Table of Contents

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, 2021

☐ **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: 001-40366

WEREWOLF THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**82-3523180**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
1030 Massachusetts Avenue, Suite 210	
Cambridge, Massachusetts	**02138**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (617) 952-0555

(Former name, former address and former fiscal year, if changed since last report)

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, $0.0001 par value per share	HOWL	The Nasdaq Global Select Market

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

None

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

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

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

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

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

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

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

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

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

As of June 30, 2021, the last business day of the registrant's most recently completed second fiscal quarter, the aggregate market value of the registrant's Common Stock held by non-affiliates of the registrant was approximately $201,872,133, based upon the closing price of the registrant's Common Stock on June 30, 2021.

As of March 18, 2022, there were 27,653,671 shares of common stock, $0.0001 par value per share, outstanding.

Documents Incorporated by Reference

Portions of the registrant's Definitive Proxy Statement on Schedule 14A relating to its 2022 Annual Meeting of Stockholders to be filed within 120 days of the registrant's fiscal year ended December 31, 2021 are incorporated by reference into Part III of this Annual Report on Form 10-K to the extent stated herein.

Table of Contents

References to Werewolf

Throughout this Annual Report on Form 10-K, or Annual Report, the "Company," "Werewolf," "Werewolf Therapeutics," "we," "us," "our," and similar references, except where the context requires otherwise, refer to Werewolf Therapeutics, Inc. and its consolidated subsidiary, and "board of directors" refers to the board of directors of Werewolf Therapeutics, Inc.

Cautionary Note Regarding Forward-Looking Statements and Industry Data

This Annual Report contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, or the Exchange Act, that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this Annual Report, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth, are forward-looking statements.

The words "aim," "anticipate," "believe," "contemplate," "continue," "could," "estimate," "expect," "goal," "intend," "may," "might," "objective," "ongoing," "plan," "potential," "predict," "project," "should," "target," "will," "would," or the negative of these words or other similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

These forward-looking statements include, among other things, statements about:

- the initiation, timing, progress and results of our research and development programs and preclinical studies and planned clinical trials;
- the anticipated timing of the submission of investigational new drug applications to the U.S. Food and Drug Administration for our product candidates WTX-124, WTX-330 and WTX-613;
- our estimates regarding expenses, capital requirements, need for additional financing and the period over which we believe our existing cash and cash equivalents will be sufficient to fund our operating expenses and capital expenditure requirements;
- our plans to develop and, if approved, subsequently commercialize product candidates;
- the timing of and our ability to submit applications and obtain and maintain regulatory approvals for product candidates;
- the potential advantages of our PREDATOR platform and our ability to use our platform to identify and develop future product candidates;
- our estimates regarding the potential market opportunities for our product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position and our expectations regarding our ability to obtain and maintain intellectual property protection;
- our ability to identify additional products, product candidates or technologies with significant commercial potential that are consistent with our commercial objectives;
- the impact of government laws and regulations;
- our competitive position and expectations regarding developments and projections relating to our competitors and any competing therapies that are or become available;
- developments and expectations regarding developments and projections relating to our competitors and our industry;
- the impact of the COVID-19 pandemic on our business, including our preclinical studies and clinical trials; and
- our expectations regarding the time during which we will be an emerging growth company under the Jumpstart our Business Startup Act of 2012.

There are a number of important risks and uncertainties that could cause our actual results to differ materially from those indicated by forward-looking statements. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report, particularly in Part I, Item 1A. "Risk Factors", that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. 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, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, collaborations, joint ventures or investments that we may make or enter into.

You should read this Annual Report and the documents that we have filed or incorporated by reference as exhibits to this Annual Report completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements contained in this Annual Report are made as of the date of this Annual Report, and we do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by applicable law.

In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this Annual Report, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete. Our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain, and you are cautioned not to unduly rely on these statements.

Trademarks and Trade names

We own or have rights to trademarks, service marks and trade names that we use in connection with the operation of our business, including our corporate name, logos and website names. The service marks and trademarks that we own include the marks PREDATOR™ and INDUKINE™. Other trademarks, service marks and trade names appearing in this Annual Report are the property of their respective owners. Solely for convenience, some of the trademarks, service marks and trade names referred to in this Annual Report are listed without the ® and ™ symbols, but we will assert, to the fullest extent under applicable law, our rights to our trademarks, service marks and trade names.

Risk Factor Summary

Our business is subject to numerous risks that, if realized, could materially and adversely affect our business, financial condition, results of operations and future growth prospects. These risks are discussed more fully in Part I, Item 1A. Risk Factors in this Annual Report. These risks include, but are not limited to, the following:

- We have a limited operating history, have incurred significant operating losses since our inception and expect to incur significant losses for the foreseeable future.
- We have no products approved for commercial sale and have not generated any revenue from product sales. We may never generate any revenue or become profitable or, if we achieve profitability, we may not be able to sustain it.
- We will need to obtain substantial additional funding to finance our operations and complete the development and any commercialization of WTX-124, WTX-330, WTX-613 and any future product candidates.
- We are early in our development efforts. All of our product candidates are still in preclinical development and will require successful completion of preclinical development before we can submit an IND to the FDA to commence clinical development.Our business is highly dependent on the success of our initial INDUKINE molecules, which are in the early stages of development and will require significant additional preclinical and clinical development before we can seek regulatory approval for and launch a product commercially.
- Our approach to the discovery and development of product candidates based on our PREDATOR platform is unproven, and we do not know whether we will be able to develop any products of commercial value.
- Manufacturing INDUKINE molecules is subject to risk since they are a novel class of multi-domain biologics that include protease cleavable linkers, and they have never been produced on a clinical or commercial scale. We may be unable to manufacture INDUKINE molecules at the scale needed for clinical development and commercial production on a timely basis or at all.
- Preclinical studies and clinical trials are expensive, time-consuming and difficult to design and implement, and involve uncertain outcomes.
- We may encounter substantial delays in the commencement or completion, or termination or suspension, of our clinical trials, which could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our commercial prospects.
- If we experience delays or difficulties in the enrollment of patients in clinical trials, our clinical development activities could be delayed or otherwise adversely affected.
- We expect to develop WTX-124 and WTX-330, and potentially future product candidates, in combination with third-party drugs, some of which may still be in development, and we will have limited or no control over the safety, supply, regulatory status or regulatory approval of such drugs.
- We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.
- We rely, and expect to continue to rely, on third parties to conduct our preclinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines or comply with regulatory requirements, we may not be able to obtain regulatory approval of or commercialize any product candidates.
- The manufacturing of biologics is complex and we do not have our own clinical manufacturing capabilities. We will rely on third parties to produce preclinical, clinical and commercial supplies of all current and any future product candidates.
- We rely on our license agreement with Harpoon Therapeutics, Inc. for patent rights with respect to our product candidates and may in the future acquire additional third-party intellectual property rights on which we may similarly rely. We face risks with respect to such

reliance, including the risk that we could lose these rights that are important to our business if we fail to comply with our obligations under these licenses.

- Our proprietary position in part depends upon patents that are manufacturing, formulation or method-of-use patents, which may not prevent a competitor or other third party from using the same product candidate for another use.
- In the past, we have identified material weaknesses in our internal control over financial reporting, and if we are unable to implement and maintain effective internal control over financial reporting in the future, investors may lose confidence in the accuracy and completeness of our financial reports, and the market price of our common stock may be materially adversely affected.

PART I

Item 1. Business

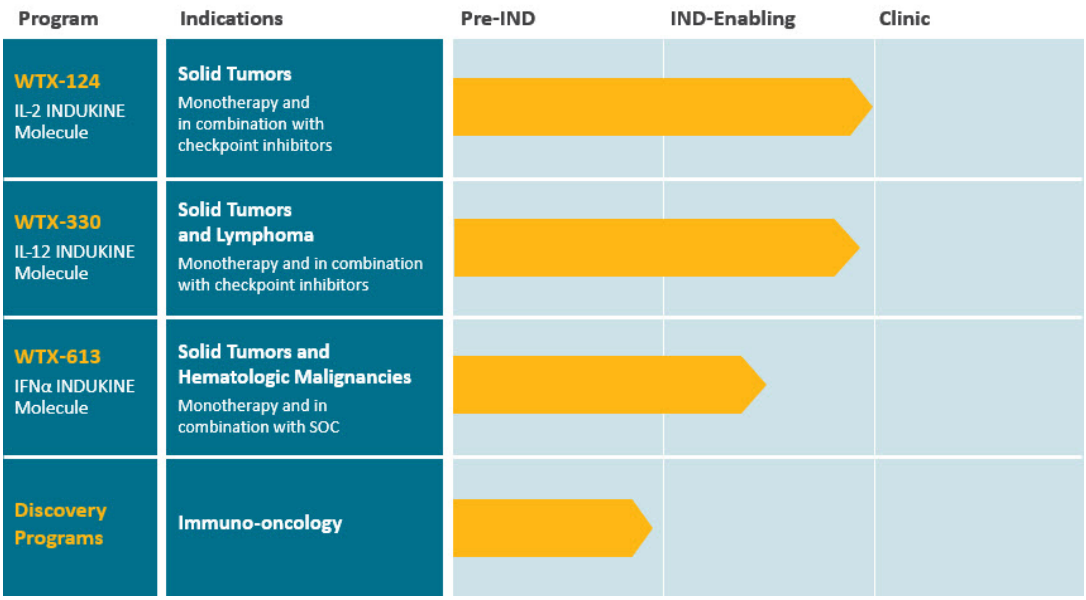
Company Overview

We are an innovative biopharmaceutical company pioneering the development of therapeutics engineered to stimulate the body's immune system for the treatment of cancer. We are leveraging our proprietary PREDATOR platform to design conditionally activated molecules that stimulate both adaptive and innate immunity with the goal of addressing the limitations of conventional proinflammatory immune therapies. Our molecules, which we refer to as INDUKINE molecules, are intended to activate selectively in the tumor microenvironment, or TME. Our most advanced product candidates, WTX-124 and WTX-330, are systemically delivered, conditionally activated Interleukin-2, or IL-2, and Interleukin-12, or IL-12, respectively, INDUKINE molecules for the treatment of solid tumors. We plan to submit an investigational new drug application, or IND, to the U.S. Food and Drug Administration, or FDA, for WTX-124 in the second quarter of 2022, an IND for WTX-330 in the third quarter of 2022, and thereafter initiate a Phase 1/1b clinical trial for each candidate in multiple tumor types as a single agent and in combination with an immune checkpoint inhibitor.

We are building our PREDATOR platform to generate a pipeline of innovative therapeutics that cover a diversity of immune stimulating mechanisms with the potential to address significant unmet medical need in cancer. Our PREDATOR platform consists of our protein engineering technologies and our know-how, which we use to generate INDUKINE molecules with multiple functional domains rationally engineered into a single protein to achieve the desired pharmaceutical profile. Each of our lead INDUKINE molecules consists of four components: a cytokine, an inactivation domain, a half-life extension domain and a proprietary protease-cleavable linker. Our INDUKINE molecules contain cytokines that mediate pro-inflammatory, anti-cancer mechanisms within the TME, with full potency and functionality observed in preclinical studies. The inactivation domain physically blocks the cytokine portion of the INDUKINE molecule in non-tumor tissue throughout the body, or the periphery, preventing it from binding to its receptor until it is cleaved and thereby activated in the TME. We engineer the half-life extension domain to overcome the short half-lives of cytokines *in vivo*, which typically range from a few minutes to a few hours. The half-life extension domain enables high systemic and tumor tissue exposure for the INDUKINE molecule prior to its cleavage in the tumor. After cleavage in the tumor, the half-life extension domain is removed and the cytokine is released to activate immune cells. We select the proprietary protease-cleavable linker to enable conditional activation of the cytokine portion of the INDUKINE molecule within tumor tissue. This selection is based on our extensive screening in preclinical studies to identify protease-cleavable linkers that are efficiently cleaved by a broad array of human tumor tissues with minimal cleavage in non-tumor tissues.

Our Pipeline

We are leveraging our novel PREDATOR platform to engineer conditionally activated proinflammatory immunomodulators, or INDUKINE molecules, which are delivered systemically but activated only in the TME, with the goal of generating potent anti-tumor response while minimizing toxicities. We have worldwide rights to our PREDATOR platform and our portfolio of INDUKINE product candidates, all of which we have developed internally. We believe our approach has the potential to overcome current limitations of systemic proinflammatory immunomodulatory therapies, such as cytokines, for the treatment of cancer. Our current pipeline is summarized below:



Using our PREDATOR platform, we have developed three initial product candidates: WTX-124, WTX-330 and WTX-613. In addition to these product candidates, we are pursuing additional immuno-oncology discovery programs in which we are applying our novel engineering approach to other targets.

Our Strategy

Our goal is to utilize our proprietary PREDATOR platform to redefine the cancer treatment landscape with therapies to transform the lives of cancer patients. Key elements of our strategy include:

- Advancing our lead product candidate, IL-2 INDUKINE molecule (WTX-124), into and through clinical development in selected solid tumor indications.
- Advancing our IL-12 INDUKINE molecule (WTX-330) into clinical development in selected solid tumors and lymphoma.
- Leveraging our proprietary PREDATOR platform to advance our IFNα INDUKINE molecule (WTX-613) through preclinical development and expand our pipeline of product candidates.
- Establishing a leading position in protein engineering and developing optimized conditionally activated molecules.
- Selectively entering into strategic partnerships while retaining key rights to our programs and platform in major pharmaceutical markets.

Traditional Cancer Therapy, Immunotherapy and the Need for New Treatment Options

The treatment of certain cancers has improved markedly over the past decade. Whereas many cancer treatments were historically limited to surgical removal, chemotherapy and radiation, recent advances target specific genetic changes in individual tumors or redirect the patient's immune system to eliminate tumors and improve patient outcomes.

The latter approach, referred to as immunotherapy, represents one of the fastest growing segments in cancer treatment. The goal of immunotherapy is to harness an individual's immune system to better enable it to identify, attack and kill tumor cells and to form long-term immunologic memory against tumors. The immune system is generally divided into the innate and adaptive arms, which are responsible for driving immediate and lasting anti-tumor responses, respectively. The innate immune system involves a diverse set of cells, including natural killer, or NK, cells, mast cells, eosinophils, basophils, neutrophils, macrophages and dendritic cells, or DCs, all of which generate a rapid local response to a foreign body, pathogen or tumor cell and release signals to activate and recruit cells, specifically lymphocytes, from the adaptive immune system. The adaptive immune system is the line of defense that is specific to a pathogen or tumor antigen and is composed of T cells and B cells, which work in concert to kill cells directly, produce antibodies and form immunologic memory. The latter is critical for the body's immune response upon re-exposure to the initial antigen or pathogen. Many of the recent advances in immuno-oncology, such as immune checkpoint inhibitors, have focused on improving the function of T cells.

Over the past decade, the development of immune checkpoint inhibitors, in particular programmed cell death protein 1, or PD-1, and programmed death-ligand 1, or PD-L1, inhibitors, has revolutionized the treatment of many cancers. The efficacy of these T cell targeted immunomodulators, both as single agents or in combination with standard of care therapies, including chemotherapy, has resulted in many of these regimens moving up the treatment paradigm to become first- or second-line treatment options in numerous cancer types, and the landscape for immunotherapy continues to rapidly evolve. However, features of the tumor cells or the TME play a role in the efficacy of immune checkpoint inhibitors, leaving many patients with advanced or metastatic disease either ineligible for or unresponsive to treatment with immune checkpoint inhibitors. The majority of patients who do respond to these therapies ultimately develop resistance and experience disease progression. As a result, many patients are still underserved and could benefit from novel approaches to immunotherapy that complement and/or enhance checkpoint inhibition, whether as monotherapy or in combination. We believe that the best way to improve outcomes for cancer patients is to stimulate additional or *de novo* immune cell responses within the innate and adaptive arms of the immune system to complement immune checkpoint inhibitor therapy.

Leveraging our PREDATOR platform and drug development capabilities, we are creating a portfolio of conditionally activated proinflammatory immunomodulators, including cytokines, designed to be optimized for the treatment of cancer. Cytokines are small biologically active proteins that play an essential role in immune cell function of both the innate and adaptive arms of the immune system. These proteins regulate immune responses by acting as chemical messengers for the body's immune cells through receptor site binding. Interleukins, such as IL-2 and IL-12, and IFNα are specific types of cytokines, produced primarily by cells of the immune system to signal and organize the immune response. In cancer, cytokines facilitate the ability of the immune system to recognize tumor cells as abnormal and harmful to the host. Cytokines further increase the proliferation of, enhance the survival of and direct a variety of immune cell types to infiltrate the TME and promote potent anti-tumor immune responses resulting in tumor cell killing and tumor clearance. Two cytokine therapies have received FDA approval for cancer treatment: (1) aldesleukin for the treatment of metastatic RCC and metastatic melanoma and (2) interferon-alfa2b for the treatment of several malignancies, including advanced melanoma.

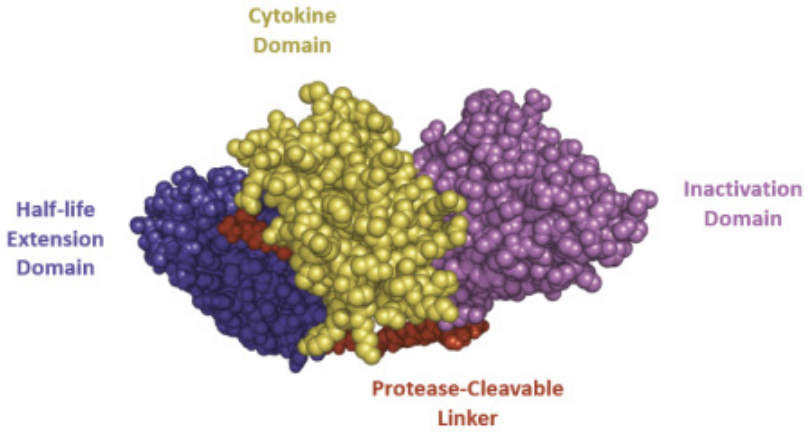
However, despite promising anti-tumor activity, the clinical utility of approved cytokine therapies is limited due to toxicity and poor pharmaceutical properties, such as short half-life, reduced exposure of active drug in the tumor and the requirement for frequent administration. The efficacy observed is often accompanied by side effects that can be severe and can make treatment difficult for many patients to tolerate, which limits the ability of patients to remain on therapy long-term. The need to improve the pharmaceutical properties of cytokines to achieve increased therapeutic indexes provides an opportunity to address a large unmet need for safer, and potentially more efficacious, cytokine therapeutics for the treatment of cancer. Our PREDATOR platform allows us to engineer cytokines that can be delivered systemically and have activity selectively upon reaching the TME, thus potentially limiting systemic toxicity. We believe this unique profile will help overcome the limitations seen with other cytokine approaches.

Our Solution

Our PREDATOR Platform

We designed our PREDATOR platform to overcome the current limitations of systemic proinflammatory therapies. We use our PREDATOR platform to design molecules with superior tolerability and optimal pharmaceutical properties when administered systemically as inactive pro-drugs. They then undergo transformation to an active state upon reaching the TME, thereby delivering the full biological potency of antitumor immune modulation for maximum therapeutic potential.

Our PREDATOR platform is based on protein engineering to combine four critical components into a single INDUKINE molecule, as shown in the figure below.



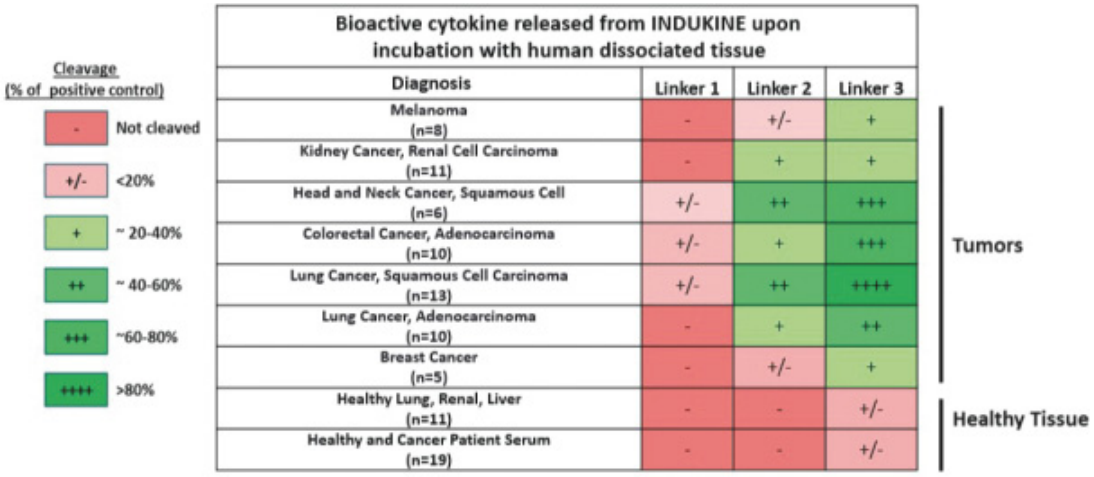
- **Cytokine Domain**: An immunostimulatory molecule with no muteins or sequence alteration. Upon tumor specific conditional activation, the released cytokine works as a fully potent agonist, displaying the expected pro-inflammatory mechanism and pharmacology.
- **Inactivation Domain**: A domain that blocks the activity of the immunostimulatory molecule outside of the tumor, for which we have identified and optimized multiple formats with high affinity blockade to achieve minimal off-tumor toxicity and low peripheral target receptor-mediated clearance.
- **Half-Life Extension Domain**: A domain that imparts a longer half-life to the INDUKINE molecule until cleavage within the tumor, when the immunostimulatory cytokine is released. We have selected multiple domain formats to enable our INDUKINE product candidates to maintain high systemic and tumor tissue exposure.
- **Protease-Cleavable Linker**: A novel, proprietary protease-cleavable linker substrate with optimal tumor selectivity that is used to impart conditional activation of the INDUKINE molecule through its cleavage, which releases the active cytokine. We have observed high stability of these proprietary protease-cleavable linker substrates in rodents and non-human primates, or NHPs, with minimal non-tumor tissue cleavage.

Linker Selection

A key challenge in the design of tumor-selective conditionally activated immunomodulators is the heterogeneity of tumor protease profiles. There is no single protease that is uniquely dysregulated in human tumors. Therefore, the identification of a linker substrate with the optimal profile cannot be achieved by biasing the linker sequence towards any single protease or protease family.

To ensure INDUKINE molecules are broadly activated across multiple tumor types, the linker substrate must be efficiently cleaved in the TME of many different tumors while remaining stable in circulation and in normal non-tumor tissues. We achieve this by utilizing a differentiated approach for linker identification and let the tumors select the substrate, rather than screening for linkers sensitive to cleavage by a single protease. Our process begins with a novel proprietary library of peptide sequences designed to target the universe of protease families known to be dysregulated in tumors. We initially screen these libraries for a high efficiency of cleavage and, based on the result, generate additional libraries to optimize the sequence motifs. We then screen the prioritized linker sequences that we have identified from the initial novel proprietary library of peptide sequences for cleavage by a panel of primary human tumor specimens and for stability when incubated with human serum or normal tissues. This step allows us to eliminate linkers that are not efficiently cleaved by human tumor samples and identify proprietary linkers that are efficiently cleaved by human tumor specimens. Leveraging this screening process, we initially screened several thousand linker sequences for optimal biochemical properties, and then screened the lead sequences for cleavage by a panel of primary human tumor specimens and normal non-tumor tissues. Linker sequences that were not efficiently cleaved by human tumor samples (for example, the linker shown as Linker 1 in the diagram below) were eliminated in the screening and those that were efficiently cleaved by human tumors but not cleaved by normal serum or tissues (for example, the linker shown as Linker 3 in the diagram below) were selected for incorporation into our INDUKINE molecules to confirm their activity *in vitro* and *in vivo*. We have selected linkers for our INDUKINE molecules with characteristics similar to those of Linker 3 in the table below.

Human Tissue Screening for Selection of Optimized Linker Candidates



We seek to protect aspects of our PREDATOR platform technology by obtaining patent protection in the United States and internationally. Currently, our patent portfolio for our PREDATOR platform technology includes two families of pending patent applications, which disclose and claim protease cleavable linkers and libraries of protease cleavable linkers, as well as polypeptides that contain such linkers, methods of making libraries and methods of screening libraries to identify linkers with desired properties. These patent families were recently filed and no patents have granted. For more information see “Intellectual Property” described in this Part I, Item 1.

INDUKINE Molecules

We have rationally engineered INDUKINE molecules to have four key characteristics that we believe provide our product candidates with a unique profile and potential advantages in clinical settings when compared to other cytokines currently approved or in development:

- **Optimized Anti-tumor Activity**: The active portion of our INDUKINE molecules consists of a wild-type cytokine. We believe that delivery of a fully potent and functional cytokine molecule, as opposed to a mutein or cytokine with sequence alterations, into the TME will enable our product candidates to capture the full proinflammatory and immunomodulatory potential of cytokines and potentially result in optimal anti-tumor activity.
- **Enhanced Tolerability**: In order to improve tolerability, our INDUKINE molecules are designed to be administered as inactive pro-drugs that employ a tailored, high affinity blockade to minimize off-target toxicity. We aim to prevent peripheral pathway activation, as well as target-mediated disposition in normal tissues, with the goal of minimizing potential toxicity.
- **Optimized Pharmaceutical Properties**: We design INDUKINE molecules to be stable in the bloodstream and periphery and to have a long serum half-life in order to achieve efficacy without requiring the frequent dosing that is a limiting requirement of approved recombinant cytokines, such as aldesleukin, an rhIL-2 therapy. Our design allows us to achieve high, biologically relevant tumor tissue exposure with our INDUKINE molecules. Once our molecules are cleaved within the tumor, the cytokine is released for either intratumoral target binding or rapid systemic clearance.
- **Conditional Activation**: Upon reaching the TME, INDUKINE molecules are activated via cleavage of our proprietary linkers by tumor-specific proteases which results in release of the cytokines in the tumor. We select our linkers to be specifically cleaved in the tumor and be stable in circulation and normal non-tumor tissues, with the goal enhancing the tolerability profile of our INDUKINE molecules.

Our Programs

WTX-124: Our IL-2 INDUKINE Molecule

Overview

Our lead product candidate, WTX-124, is a systemically delivered, conditionally activated IL-2 INDUKINE molecule that we are developing to minimize the severe toxicities observed with recombinant human IL-2, or rhIL-2, therapy and maximize clinical benefit when administered as monotherapy or in combination with immune checkpoint inhibitors in advanced or metastatic tumors. We believe that these properties will also allow WTX-124 to have potential applicability in indications beyond those for which rhIL-2 therapy is currently approved. Key features of WTX-124 include preservation of full IL-2 potency and function as observed in preclinical trials, high affinity blockade of IL2—IL2R interaction in systemic circulation and non-tumor tissues, half-life extension for optimal tumor exposure and conditional protease activation within the TME due to our proprietary linker.

We designed WTX-124 to address the limitations of next generation IL-2 therapies in development by blocking the binding of IL-2 to the IL-2R in the periphery, thereby inhibiting IL-2 signaling and potentially minimizing toxicities, while maintaining binding to the high affinity IL-2Ra/ß/g in tumors to ensure the full pharmacology of IL-2.

WTX-124 consists of wild-type human IL-2, an IL-2Rß/g blockade element that eliminates binding to both high and medium affinity IL-2Rs expressed in normal tissues to neutralize IL-2 activity in the periphery, an antibody fragment that extends the circulation half-life and a proprietary linker for cleavage in the TME. As a prodrug, WTX-124 is conditionally activated in the TME to release an IL-2 cytokine to stimulate an anti-tumor immune response but with reduced peripheral toxicities. In preclinical studies, WTX-124 has exhibited favorable pharmacokinetic and tolerability profile with robust anti-tumor activity driven by the differentiation, activation and expansion of T effector and memory lymphocyte immune responses.

Market Opportunity

We are initially developing WTX-124 in tumor types known to be responsive to IL-2 and PD-1 targeting therapies including melanoma, RCC and non-small cell lung cancer. These are aggressive tumor types and many patients will eventually progress following treatment with standard of care. As a result, we believe there is a need for new therapies to improve response and durability. If successfully developed and approved, we believe WTX-124 represents a promising therapeutic option for patients with life-threatening diseases with high unmet medical need, either as monotherapy or in combination with immune checkpoint inhibitors or current or potential future standard of care agents. The global checkpoint inhibitors market is expected to grow from $15.29 billion in 2020 to $18.04 billion in 2021 at a compound annual growth rate (CAGR) of 18%. The market is expected to reach $39.81 billion in 2025 at a CAGR of 22%. We intend to develop WTX-124 as monotherapy and in combination with pembrolizumab, and eventually in combination with other standard of care therapeutics across different lines of therapy.

WTX-124 Preclinical Results

In November 2021, we presented “WTX-124 is a novel IL-2 pro-drug that is conditionally activated in tumors and drives anti-tumor immunity in murine syngeneic cancer models” at the 36th Annual Meeting of the Society for Immunotherapy of Cancer (SITC) summarizing the biochemical, cellular, and *in vivo* activity of our lead IL-2 INDUKINE molecule, WTX-124. Preclinical data from the presentation for WTX-124 demonstrated that:

- WTX-124, a pro-drug containing wild-type IL-2, is selectively processed and activated in tumors and is efficacious in murine models, even in the presence of regulatory T cells;
- WTX-124 activity is dependent on the processing of the pro-drug, as a non-cleavable version of WTX-124 (WTX-124-NC) is not efficacious in our models;
- Mechanistically, WTX-124 induces intratumoral activation of NK cells and CD8+ T cells and generates long-term memory in treated animals; and
- WTX-124 possesses good PK characteristics in mouse and NHP models and is stable in the periphery, with minimal release of free IL-2.

These data will be used to support our planned IND submission for WTX-124.

Clinical Development Plan for WTX-124

We have designed our clinical development strategy for WTX-124 with the goal of achieving rapid proof-of-concept in historically immunotherapy-sensitive tumor types, including melanoma and RCC, indications for which aldesleukin is approved. First, we intend to initiate a Phase 1/1b clinical trial of WTX-124 for the treatment of relapsed or refractory advanced or metastatic solid tumors as monotherapy or in combination with pembrolizumab. During the dose escalation phase of the trial, we expect to identify safe and pharmacodynamically active doses of WTX-124 for the respective dose escalation arms, following which we will open expansion arms for both monotherapy and in combination with pembrolizumab or other standard of care therapy in advanced or metastatic renal cell cancer and advanced or metastatic cutaneous malignant melanoma.

The rationale for our clinical development strategy is as follows:

- **IL-2 has been shown to have single agent activity in some cancers**. Aldesleukin is approved for the treatment of metastatic RCC and metastatic melanoma. However, due to the toxicity associated with aldesleukin, which is noted in a black box warning, the drug is used infrequently. We believe, based on the mechanism of action of WTX-124, that it may be able to achieve higher intratumoral exposures of IL-2 than aldesleukin with minimal systemic toxicity, leading to monotherapy anti-tumor immune responses in patients with historically immunotherapy-sensitive tumor types who have progressed on or subsequent to immune checkpoint inhibitor therapy. Our preclinical data with WTX-124 shows that WTX-124 has single agent anti-tumor activity in mouse tumor models and was well-tolerated. WTX-124 was also tolerated in NHPs at doses greater than predicted to be required for anti-tumor activity based on modeling the mouse tumor data. Single agent activity with competitor IL-2 compounds has been limited, potentially affording an opportunity for us to pursue an expedited clinical development and regulatory strategy for WTX-124 if we can show positive single arm efficacy data in a relapsed or refractory tumor type with high unmet medical need.
- **IL-2 agonists and immune checkpoint inhibitors may act synergistically to enhance anti-tumor immune response**. Clinical results have shown that aldesleukin induces responses as a single agent in patients who progressed on immune checkpoint inhibitors. Our preclinical data with WTX-124 highlight the potential benefit of WTX-124 when combined with an anti-PD-1 antibody. These results suggest that combining novel IL-2 therapies with checkpoint inhibitors merits further evaluation as a regimen for treating cancer.

WTX-330: Our IL-12 INDUKINE Molecule

Overview

Our second product candidate, WTX-330, is a systemically delivered, conditionally activated IL-12 INDUKINE molecule that we are developing to minimize the severe toxicities observed with rhIL-12 therapy and maximize clinical benefit when administered as monotherapy or in combination with immune checkpoint inhibitors in relapsed or refractory advanced or metastatic solid tumors or lymphoma.

IL-12 is a potent, pleiotropic cytokine for immune-mediated killing of cancer cells, whose mechanism of action includes stimulation of both innate and adaptive immune responses. IL-12 is a heterodimeric cytokine (p70) containing two subunits (p35 and p40). A subset of antigen-presenting cells, such as DCs, produce IL-12 upon activation, during the antigen presentation process. Binding of IL-12 to the IL-12R expressed on multiple immune cell populations activates the JAK/STAT signaling pathway resulting in helper T cell differentiation, activation of cytotoxic NK and T cells, and inhibition or reprograming of immunosuppressive cells such as tumor-associated macrophages or myeloid-derived suppressor cells. IL-12 also increases the expression of antigen-presentation machinery, which is necessary to initiate an immune response in tumors that have not naturally stimulated an anti-tumor immune response, also referred to as "cold" tumors. IL-12 induces the production of interferon gamma, or IFNγ, a potent proinflammatory mediator of the downstream activities of IL-12 signaling. IFNγ, in turn, increases the production of IL-12 by mature DCs aiding in their antigen presentation capacity and driving activation of effector T cells. Numerous studies conducted by others have demonstrated that IL-12 treatment has significant anti-tumor activity in a range of preclinical models, with the induction of a long-lasting anti-tumor immune memory.

Due to the robust anti-tumor activity seen in preclinical studies, there has been significant interest in developing rhIL-12 therapy for advanced solid tumors. In early clinical trials conducted by a third party, the use of systemically administered rhIL-12 produced evidence of clinical activity in several tumor types, including RCC, melanoma and non-Hodgkin's lymphoma. However, the systemic administration of rhIL-12 was shown to be toxic, resulting in the death of two patients in one Phase 2 trial and multiple hospitalizations. Additional trials at tolerated doses yielded modest clinical activity, potentially due to a lack of sufficient and durable exposure of rhIL-12 in the TME at lower doses.

WTX-330 is designed to improve the pharmacological properties of IL-12 and require less frequent systemic administration. The prodrug is designed to remain inactive while circulating in the periphery and is activated preferentially in the TME to release an IL-12 cytokine. We believe activation of WTX-330 in the TME has the potential to stimulate a robust anti-tumor immune response while minimizing the peripheral toxicities that have been associated with systemic administration of rhIL-12 therapy. Key features of WTX-330 include high affinity blockade of IL-12 – IL-12R interaction in systemic circulation and non-tumor tissues, half-life extension for optimal tumor exposure and conditional protease activation due to our proprietary linker. In preclinical studies, we have observed high anti-tumor activity of an IL-12 INDUKINE surrogate molecule across a broad range of preclinical tumor models and that it has a favorable pharmacokinetic and tolerability profile.

WTX-330 Preclinical Results

In November 2021, we presented "WTX-330, a conditionally activated IL-12 INDUKINE therapy, releases IL-12 selectively in the tumor microenvironment to activate anti-tumor immune responses and induce regression in mouse tumor models" at the 36th Annual Meeting of SITC summarizing the biochemical, cellular, and in vivo activity of our IL-12 INDUKINE molecule, WTX-330. Based on the preclinical data summarized in the presentation for WTX-330, we concluded that:

- Proof-of-concept assays of WTX-330 demonstrate anti-tumor activity in syngeneic mouse models and better tolerability compared with rIL-12;
- WTX-330 potently inhibits tumor growth in MC38, CT26, B16F10 and EMT6 mouse tumor models;
- Changes in immune profiles in mouse tumors after IL-12 INDUKINE therapy support a mechanism of action similar to rIL-12; and
- WTX-330 is tolerated in NHPs and reaches Cmax and area under the curve, or AUC, exposures higher than the efficacious exposures seen in mice.

These data will be used to support our planned IND submission for WTX-330.

Clinical Development Plan for WTX-330

We plan to submit an IND with the FDA in the third quarter of 2022 to initiate a Phase 1/1b clinical trial of WTX-330 for the treatment of immunotherapy resistant advanced or metastatic solid tumors or lymphoma, followed by expansion arms in relapsed/refractory tumors following treatment with checkpoint inhibitors or tumors for which checkpoint inhibitors are not approved. In this Phase 1/1b trial, we plan to evaluate safety and tolerability, pharmacokinetics, biomarker changes and preliminary signs of anti-tumor activity. We believe the administration of WTX-330 to patients with relapsed or refractory advanced or metastatic solid tumors or lymphoma, in particular those who are resistant to checkpoint inhibitors or for whom checkpoint inhibitors are not indicated, could demonstrate clinical benefit as monotherapy, with the potential for us to pursue an expedited clinical development and regulatory strategy if we are able to show positive single arm efficacy data in a relapsed or refractory tumor type with high unmet medical need.

WTX-613: Our IFNα INDUKINE Molecule

Overview

WTX-613 is a systemically delivered, conditionally activated IFNα INDUKINE molecule that we are developing to minimize the severe toxicities that have been observed with rhIFNα therapy and maximize clinical benefit when administered as monotherapy or in combination with checkpoint inhibitors or other standard of care therapy.

IFNα is a member of the type-I IFN family and a proinflammatory cytokine that exerts dual mechanisms of inhibiting tumor cell growth through both cytotoxic effects directly on tumor cells as well as driving anti-tumor immune responses. IFNα binds and signals through a heterodimeric receptor formed by the subunits IFNAR1 and IFNAR2, resulting in the phosphorylation and activation of the JAK/STATs pathway, as well as activation of the PI3K, NFkB and MAPK pathways. While IFNα can inhibit proliferation and induce direct cell apoptosis of some cancer cell types, this mechanism by itself is unlikely to be sufficient to fully control tumor growth. The additional ability of IFNα to activate and engage different cells of the immune system makes IFNα a potentially effective anti-tumor agent. IFNα activation of the immune response can occur directly by engagement of IFNARs on immune cells or indirectly by the induction of chemokines that attract immune cells to the tumor site. IFNα can activate NK cells, enhance their ability to kill and increase their production of IFNγ. Furthermore, it can increase macrophage activation and support differentiation and activation of DCs. Lastly, IFNα can have a direct effect on B lymphocytes as well as T lymphocytes where IFNα favors the differentiation of naïve CD4+ T cells into helper T cells and directly activates CD8+ T cells, augmenting their IFNγ production and survival.

IFNα was one of the first cytokines clinically tested as a therapy for patients with cancer. Encouraging clinical benefit, although limited, resulted in regulatory approvals for the treatment of several hematological malignancies and solid tumors, such as chronic myelogenous leukemia, lymphoma and malignant melanoma. Widespread use of IFNα for hematologic and oncologic indications has unfortunately been hampered by adverse events linked to the on-target, off-tumor activity of the native or pegylated formulations of the molecule and its use in clinical practice has been supplanted by other therapies. In our preclinical studies, we observed the potential benefit of IFNα treatment in syngeneic mouse tumor models using colon, melanoma and breast tumor cell lines and the superior response obtained by the INDUKINE molecule format when compared to the dosing of recombinant cytokine.

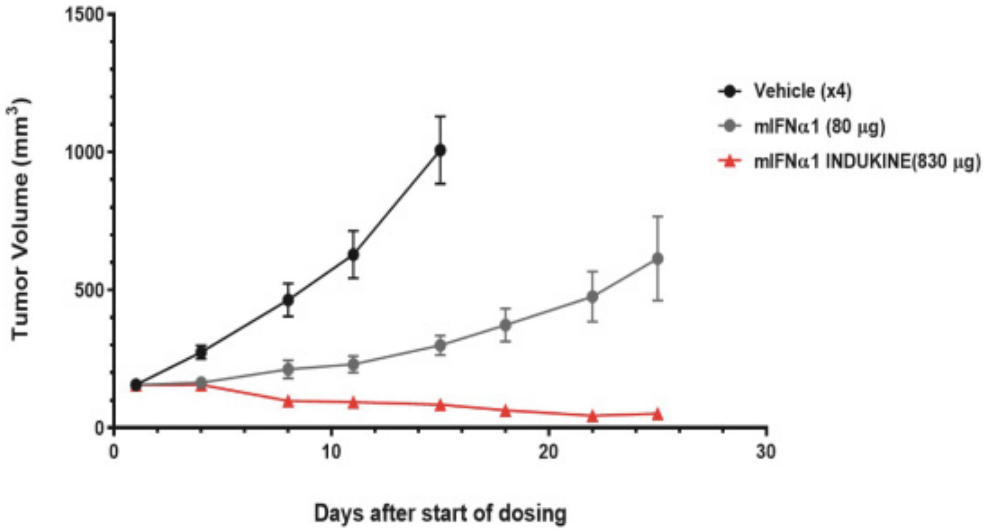
We designed WTX-613 to improve the pharmacological properties of IFNα to support less frequent systemic administration and potentially enhance its therapeutic index compared to current IFNα based therapies. WTX-613 is designed to have minimal activity in the periphery and is activated preferentially in the TME to release wild-type IFNα in the tumor and potentially stimulate an anti-tumor immune response while reducing the peripheral toxicities associated with systemic administration of approved rIFNα therapy. Key features of WTX-613 include high efficiency blockade of IFNα – IFNR interaction in systemic circulation and non-tumor tissues, half-life extension for optimal tumor exposure and proprietary conditional protease activation. In preclinical studies, an IFNα INDUKINE surrogate molecule has exhibited robust anti-tumor activity mediated through stimulation of a type I interferon immune response with favorable pharmacokinetics and tolerability.

WTX-613 Preclinical Results

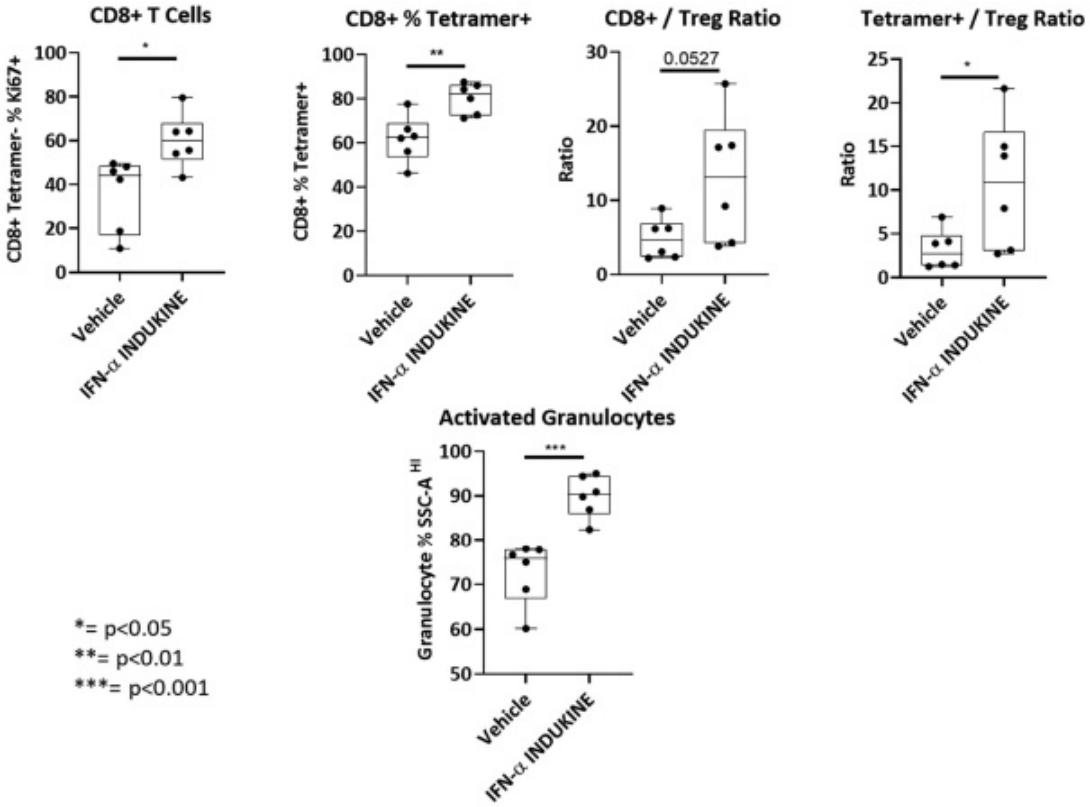
We have conducted multiple preclinical studies to assess the pharmacological activity of WTX-613.

The cytokine domain of WTX-613 consists of human IFNα2b, which does not bind to the mouse IFNR. As a result, laboratory mice cannot be used to study the pharmacology of WTX-613. Accordingly, we have utilized a surrogate IFNα INDUKINE molecule consisting of mouse IFNα which is otherwise identical to WTX-613, to assess its pharmacological properties. To assess anti-tumor activity, we treated MC38 mice twice each week with vehicle or the IFNα INDUKINE molecule at a dose of 830 µg. A total of six doses were administered. In addition, an 80 µg dose of recombinant mouse IFNα1, or mIFNα1, was administered to a third group of mice twice per day, for five days on, two days' rest, five days on, for a total of 20 doses. This 80 µg dose of mIFNα1 was equimolar to the dose of the IFNα INDUKINE molecule. As shown in the figure below, animals treated with the IFNα INDUKINE molecule displayed long-lasting tumor growth control resulting in durable tumor stasis. Overall anti-tumor activity of mIFNα1 was modest, even though the treatment initially provided some tumor growth control. Both treatments were well tolerated at these dose levels with no signs of body weight loss or premature death. These data suggest that the IFNα INDUKINE molecule could be dosed less frequently and with lower molar amount than mIFNα1 while still maintaining greater anti-tumor activity and acceptable tolerability.

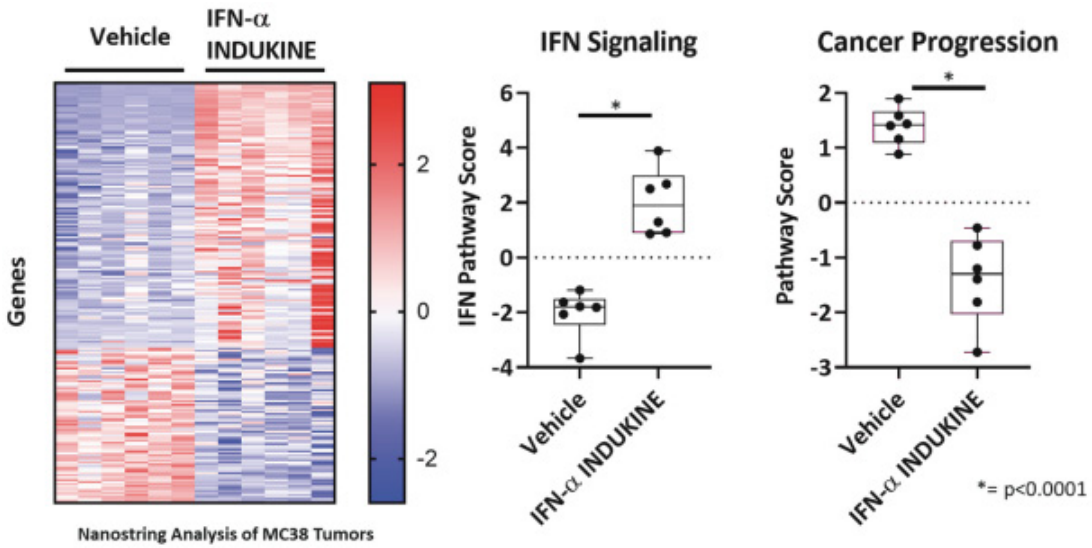
Anti-tumor Activity in MC38 Model



To better understand the mechanism by which the IFNα INDUKINE molecule treatment induced tumor regression, MC38 tumors from animals treated with either vehicle or the IFNα INDUKINE molecule were harvested 24 hours after their second dose in the first week, and tumor infiltrating lymphocytes were collected and analyzed by flow cytometry. As shown in the figure below, within five days after the initial dose, treatment with the IFNα INDUKINE molecule resulted in a large influx and activation of immune cells, specifically CD8+ T effector cells and tumor specific tetramer+ CD8+ T effector cells which resulted in a significant increase in the CD8+/Treg ratio. Furthermore, granulocytes were strongly activated following treatment with the IFNα INDUKINE molecule, providing evidence of induction of a pro-inflammatory phenotype in the tumors.



To determine changes in gene expression following treatment with the INDUKINE molecule, we subjected the same tumor material to Nanostring analysis using mRNA extracted from MC38 tumors isolated from animals treated with either vehicle or the IFNα INDUKINE molecule. A comparison of the gene expression changes in tumors isolated from mice treated with the INDUKINE molecule or vehicle control is shown in the heat-map in the figure below. We observed that genes in the IFN pathway were strongly upregulated, while genes representing cancer progression were downregulated. Together, these data demonstrate that treatment with an IFNα INDUKINE molecule increased immune cell tumor infiltration and activation, thereby driving anti-tumor immunity in this model.



In addition to these studies completed to date, we plan to conduct additional *in vivo* and *in vitro* pharmacology and toxicology studies to support our planned submission to the FDA of an IND for WTX-613.

Clinical Development Plan for WTX-613

We plan to submit an IND to the FDA in the first half of 2023 for a clinical trial of WTX-613, which we anticipate will evaluate safety and tolerability, pharmacokinetics, biomarker changes and preliminary signs of anti-tumor activity.

Our Early Stage Programs

In addition to IL-2, IL-12 and IFNα, we are also applying our novel engineering approach to other targets. We believe that additional pro-inflammatory cytokines have the potential to empower the immune system in its fight against cancer. The most efficacious immune responses to tumors require a coordinated activation of both the innate and adaptive immune responses. Cytokines are diverse in the nature and extent of their effect, with some having a more direct impact on the innate immune system and others favoring or aiding the activation of the adaptive immune system.

Our goal is to better understand how the localized tumor delivery of these cytokines using our INDUKINE molecules might contribute to control tumor progression while reducing the toxicity that in many cases accompany the systemic delivery of these cytokines.

Competition

The pharmaceutical industry is characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary drugs. While we believe that our technology, knowledge, experience and scientific resources provide us with certain competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies; academic institutions; governmental agencies; and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing treatments and new treatments that may become available in the future.

We compete with other companies working to develop immunotherapies for the treatment of cancer including divisions of large pharmaceutical and biotechnology companies of various sizes. These companies are developing cytokines as immunotherapies using different modalities, including monoclonal antibodies, cell therapies, oncolytic viruses and vaccines.

Our lead product candidate, WTX-124, if approved, may face competition from other IL-2 based cancer therapies. Proleukin® (aldesleukin) has been approved and is marketed for the treatment of both metastatic RCC and metastatic melanoma. In addition, we are aware of numerous clinical and preclinical IL-2 programs using different platforms being developed for oncology indications, including programs from Alkermes Plc, BioNTech SE, Medicenna Therapeutics Corp., Nektar Therapeutics (Bristol-Myers Squibb Company), Neoleukin Therapeutics, Inc., F. Hoffmann-La Roche AG, or Roche, Synthorx, Inc. (Sanofi) and Xilio Therapeutics, Inc.

There are no approved IL-12 therapies currently on the market for the treatment of cancer. However, if approved, WTX-330 may face competition from other IL-12 cytokine programs in clinical and pre-clinical development for oncology indications, including programs from Sanofi S.A. (Amunix), DragonFly Therapeutics, Inc., Juno Therapeutics, Inc. (Bristol-Myers Squibb Company), Oncorus, Inc., Turnstone Biologics Corp. (partnered with Takeda Pharmaceutical Corporation, or Takeda) and Oncosec Medical Incorporated.

If approved, WTX-613 may face competition from other IFNα cancer therapies. Intron-A, a recombinant IFNα-2b molecule marketed by Merck, has been approved by the FDA for the treatment of several forms of cancer, including specific types of leukemia and lymphoma, and we are aware of other IFNα programs targeting the treatment of cancer in development by Immunomedics (acquired by Gilead Sciences, Inc.), International Center for Genetic Engineering and Biotechnology (ICGEB) and Takeda. Roferon A, a recombinant IFNα-2a molecule developed and marketed by Roche for the treatment of specific types of leukemia, was discontinued globally in 2020.

We are developing WTX-124, WTX-330 and WTX-613 as potential monotherapies in relapsed or refractory tumor types or in combination with checkpoint inhibitors or other standard of care therapies in advanced or metastatic malignancies with high unmet medical need. Standard of care therapies include chemotherapy, targeted therapy, and more recently, immunotherapies, including monoclonal antibodies and bispecific formats, antibody drug conjugates, adoptive cellular therapies, and cytokines. In addition, there are numerous investigational agents in clinical development. Combining agents to improve patient outcomes and prevent emergence of resistance has become the norm for treatment of cancer.

Many of our competitors, either alone or with their collaboration partners, have significantly greater financial resources and expertise in research and development, preclinical testing, clinical trials, manufacturing and marketing than we do. Future collaborations and mergers and acquisitions may result in further resource concentration among a smaller number of competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors will also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and subject registration for clinical trials, as well as in acquiring technologies complementary to, or that may be necessary for, our programs.

Our commercial potential could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market or make our development more complicated. The key competitive factors affecting the success of all of our programs are likely to be efficacy, safety and convenience.

Manufacturing

To date, we have produced limited quantities of our product candidates at our own facilities for preclinical evaluation. We do not own manufacturing facilities capable of producing drug product for clinical trials or at clinical scale. We must manufacture drug product for clinical trial use in compliance with current Good Manufacturing Practices, or cGMPs, or similar foreign standards. The cGMP regulations include requirements relating to organization of personnel, buildings and facilities, equipment, control of components and drug product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports, and returned or salvaged products. We do not have and we do not currently plan to acquire or develop the facilities or capabilities to manufacture cGMP drug substance or filled drug product for use in human clinical trials. Going forward, we will rely on third-party contract manufacturers to manufacture some of our preclinical product candidate supplies and will rely on third-party contract manufacturers to manufacture all of our clinical trial product supplies. We will also contract with additional third parties for the filling, labeling, packaging, storage and distribution of our product candidates investigational drug products.

The manufacturing facilities for our product candidates must meet cGMP requirements and FDA certification before any product is approved and we can manufacture commercial products. Our third-party manufacturers will also be subject to periodic inspections of facilities by the FDA and other authorities, including procedures and operations used in the testing and manufacture of our products to assess our compliance with applicable regulations.

Commercialization Plan

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 major pharmaceutical markets. 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.

Intellectual Property

Our intellectual property is critical to our business and we strive to protect it, including by seeking to obtain and maintaining patent protection in the United States and internationally to cover our product candidates, their methods of use and processes for their manufacture and any other inventions that are commercially important to the development of our business. We also rely on trade secrets and proprietary know-how to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Our patent portfolio includes patents and patent applications with composition of matter and method of use claims with respect to our product candidates, WTX-124, WTX-330 and WTX-613, and claims directed to our PREDATOR platform technology. For our product candidates, we will, in general, initially pursue patent protection covering compositions of matter and methods of use. Throughout the development of our product candidates, we will seek to identify additional opportunities for obtaining patent protection that would potentially enhance commercial success, including through additional methods of use, processes for manufacture, formulation and dosing regimen-related claims.

Our commercial success depends in part on our ability to obtain and maintain proprietary protection for our current and future product candidates, platform technologies, novel discoveries, product development technologies and know-how, to operate without infringing on the proprietary rights of others and to prevent others from infringing our proprietary rights. We seek to protect our proprietary position by, among other methods, filing or in-licensing U.S. and foreign patents and patent applications related to technology, inventions and improvements that are important to the development and implementation of our business. We also rely on or may rely in the future on trademarks, trade secrets, copyright protection, know-how, continuing technological innovation and confidential information to develop and maintain our proprietary position. For the product candidates we develop and plan to commercialize, as a normal course of business, we have been granted and intend to continue to pursue composition and method of manufacture and use, including therapeutic use patents, as well as novel indications for our product candidates. We also have obtained and will continue to seek patent protection with respect to novel discoveries. We have sought and plan to continue to seek patent protection, either alone or jointly with our collaborators, as our agreements may dictate.

In some instances, we submit patent applications directly with the United States Patent and Trademark Office, or USPTO, as provisional patent applications. Provisional applications for patents were designed to provide a lower-cost first patent filing in the United States. Corresponding non-provisional patent applications must be filed not later than 12 months after the provisional application filing date. The corresponding non-provisional application benefits in that the priority date(s) of the patent application is/are the earlier provisional application filing date(s), and the patent term of the finally issued patent is calculated from the later non-provisional application filing date. This system allows us to obtain an early priority date, add material to the patent application(s) during the priority year, obtain a later start to the patent term and to delay prosecution costs, which may be useful in the event that we decide not to pursue examination in an application. While we intend to timely file non-provisional patent applications relating to our provisional patent applications, we cannot predict whether any such patent applications will result in the issuance of patents that provide us with any competitive advantage.

We file U.S. non-provisional applications and Patent Cooperation Treaty, or PCT, applications that claim the benefit of the priority date of earlier filed provisional applications, when applicable. The PCT system allows a single application to be filed within 12 months of the original priority date of the patent application, and to designate all of the PCT member states in which national patent applications can later be pursued based on the international patent application filed under the PCT. The PCT searching authority performs a patentability search and issues a non-binding patentability opinion, which can be used to evaluate the chances of success for the national applications in foreign countries prior to having to incur the filing fees. Although a PCT application does not issue as a patent, it allows the applicant to seek protection in any of the member states through national-phase applications.

At the end of the period of two and a half years from the first priority date of the patent application, separate patent applications can be pursued in any of the PCT member states either by direct national filing or, in some cases by filing through a regional patent organization, such as the European Patent Organization. The PCT system delays expenses, allows a limited evaluation of the chances of success for national/regional patent applications and enables substantial savings where applications are abandoned within the first two and a half years of filing.

For all patent applications, we determine claiming strategy on a case-by-case basis. Advice of counsel and our business model and needs are always considered. We file patent applications containing claims for protection of all useful applications of our proprietary technologies and any products, as well as all new applications and/or uses we discover for existing technologies and products, assuming these are strategically valuable. We continuously reassess the number and type of patent applications, as well as the existing patent claims to ensure that maximum coverage and value are obtained for our processes and compositions, given existing patent office rules and regulations. Further, claims may be modified during patent prosecution to meet our intellectual property and business needs.

We recognize that the ability to obtain patent protection and the degree of such protection depends on a number of factors, including the extent of the prior art, the novelty and non-obviousness of the invention and the ability to satisfy the enablement requirement of the patent laws. The patent positions of therapeutic polypeptide companies like ours are generally uncertain and involve complex legal, scientific and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted or further altered even after patent issuance. Consequently, we may not obtain or maintain adequate patent protection for any of our future product candidates or for our platform technology. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient proprietary protection from competitors. Any patents that we hold may be challenged, circumvented or invalidated by third parties.

Regardless of the coverage we seek under our existing patent applications, there is always a risk that an alteration to the product or process may provide sufficient basis for a competitor to avoid infringement claims. In addition, the coverage claimed in a patent application can be significantly reduced before a patent is issued, and courts can reinterpret patent scope after issuance. Moreover, many jurisdictions, including the United States, permit third parties to challenge allowed or issued patents in administrative proceedings, which may result in further narrowing or even cancellation of patent claims. Moreover, we cannot provide any assurance that any patents will be issued from our pending or any future applications or that any current or future issued patents will adequately protect our products.

Our patent portfolio, including patents and patent applications that we own and that we license from Harpoon Therapeutics, Inc., or Harpoon, comprises eight patent families that are in various stages of the patent application filing and examination process in various jurisdictions worldwide, and include claims to our product candidates and claims directed to our PREDATOR platform technology for potential products and developments. The status of our patent portfolio changes frequently in the ordinary course of patent prosecution. As of March 9, 2022, our patent portfolio related to the PREDATOR platform technology included approximately two issued patents in the United States, approximately 17 pending U.S. provisional or non-provisional patent applications, two pending international patent applications filed under the PCT and approximately 53 pending foreign patent applications, including pending applications in Australia, Brazil, Canada, China, European Patent Office, Hong Kong, India, Israel, Japan, Republic of Korea, Mexico, Russian Federation, Singapore, and South Africa. These patent applications, if issued, are expected to expire on various dates from 2039 through about 2043, in each case without taking into account any possible patent term extension that may be available.

Our patent portfolio on our PREDATOR platform technology includes two patent families directed to protease cleavable linkers and libraries of protease cleavable linkers, as well as polypeptides that contain such linkers and methods of making libraries and screening libraries to identify linkers with desired properties. One of the patent families includes pending applications in Australia, Brazil, Canada, China, European Patent Office, Israel, India, Japan, Republic of Korea, Mexico, and Singapore. The 20-year term for patents in this family runs through 2040, excluding any extension of patent term that may be available. The second patent family currently consists of a pending U.S. provisional application. We plan to file an international patent application under the PCT based on this provisional application before applicable deadlines.

Our patent portfolio for each of the product candidates is summarized below.

WTX-124

We own two patent families directed to IL-2 INDUKINE molecules and our WTX-124 product candidate. One of the families includes an issued U.S. patent with certain composition of matter claims with respect to WTX-124. We have also filed pending U.S. applications and pending foreign patent applications in Australia, Brazil, Canada, China, European Patent Office, Hong Kong, India, Israel, Japan, Republic of Korea, Mexico, Russian Federation, Singapore and South Africa that claim certain compositions of matter and methods of use with respect to WTX-124. The 20-year term for patents in this family runs through 2039, excluding any extension of patent term that may be available. A second patent family currently includes one pending international patent application filed under the PCT that claims certain compositions of matter and methods of use with respect to WTX-124. This PCT application also claims certain compositions of matter and method of use with respect to WTX-613. We intend to file national phase applications in the United States and various foreign jurisdictions based on this PCT application before applicable deadlines. The 20-year term for patents in this family runs through to 2040, excluding any extension of patent term that may be available.

WTX-330

We own two families directed to IL-12 INDUKINE molecules and our WTX-330 product candidate. One of the families includes an issued U.S. patent with certain composition of matter claims with respect to IL-12 INDUKINE molecules. We have also filed a pending U.S. application and pending foreign applications in Australia, Brazil, Canada, China, European Patent Office, Hong Kong, India, Israel, Japan, Republic of Korea, Mexico, Russian Federation, Singapore and South Africa that claim certain compositions of matter and methods of use with respect to IL-12 INDUKINE molecules and WTX-330. The 20-year term for patents in this family runs through 2039, excluding any extension of patent term that may be available. A second patent family currently consists of a pending international patent application filed under the PCT directed to certain compositions of matter and methods of use with respect to WTX-330. The 20-year term for patents in this family runs through to 2041, excluding any extension of patent term that may be available.

WTX-613

We own two patent families directed to our INF-a INDUKINE molecules and our WTX-613 product candidate. We own a first patent family that includes pending foreign applications in Australia, Brazil, Canada, China, European Patent Office, Hong Kong, India, Israel, Japan, Republic of Korea, Mexico, Russian Federation, Singapore and South Africa that claim certain compositions of matter and methods of use with respect to WTX-613. The 20-year term for patents in this family runs through 2039, excluding any extension of patent term that may be available. A second patent family currently includes one pending international patent application filed under the PCT that claims certain compositions of matter and methods of use with respect to WTX-613. This PCT application also claims certain compositions of matter and method of use with respect to WTX-124. We intend to file national phase applications in various foreign jurisdictions based on this PCT application before applicable deadlines. We filed a pending application in the United States that combined the disclosures of the first and second families, and claims compositions of matter and certain methods of use with respect to WTX-613. The 20-year term for patents based on the pending U.S. application will run through to 2039 or 2040, depending on the particular claims, excluding any extension of patent term that may be available.

In-Licensed Patents

We have licensed from Harpoon certain patents that are directed to single immunoglobulin variable domains that bind human serum albumin. We use the licensed technology in our current product candidates and may use the technology in additional development candidates we discover in the future. The licensed patent family includes granted U.S. patents and pending applications, and pending applications in Brazil, India, Canada, Japan, Mexico, Singapore, Australia, Eurasian Patent Organization, Republic of Korea, European Patent Office, China, and Israel. The 20-year term for the licensed patents runs through 2037, excluding any extension of patent term that may be available. See the discussion under “License Agreement with Harpoon Therapeutics, Inc.”, and Item 13. Certain Relationships and Related Transactions, and Director Independence, within this Annual Report for more information regarding our license agreement with Harpoon.

Patent Term and Patent Term Extensions

The term of individual patents depends upon the legal term for patents in the countries in which they are obtained. In most countries, including the United States, the patent term is 20 years from the earliest filing date of a non-provisional patent application. In addition, in certain instances, the term of a U.S. patent can be extended to compensate a patentee for administrative delays by the USPTO in examining and granting a patent. The term of a patent that covers a drug, biological product or medical device approved pursuant to a pre-market approval may also be eligible for patent term extension when FDA approval is granted, provided statutory and regulatory requirements are met. The length of the patent term extension is related to the length of time the drug is under regulatory review while the patent is in force. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Amendments, permits a patent term extension of up to five years beyond the expiration date set for the patent. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to each regulatory review period may be granted an extension and only those claims reading on the approved drug are extended. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug. We will, in general, pursue available patent term extensions in the United States and in foreign jurisdictions that provide for patent term extensions, however, there is no guarantee that the applicable authorities, including the FDA in the United States, will agree with our assessment of whether such extensions should be granted, and if granted, the length of such extensions.

Trademarks, Trade Secrets and Know-How

In connection with the ongoing development and advancement of our product candidates in the United States and various international jurisdictions, we seek to create protection for our marks and enhance their value by pursuing trademarks where available and when appropriate. In addition to patent and trademark protection, we rely upon trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, using confidentiality agreements with our commercial partners, collaborators, employees and consultants and invention assignment agreements with our employees and selected consultants. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached and our trade secrets and other proprietary information may be disclosed. We may not have adequate remedies for any breach and could lose our trade secrets and other proprietary information through such a breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our consultants, contractors or collaborators use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting trade secrets, know-how and inventions.

Our commercial success will also depend in part on not infringing the proprietary rights of third parties. In addition, we have licensed rights under proprietary technologies of third parties to develop, manufacture and commercialize specific aspects of our future products and services. It is uncertain whether the issuance of any third-party patent would require us to alter our development or commercial strategies, alter our processes, obtain licenses or cease certain activities. The expiration of patents or patent applications licensed from third parties or our breach of any license agreements or failure to obtain a license to proprietary rights that we may require to develop or commercialize our future technology may have a material adverse impact on us. If third parties prepare and file patent applications in the United States that also claim technology to which we have rights, we may have to participate in interference proceedings in the USPTO to determine priority of invention.

For more information regarding the risks related to our intellectual property, please see “Risks Related to Our Intellectual Property” under Part I, Item 1A. Risk Factors in this Annual Report.

License and Royalty Agreements

License Agreement with Harpoon Therapeutics, Inc.

In March 2018, we entered into an assignment and license agreement, or the Harpoon Agreement, with Harpoon, pursuant to which we assigned to Harpoon certain patents related to adoptive cell therapies and binding moieties for conditional activation of immunoglobulin and non-immunoglobulin molecules, and Harpoon assigned to us certain patents related to certain inducible polypeptides and a binding moiety for conditional activation of certain polypeptides. Harpoon also granted to us a worldwide, non-exclusive, royalty-bearing, sublicensable license under certain other patents owned by Harpoon and related to certain proteins to make, have made, use, sell, offer for sale and import products that are covered by such patents in the field of molecules comprising a certain polypeptide. Under the Harpoon Agreement, we agreed to pay to Harpoon an upfront fee of $0.5 million and, if we commercialize any products covered by these licensed patents, a low single digit percentage royalty on net sales of such products by us or any of our affiliates or licensees, subject to an obligation to make a minimum annual royalty payment at an amount in the low hundreds of thousands of dollars beginning with the first commercial sale of any such product by us.

In October, 2018, we and Harpoon amended the Harpoon Agreement by entering into a First Amended and Restated Assignment and License Agreement, which amended certain terms of the original agreement, but did not change the terms of the license to the Company, patent assignments between the parties or payments due to Harpoon.

In December 2019, we and Harpoon amended the Harpoon Agreement by entering into a Second Amended and Restated Assignment and License Agreement, or the Second Amended Harpoon Agreement, which granted to us an additional worldwide, exclusive, irrevocable, royalty-bearing, transferable, assignable, sublicensable license under certain patents owned by Harpoon and related to certain proteins, to make, have made, use, sell, offer for sale and import products that are covered by such patents in the field of molecules comprising a certain protein. Under the Second Amended Harpoon Agreement, we agreed to pay to Harpoon a low single digit percentage royalty on net sales by us or any of our affiliates or licensees of any products that we commercialize covered by these additional licensed patents. In addition, we also agreed to grant to Harpoon, and Harpoon agreed to grant to us, a perpetual, non-exclusive, irrevocable, royalty-free license under certain other patents directed to a certain binding domain of a certain protein, to make, have made, use, sell, offer for sale and import products that are covered by such patents in a field defined by a certain type of molecule with respect to each party.

Unless earlier terminated, our obligations to pay any royalties under the Second Amended Harpoon Agreement will expire on a country-by-country basis upon expiration of the last to expire valid claim of the relevant patents covering the manufacture, use or sale of such covered products in the applicable country. Harpoon may terminate the Second Amended Harpoon Agreement in the event of a material breach by us and our failure to cure such breach within a specified period and may terminate certain licenses if we become insolvent or bankrupt. We may terminate the Second Amended Harpoon Agreement voluntarily with prior written notice to Harpoon.

Amended and Restated Royalty Transfer Agreement

In December 2017, in connection with our sale of convertible promissory notes, we entered into a royalty transfer agreement with MPM Oncology Impact Fund Charitable Foundation, Inc., or MPM Charitable Foundation, and UBS Optimus Foundation, or the Royalty Transfer Agreement. Under the Royalty Transfer Agreement, we agreed to pay a royalty of 0.5% of net sales of our products to each of MPM Charitable Foundation and UBS Optimus Foundation. In August 2019, we amended the Royalty Transfer Agreement by entering into an amended and restated royalty transfer agreement, or the Amended Royalty Transfer Agreement, which provided that only products in our product pipeline at the time of our initial public offering or a change in control would be subject to the royalty on net sales. Under the Amended Royalty Transfer Agreement, our obligation to pay a royalty expires on a product-by-product and country-by-country basis upon

the later of the 12th anniversary of the first commercial sale of such product in such country and expiration of the last valid claim in such country covering such product. The royalty rate is subject to a specified reduction for lack of any valid claim covering such product in a country. The obligation to pay royalties under the Amended Royalty Transfer Agreement shall not apply to any product that would only infringe our intellectual property rights that are discovered or developed after this offering or to any product of an acquirer, assignee of the agreement or merger partner of the company so long as such product does not incorporate any of our pre-acquisition intellectual property.

Government Regulation and Product Approval

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

Review and Approval of Drugs and Biologics in the United States

In the United States, the FDA approves and regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and related regulations. Biological products are licensed for marketing under the Public Health Service Act, or PHSA, and subject to regulation under the FDCA and related regulations. A company, institution, or organization which takes responsibility for the initiation and management of a clinical development program for such products, and for their regulatory approval, is typically referred to as a sponsor. A sponsor seeking approval to market and distribute a new drug or biological product in the United States must typically secure the following:

- completion of preclinical laboratory tests in compliance with the FDA's good laboratory practice, or GLP, standards and applicable regulations;
- design of a clinical protocol and submission to the FDA of an IND, which must take effect before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCPs, to establish the safety and efficacy of the proposed drug product for each proposed indication;
- submission to the FDA of an NDA for a drug candidate product and a biological licensing application, or BLA, for a biological product requesting marketing for one or more proposed indications;
- review of the request for approval by an FDA advisory committee, where appropriate or if applicable;
- completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with cGMPs to assure the product's identity, strength, quality and purity;
- completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;
- payment of user fees and securing FDA approval of the NDA or BLA; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct post-approval studies.

Preclinical Studies

Before a sponsor begins testing a compound with potential therapeutic value in humans, the product candidate enters the preclinical testing stage. Preclinical studies include laboratory evaluation of the purity and stability of the manufactured substance or active pharmaceutical ingredient and the formulated product, as well as *in vitro* and animal studies to assess the safety and activity of the product candidate for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP standards and regulations and the United States Department of Agriculture's Animal Welfare Act, if applicable. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, and long-term toxicity studies, may continue after the IND is submitted.

The IND and IRB Processes

An IND is a request for FDA authorization to administer an investigational product candidate to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug or biologic that is not the subject of an approved NDA or BLA. In support of a request for an IND, sponsors must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the filing of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research subjects and patients will be exposed to unreasonable health risks. At any time during this 30-day period, or thereafter, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold or partial clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin. The FDA's primary objectives in reviewing an IND are to assure the safety and rights of patients and to help assure that the quality of the investigation will be adequate to permit an evaluation of the drug's effectiveness and safety and of the biological product's safety, purity and potency.

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. Clinical holds are imposed by the FDA whenever there is concern for patient safety and may be a result of new data, findings, or developments in clinical, nonclinical, and/or chemistry, manufacturing, and controls, or CMC. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a specific protocol or part of a protocol is not allowed to proceed, while other protocols may do so. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all IND requirements must be met unless waived. When a foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA in order to use the study as support for an IND or application for marketing approval in the United States. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

In addition to the foregoing IND requirements, 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.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board, or DSMB, or committee. This group provides authorization for whether a trial may move forward at designated check points based on access that only the group maintains to available data from the trial. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made based on evolving business objectives and/or competitive climate.

Human Clinical Studies in Support of an NDA or BLA

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written trial protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

The clinical investigation of an investigational drug or biological product is generally divided into four phases. Although the phases are usually conducted sequentially, they may overlap or be combined. The four phases of an investigation are as follows:

- Phase 1. Phase 1 studies include the initial introduction of an investigational new drug or biological product into humans. These studies are designed to evaluate the safety, dosage tolerance, metabolism and pharmacologic actions of the investigational drug or biological product in humans, the side effects associated with increasing doses, and if possible, to gain early evidence on effectiveness.
- Phase 2. Phase 2 includes the controlled clinical trials conducted to preliminarily or further evaluate the effectiveness of the investigational drug or biological product for a particular indication(s) in patients with the disease or condition under trial, to determine dosage tolerance and optimal dosage, and to identify possible adverse side effects and safety risks associated with the drug or biological product. Phase 2 clinical trials are typically well-controlled, closely monitored, and conducted in a limited patient population.
- Phase 3. Phase 3 clinical trials are generally controlled clinical trials conducted in an expanded patient population generally at geographically dispersed clinical trial sites. They are performed after preliminary evidence suggesting effectiveness of the drug or biological product has been obtained, and are intended to further evaluate dosage, clinical effectiveness and safety, to establish the overall benefit-risk relationship of the investigational drug or biological product, and to provide an adequate basis for product approval.
- Phase 4. Post-approval studies may be conducted after initial marketing approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication.

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

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator

brochure. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

In August 2018, the FDA released a draft 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.

Finally, sponsors of clinical trials are required to register and disclose certain clinical trial information on a public registry (clinicaltrials.gov) maintained by the U.S. National Institutes of Health, or NIH. In particular, information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. Both the NIH and the FDA have recently signaled the government's willingness to begin enforcing those requirements against non-compliant clinical trial sponsors. The failure to submit clinical trial information to clinicaltrials.gov, as required, is a prohibited act under the FDCA with violations subject to potential civil monetary penalties of up to $10,000 for each day the violation continues.

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

Pediatric Studies

Under the Pediatric Research Equity Act of 2003, or PREA, an application or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. Sponsors must also submit an initial Pediatric Study Plan, or PSP, prior to the assessment data. The PSP must contain an outline of the proposed pediatric study or studies the sponsor plans to conduct, including study objectives and design, any deferral or waiver requests and other information required by regulation. The sponsor, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other and agree upon a final plan. The FDA or the sponsor may request an amendment to the plan at any time.

For investigational products intended to treat a serious or life-threatening disease or condition, the FDA must, upon the request of a sponsor, meet to discuss preparation of the initial pediatric study plan or to discuss deferral or waiver of pediatric assessments. In addition, the FDA will meet early in the development process to discuss pediatric study plans with sponsors, and the FDA must meet with sponsors by no later than the end-of-phase 1 meeting for serious or life-threatening diseases and by no later than ninety (90) days after the FDA's receipt of the study plan.

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

FDARA also established new requirements to govern certain molecularly targeted cancer indications. Any company that submits an application three years after the date of enactment of that statute must submit pediatric assessments with the application if the product is intended for the treatment of an adult cancer and is directed at a molecular target that the FDA determines to be substantially relevant to the growth or progression of a pediatric cancer. The investigation must be designed to yield clinically meaningful pediatric study data regarding the dosing, safety and preliminary efficacy to inform pediatric labeling for the product.

Submission and Review of an NDA or BLA by the FDA

In order to obtain approval to market a drug or biological product in the United States, a marketing application must be submitted to the FDA that provides data establishing the safety and effectiveness of the proposed drug product for the proposed indication, and the safety, purity and potency of the biological product for its intended indication. The application includes all relevant data available from pertinent preclinical and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls and proposed labeling, among other things. Data can come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including studies initiated by investigators.

The application is the vehicle through which sponsors formally propose that the FDA approve a new product for marketing and sale in the United States for one or more indications. Every new product candidate must be the subject of an approved NDA or BLA before it may be commercialized in the United States. Under federal law, the submission of most applications is subject to an application user fee. The sponsor of an approved application is also subject to an annual program fee. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for products with orphan designation and a waiver for certain small businesses. If an application is

withdrawn prior to the FDA acceptance for filing, 75% of these fees may be refunded to the sponsor. If an application is withdrawn after filing, a lower portion of these fees may be refunded in certain circumstances.

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

Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review process of NDAs and BLAs. Under that agreement, 90% of applications seeking approval of New Molecular Entities, or NMEs, are meant to be reviewed within ten months from the date on which FDA accepts the NDA for filing, and 90% of applications for NMEs that have been designated for "priority review" are meant to be reviewed within six months of the filing date. The review process and the Prescription Drug User Fee Act goal date may be extended by the FDA for three additional months to consider new information or clarification provided by the sponsor to address an outstanding deficiency identified by the FDA following the original submission.

In connection with its review of an application, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA or BLA submission, including drug component manufacturing (e.g., active pharmaceutical ingredients), finished drug product manufacturing, and control testing laboratories. The FDA will not approve an application 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 an NDA or BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP standards and the integrity of the clinical data supporting the application.

The FDA may also refer an application for a novel product to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

The FDA's Decision on an NDA or BLA

After evaluating the application and all related information, including the advisory committee recommendations, if any, and inspection reports of manufacturing facilities and clinical trial sites, the FDA will issue either a Complete Response Letter, or CRL, or an approval letter. To reach this determination, the FDA must determine that the expected benefits of the proposed product outweigh its potential risks to patients. This "benefit-risk" assessment is informed by the extensive body of evidence about the product's safety and efficacy in the NDA or BLA.

If the FDA decides not to license or approve the application, it will issue a CRL. A CRL will describe all of the deficiencies that the FDA has identified in the application, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the CRL without first conducting required inspections, testing submitted product lots, and/or reviewing proposed labeling. In issuing the CRL, the FDA may recommend actions that the applicant might take to place the application in condition for approval, including requests for additional information or clarification. The FDA may delay or refuse approval of an application 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 CRL is issued, the applicant will have one year to respond to the deficiencies identified by the FDA, at which time the FDA can deem the application withdrawn or, in its discretion, grant the applicant an additional six month extension to respond.

An approval letter, on the other hand, authorizes commercial marketing of the product with specific prescribing information for specific indications. If the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including phase 4 clinical trials, be conducted to further assess the drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Fast Track, Breakthrough Therapy and Priority Review Designations

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs include fast track designation, breakthrough therapy designation and priority review designation. None of these expedited programs changes the standards for approval but each may help expedite the development or approval process governing product candidates.

Specifically, the FDA may designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a Fast Track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a Fast Track application does not begin until the last section of the

application is submitted. In addition, the Fast Track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, a product may be designated as a Breakthrough Therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to Breakthrough Therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to help the sponsor design the clinical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a product that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a product for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. Products granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a product.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a product, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of products for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit. Thus, the benefit of accelerated approval derives from the potential to receive approval based on surrogate endpoints sooner than possible for trials with clinical or survival endpoints, rather than deriving from any explicit shortening of the FDA approval timeline, as is the case with priority review.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the product's clinical benefit. As a result, a product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to initiate expedited proceedings to withdraw approval of the product. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

Post-Approval Regulation

Drugs and biologics manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

In addition, manufacturers and other entities involved in the manufacture and distribution of approved products are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse

events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

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

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

Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress established an abbreviated regulatory scheme authorizing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs. To obtain approval of a generic drug, a sponsor must submit an abbreviated new drug application, or ANDA, to the agency. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the active pharmaceutical ingredient, bioequivalence, drug product formulation, specifications and stability of the generic drug, as well as analytical methods, manufacturing process validation data and quality control procedures. ANDAs are “abbreviated” because they generally do not include preclinical and clinical data to demonstrate safety and effectiveness. Instead, in support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference-listed drug, or RLD.

Under the Hatch-Waxman Amendments, the FDA may not approve an ANDA until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity. For the purposes of this provision, a new chemical entity, or NCE, is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. This interpretation of the FDCA by the FDA was confirmed with enactment of the Ensuring Innovation Act in April 2021. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the sponsor may submit its application four years following the original product approval. The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the sponsor and are essential to the approval of the application.

Biosimilars

The 2010 Patient Protection and Affordable Care Act, or ACA, which was signed into law on March 23, 2010, included a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA. The BPCIA established a regulatory scheme authorizing the FDA to approve biosimilars and interchangeable biosimilars. To date, the FDA has approved a number of biosimilars and the first interchangeable biosimilar product was approved on July 30, 2021 and a second product previously approved as a biosimilar was designated as interchangeable in October 2021.

Under the BPCIA, a manufacturer may submit an application for licensure of a biologic product that is “biosimilar to” or “interchangeable with” a previously approved biological product or “reference product.” In order for the FDA to approve a biosimilar product, it must find that there are no clinically meaningful differences between the reference product and proposed biosimilar product in terms of safety, purity, and potency. For the FDA to approve a biosimilar product as interchangeable with a reference product, the agency must find that the biosimilar product can be expected to produce the same clinical results as the reference product, and (for products administered multiple times) that the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

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

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition, generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product. A company must request orphan drug designation before submitting an NDA or BLA for the candidate product. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan drug designation does not shorten the Prescription Drug User Fee Act, or PDUFA, goal dates for the regulatory review and approval process, although it does convey certain advantages such as tax benefits and exemption from the PDUFA application fee.

If a product with orphan designation receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor's marketing application for the same drug for the same indication for seven years, except in certain limited circumstances. Orphan exclusivity does not block the approval of a different product for the same rare disease or condition, nor does it block the approval of the same product for different indications. If a drug or biologic designated as an orphan drug ultimately receives marketing approval for an indication broader than what was designated in its orphan drug application, it may not be entitled to exclusivity.

Orphan exclusivity will not bar approval of another product under certain circumstances, including if a company with orphan drug exclusivity is not able to meet market demand and in cases where a subsequent product with the same drug or biologic for the same indication is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care. Under Omnibus legislation signed by President Trump on December 27, 2020, the requirement for a subsequent product to show clinical superiority in order to break the previous product's orphan drug exclusivity applies to drugs and biologics that received orphan drug designation before enactment of FDARA in 2017 but have not yet been approved or licensed by FDA.

In September 2021, the Court of Appeals for the 11th Circuit held that, for the purpose of determining the scope of market exclusivity, the term "same disease or condition" in the statute means the designated "rare disease or condition" and could not be interpreted by the FDA to mean the "indication or use." Thus, the court concluded, orphan drug exclusivity applies to the entire designated disease or condition rather than the "indication or use." It is unclear how this court decision will be implemented by the FDA.

Pediatric Exclusivity

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of regulatory exclusivity. For drug products, the six-month exclusivity may be attached to the term of any existing patent or regulatory exclusivity. For biologic products, the six-month period may only be attached to any existing regulatory exclusivities but not to any patent terms. This six-month exclusivity may be granted if an NDA or BLA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of non-patent exclusivity for drugs and biologics, or patent protection that covers a drug product, are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application.

Patent Term Restoration and Extension

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

Pharmaceutical Coverage, Pricing 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. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. 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. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product candidate could reduce physician utilization once the

product is approved and have a material adverse effect on sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a drug 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.

Healthcare Law and Regulation

Health care providers and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, patient privacy laws and regulations and other health care laws and regulations that may constrain business and/or financial arrangements.

Restrictions under applicable federal and state health care laws and regulations, include the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal health care program such as Medicare and Medicaid; the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government; the Foreign Corrupt Practices Act, or FCPA, which prohibits companies and their intermediaries from making, or offering or promising to make, improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment; and the federal transparency requirements known as the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the United States Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. As of January 1, 2022, these federal transparency reporting obligations were extended to include transfers of value made during the previous year to physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists and certified nurse midwives. In addition, the Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended, among other things, imposes limitations on certain covered healthcare providers, health plans, and healthcare clearinghouses and their respective business associates and their covered subcontractors that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information.

Further, some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. Additionally, some state and local laws require the registration of pharmaceutical sales representatives in the jurisdiction.

State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. In particular, numerous federal and state laws and regulations, including state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws, govern the collection, use, disclosure, and protection of health-related and other personal information.

Violation of the laws described above or any other governmental laws and regulations may result in significant penalties, including civil, criminal, and administrative penalties, damages, fines, the curtailment or restructuring of operations, the exclusion from participation in federal and state healthcare programs, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, imprisonment, and additional reporting requirements and oversight if a manufacturer becomes subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws. Furthermore, efforts to ensure that business activities and business arrangements comply with applicable healthcare laws and regulations can be costly.

Healthcare Reform

The containment of health care costs also 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 reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and biologics and other medical products, government control and other changes to the health care system in the United States. In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, or the PPACA, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the ACA. In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress including aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2031. These Medicare sequester reductions have been suspended through the end of March 2022. From April 2022 through June 2022 a 1% sequester cut will be in effect, with the full 2% cut resuming thereafter. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments

to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Since enactment of the PPACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, or the TCJA, which was signed by President Trump on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. In December 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the PPACA is an essential and inseverable feature of the PPACA, and therefore because the mandate was repealed as part of the TCJA, the remaining provisions of the PPACA are invalid as well. After appeal, in June 2021, the U.S. Supreme Court dismissed this action after finding that the plaintiffs do not have standing to challenge the constitutionality of the ACA. Litigation and legislation over the PPACA are likely to continue, with unpredictable and uncertain results.

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

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

In addition, in October 2020, HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program, or SIP, to import certain prescription drugs from Canada into the United States. The final rule is currently the subject of ongoing litigation, but at least six states (Vermont, Colorado, Florida, Maine, New Mexico, and New Hampshire) have passed laws allowing for the importation of drugs from Canada with the intent of developing SIPs for review and approval by the FDA. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed by the Biden administration until January 1, 2023.

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

At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. A number of states, for example, require drug manufacturers and other entities in the drug supply chain, including health carriers, pharmacy benefit managers, wholesale distributors, to disclose information about pricing of pharmaceuticals. In addition, regional health care 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 health care programs. These measures could reduce the ultimate demand for our products,

once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Human Capital

As of December 31, 2021, we had 39 full-time employees, including a total of 20 employees with M.D. or Ph.D. degrees. Of these full-time employees, 27 employees are engaged in research and development. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and additional employees. We conduct annual performance and development reviews for each of our employees to discuss the individual's strengths and development opportunities, career development goals and performance goals. In addition, each regular full-time employee is encouraged to attend appropriate job-related trainings and other professional development courses, seminars, meetings, and similar sessions. The principal purposes of our equity incentive plans are to attract, retain and motivate selected employees, consultants and directors through the granting of stock-based compensation awards. We value our employees and regularly benchmark total rewards we provide, such as short and long term compensation, 401(k) contributions, health, welfare and quality of life benefits, paid time off and personal leave, against our industry peers to ensure we remain competitive and attractive to potential new hires.

We are committed to diversity, equity and inclusion across all aspects of our organization, including in our recruitment, advancement and development practices.

Corporate Information

Our principal offices are located at 1030 Massachusetts Ave, Suite 210, Cambridge, MA 02138, and our telephone number is (617) 952-0555.

Our website address is www.werewolftx.com. Our website and the information contained on, or that can be accessed through, the website will not be deemed to be incorporated by reference in, and are not considered part of, this Annual Report or any other report or document we file with the Securities and Exchange Commission, or the SEC, and any reference to our website address is intended to be an inactive textual reference only. Through our website, we make available, free of charge, our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, any amendments to those reports, proxy and registration statements, and all of our insider Section 16 reports, as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. These SEC reports can be accessed through the "Investors" section of our website. You should not rely on any such information in making your decision whether to purchase our common stock.

Item 1A. Risk Factors

Our business is subject to numerous risks. You should carefully consider the risks described below, as well as the other information in this Annual Report, including our consolidated financial statements and the related notes and Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations. The occurrence of any of the events or developments described below could materially and adversely affect our business, financial condition, results of operations and future growth prospects. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations. This Annual Report also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in the forward-looking statements as a result of a number of factors, including the risks described below.

Risks Related to Our Limited Operating History, Financial Position and Capital Requirements

We have a limited operating history, have incurred significant operating losses since our inception and expect to incur significant losses for the foreseeable future.

We are an early-stage biopharmaceutical company with a limited operating history upon which our business and prospects can be evaluated. We commenced operations in 2017. To date, we have focused primarily on organizing and staffing our company, business planning, raising capital, developing and optimizing our platform technology, identifying potential product candidates, enhancing our intellectual property portfolio, undertaking research and preclinical studies and enabling manufacturing for our development programs. Our approach to the discovery and development of product candidates based on our PREDATOR platform is unproven, and we do not know whether we will be able to develop any approved products of commercial value. In addition, we currently only have three product candidates, WTX-124, WTX-330 and WTX-613, none of which have entered clinical development, and all of our other development programs are in discovery or preclinical stages. We have not yet demonstrated an ability to successfully submit an investigational new drug application, or IND, to the U.S. Food and Drug Administration, or the FDA, or successfully complete any Phase 1, Phase 2 or pivotal clinical trials, obtain regulatory approvals, manufacture a clinical- or commercial-scale product, or arrange for a third party to do so on our behalf, or conduct the sales and marketing activities necessary for successful product commercialization. Consequently, any predictions made about our future success or viability may not be as accurate as they could be if we had a history of successfully developing and commercializing biopharmaceutical products.

We have incurred significant operating losses since our inception and have not yet generated any revenue. If our product candidates are not successfully developed and approved, we may never generate any revenue. Our net loss was $50.0 million for the year ended December 31, 2021. As of December 31, 2021, we had an accumulated deficit of $252.9 million. We expect to continue to incur losses for the foreseeable future, and we anticipate these losses will increase substantially as WTX-124, WTX-330, WTX-613 and any future product candidates advance through preclinical studies and into clinical trials, and as we expand our clinical, regulatory, quality and manufacturing capabilities and incur additional costs associated with operating as a public company. If we obtain marketing approval for any of our product candidates, we will incur significant commercialization expenses for marketing, sales, manufacturing and distribution. We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. We will need to develop commercial capabilities, and we may not be successful in doing so. The net losses we incur may fluctuate significantly from quarter to quarter and year to year.

We have no products approved for commercial sale and have not generated any revenue from product sales. We may never generate any revenue or become profitable or, if we achieve profitability, we may not be able to sustain it.

To date, we have not generated any revenue from our product candidates or product sales, we do not expect to generate any revenue from the sale of products for a number of years and we may never generate revenue from the sale of products. Our ability to generate product revenue depends on a number of factors, including, but not limited to, our ability to:

- successfully complete our ongoing and planned preclinical studies;
- successfully submit our INDs to the FDA for WTX-124, WTX-330, WTX-613 and any future product candidates;
- successfully initiate clinical trials for WTX-124, WTX-330, WTX-613 and any future product candidates;
- successfully enroll subjects in, and complete, our planned clinical trials and future clinical trials;
- initiate and successfully complete all safety and efficacy studies to obtain U.S. and foreign regulatory approval for our product candidates;
- establish clinical and commercial manufacturing capabilities or make 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 products, if and when approved, whether alone or in collaboration with others;
- obtain and maintain acceptance of the products, if and when approved, by patients, the medical community and third-party payors;
- effectively compete with other therapies;
- obtain and maintain healthcare coverage and adequate reimbursement;
- enforce and defend intellectual property rights and claims; and

- maintain a continued acceptable safety profile of our products following approval.

Because of the numerous risks and uncertainties associated with biopharmaceutical product development, we are unable to accurately predict the timing or amount of expenses we may incur in connection with these activities prior to generating product revenue. In addition, we may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product candidates or even continue our operations. A decline in the value of our company could also cause our stockholders to lose all or part of their investment.

We will need to obtain substantial additional funding to finance our operations and complete the development and any commercialization of WTX-124, WTX-330, WTX-613 and any future product candidates. If we are unable to raise this capital when needed, we may be forced to delay, reduce or eliminate one or more of our research and development programs or other operations.

Identifying potential product candidates and conducting preclinical 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 regulatory approval and achieve product sales. We expect to incur increasing expenses and operating losses over the next several years as we pursue clinical development of our product candidates and implement the additional infrastructure necessary to support our operations as a public reporting company. Our revenue, if any, will be derived from sales of products that we do not expect to be commercially available for a number of years, if at all. If we obtain marketing approval for WTX-124, WTX-330, WTX-613 or any other product candidates that we develop, we expect to incur significant commercialization expenses related to product sales, marketing, distribution and manufacturing. Some of these expenses may be incurred in advance of marketing approval and could be substantial.

As of December 31, 2021, we had cash and cash equivalents of $157.5 million. We believe that our existing cash and cash equivalents will be sufficient to fund our operations through at least the second quarter of 2023. Our existing cash and cash equivalents will allow us to complete the development of WTX-124 through dose escalation and expansion trials as a monotherapy or in combination with an immune checkpoint inhibitor, the development of WTX-330 through dose escalation and expansion trials as a monotherapy or in combination with an immune checkpoint inhibitor and the preclinical development of WTX-613.

Our cash and cash equivalents will not be sufficient to complete development of WTX-124, WTX-330, WTX-613 or any other product candidate. Accordingly, we will be required to obtain further funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources. Adequate additional financing may not be available to us on acceptable terms, or at all. Our failure to raise capital as and when needed, on attractive terms or at all, would have a negative effect on our financial condition and our ability to develop and commercialize our current and any future product candidates, and otherwise pursue our business strategy and we may be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts.

In addition, our cash forecasts are based on assumptions that may prove to be wrong, and we could use our available capital resources earlier than we currently expect. Changing circumstances could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional financing sooner than planned. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans.

Our future capital requirements, both short-term and long-term, will depend on many factors, including:

- the scope, progress, timing, costs and results of researching and developing our current product candidates or any future product candidates, including with respect to our planned clinical trials of WTX-124 and WTX-330;
- the costs associated with attracting, hiring and retaining skilled personnel and consultants as our preclinical and clinical activities increase;
- the cost of manufacturing WTX-124, WTX-330, WTX-613 and any future product candidates for clinical trials and, if we are able to obtain marketing approval, for commercial sale;
- the costs of any third-party products used in our planned combination clinical trials that are not covered by such third parties or other sources;
- the potential additional expenses attributable to adjusting our development plans (including any supply related matters) as a result of the COVID-19 pandemic;
- the timing of, and the cost involved in, obtaining marketing approval for WTX-124, WTX-330, WTX-613 or any future product candidates, and our ability to obtain marketing approval and generate revenue from any potential commercial sales of such product candidates;
- the cost of building a sales force in anticipation of product commercialization and the cost of commercialization activities for WTX-124, WTX-330, WTX-613 or any future product candidates if we receive marketing approval, including marketing, sales and distribution costs;
- the potential emergence of competing therapies and other adverse market developments;
- the amount and timing of any payments we may be required to make pursuant to our license agreement with Harpoon Therapeutics, Inc., or Harpoon, or other future license agreements or collaboration agreements;

- our ability to establish future collaborations, licensing or other arrangements and the financial terms of any such agreements, including the timing and amount of any future milestone, royalty or other payments due under any such agreement;
- the costs involved in preparing, filing, prosecuting, maintaining, expanding, defending and enforcing patent claims, including litigation costs and the outcome of such litigation;
- any product liability or other lawsuits related to our product candidates;
- the extent to which we in-license or acquire other products and technologies; and
- the costs of operating as a public company.

We do not have any committed external source of funds and adequate additional financing may not be available to us on acceptable terms, or at all. In addition, our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions resulting from the ongoing COVID-19 pandemic and any disruptions to, or volatility in, the credit and financial markets in the United States and worldwide that arise from the pandemic. Our failure to raise capital as and when needed or on acceptable terms would have a negative impact on our financial condition and our ability to pursue our business strategy, and we may have to delay, reduce the scope of, suspend or eliminate one or more of our research-stage programs, clinical trials or future commercialization efforts or other operations.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our platform technology or product candidates.

Unless and until we can generate a substantial amount of product revenue, we expect to seek additional capital through a combination of public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources. Our issuance of additional securities, whether equity or debt, or the possibility of such issuance, may cause the market price of our common stock to decline, and our stockholders may not agree with our financing plans or the terms of such financings. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interests will be diluted and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. The incurrence of indebtedness would result in payment obligations and could require us to comply with certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to declare dividends, limitations on our ability to acquire or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. If we raise additional funds through collaborations and licensing arrangements with third parties, we may have to relinquish valuable rights to our platform technology or product candidates or grant licenses on terms unfavorable to us. In addition, securing additional financing would require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of our product candidates.

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

Changes in tax law may adversely affect our business or financial condition. The TCJA, as amended by the Coronavirus Aid, Relief, and Economic Security Act, or CARES Act, significantly revises the Internal Revenue Code of 1986, as amended, or the Code. The TCJA, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for net interest expense to 30% of adjusted taxable income (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, in each case, for losses arising in taxable years beginning after December 31, 2017 (though any such net operating losses may be carried forward indefinitely and, as a result of amendments made by the CARES Act, such net operating losses arising in taxable years beginning before January 1, 2021 are generally eligible to be carried back up to five years), one-time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits.

In addition to the CARES Act, as part of Congress's response to the COVID-19 pandemic, economic relief legislation was enacted in 2020 and 2021 containing tax provisions. Regulatory guidance under the TCJA and such additional legislation is and continues to be forthcoming, and such guidance could ultimately increase or lessen their impact on our business and financial condition. Also, as a result of the changes in the U.S. presidential administration and control of the U.S. Senate in 2021, additional tax legislation may be enacted; any such additional legislation could have an impact on us. In addition, it is uncertain if and to what extent various states will conform to the TCJA and additional tax legislation.

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

We have incurred substantial losses during our history. We do not anticipate generating revenue from sales of products for the foreseeable future, if ever, and we may never achieve profitability. As of December 31, 2021, we had federal and state net operating loss carryforwards of $80.3 million and $74.5 million, respectively. Under Section 382 of the Code, if a corporation undergoes an "ownership change" (generally defined as a greater than 50 percentage point change (by value) in the ownership of its equity by certain 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 income may be limited. As a result of our prior private placement financings or other transactions, we may have in the past experienced, and we may in the future experience as a result of subsequent changes in our stock ownership, some of which are outside our control, an ownership change for purposes of Section 382. As a result, if we earn net taxable income, our ability to use our pre-change net operating loss carryforwards and other pre-change tax attributes to offset U.S. federal taxable income may be subject to limitations, which could result in increased future tax liability to us and could have an adverse effect on our future results of operations. There is also a risk that due to regulatory changes, such as suspension of the use of net operating losses, or for other unforeseen reasons, our existing net operating

losses could expire or otherwise become unavailable to offset future income tax liabilities. As described above in "Changes in tax laws or in their implementation or interpretation could adversely affect our business and financial condition," the TCJA, as amended by the CARES Act, includes changes to U.S. federal tax rates and rules governing net operating loss carryforwards that may significantly impact our ability to utilize net operating losses to offset taxable income in the future. In addition, state net operating losses generated in one state cannot be used to offset income generated in another state. For these reasons, we may be unable to use a material portion of our net operating losses and other tax attributes.

Risks Related to the Discovery, Development, Regulatory Approval and Commercialization of Our Product Candidates

We are early in our development efforts. All of our product candidates are still in preclinical development and will require successful completion of preclinical development before we can submit an IND to the FDA to commence clinical development.

We are early in our development efforts and all of our product candidates are still in preclinical development. We have invested substantially all of our efforts and financial resources in building our PREDATOR platform and developing our initial INDUKINE molecules by leveraging our PREDATOR platform. We expect to submit an IND to the FDA with respect to WTX-124 in the second quarter of 2022 and WTX-330 in the third quarter of 2022. Additionally, we have a portfolio of programs that are in even earlier stages of preclinical development and may never advance to clinical-stage development. Our ability to generate product revenue, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our product candidates, which may never occur. We currently generate no revenue from sales of any product, and we may never be able to develop or commercialize a marketable product.

Our business is highly dependent on the success of our initial INDUKINE molecules, which are in the early stages of development and will require significant additional preclinical and clinical development before we can seek regulatory approval for and launch a product commercially.

Our business and future success is highly dependent on our ability to obtain regulatory approval of and then successfully launch and commercialize our initial INDUKINE molecules, including our most advanced product candidates, WTX-124 and WTX-330, each of which is in preclinical development.

Commencing clinical trials in the United States is subject to acceptance by the FDA of an IND and finalizing the trial design based on discussions with the FDA and other regulatory authorities. In the event that the FDA requires us to complete additional preclinical studies or we are required to satisfy other FDA requests prior to commencing clinical trials, the start of our first clinical trials may be delayed. Even after we receive and incorporate guidance from these regulatory authorities, the FDA or other regulatory authorities could disagree that we have satisfied their requirements to commence any clinical trial or change their position on the acceptability of our trial design or the clinical endpoints selected, which may require us to complete additional preclinical studies or clinical trials or impose stricter approval conditions than we currently expect. There are equivalent processes and risks applicable to clinical trial applications in other countries, including countries in the European Union.

To date, we have not submitted an IND to the FDA and have only had limited interactions with the FDA regarding our clinical development plans. We may experience issues surrounding preliminary trial execution, such as delays in FDA acceptance of our planned INDs, revisions in trial design and finalization of trial protocols, difficulties with patient recruitment and enrollment, quality and provision of clinical supplies, or early safety signals.

We are not permitted to market any biological product in the United States until we receive approval of a Biologics License Application, or BLA, from the FDA. We have not previously submitted a BLA to the FDA, or similar marketing application to comparable foreign regulatory authorities. A BLA must include extensive preclinical and clinical data and supporting information to establish that the product candidate is safe, pure and potent for each desired indication. A BLA must also include significant information regarding the chemistry, manufacturing and controls for the product, and the manufacturing facilities must complete a successful pre-license inspection.

FDA approval of a BLA is not guaranteed, and the review and approval process is expensive and uncertain and may take several years. The FDA also has substantial discretion in the approval process. The number and types of preclinical studies and clinical trials that will be required for BLA approval varies depending on the product candidate, the disease or the condition that the product candidate is designed to treat and the regulations applicable to any particular product candidate. Despite the time and expense associated with preclinical studies and clinical trials, failure can occur at any stage.

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 approval. The opinion of the Advisory Committee, although not binding, may have a significant impact on our ability to obtain approval of any product candidate that we develop based on the completed clinical trials.

Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend heavily on our ability to successful develop and commercialize of WTX-124, WTX-330, WTX-613 and any future product candidates. The success of our product candidates will depend on several factors, including the following:

- completion of preclinical studies and clinical trials with favorable results;
- acceptance of INDs by the FDA or similar regulatory filing by comparable foreign regulatory authorities for the conduct of clinical trials of our product candidates and our proposed design of future clinical trials;
- receipt of marketing approvals from applicable regulatory authorities, including BLAs from the FDA and maintaining such approvals;

- making arrangements with our third-party manufacturers for, or establishing, commercial manufacturing capabilities;
- maintaining an acceptable safety profile of our products following approval; and
- maintaining and growing an organization of scientists and business people who can develop our products and technology.

Generally, public concern regarding the safety of biopharmaceutical products could delay or limit our ability to obtain regulatory approval, result in the inclusion of unfavorable information in our labeling or require us to undertake other activities that may entail additional costs. We have not obtained FDA approval for any product. This lack of experience may impede our ability to obtain FDA approval in a timely manner, if at all, for WTX-124, WTX-330, WTX-613 or any future product candidates.

The success of our business, including our ability to finance our company and generate any revenue in the future, will primarily depend on the successful development, regulatory approval and commercialization of WTX-124, WTX-330, WTX-613 and any future product candidates, which may never occur. However, given our early stage of development, it will be years before we are able to demonstrate the safety and efficacy of a treatment sufficient to warrant approval for commercialization, and we may never be able to do so. If we are unable to develop, or obtain regulatory approval for, or, if approved, successfully commercialize our current or any future product candidates, we may not be able to generate sufficient revenue to continue our business.

Our approach to the discovery and development of product candidates based on our PREDATOR platform is unproven, and we do not know whether we will be able to develop any products of commercial value.

The success of our business depends primarily upon our ability to discover, develop and commercialize products based on our novel PREDATOR platform. While we have had favorable preclinical study results related to WTX-124, WTX-330 and WTX-613, each of which we are developing by leveraging our PREDATOR platform, we have not yet succeeded and may not succeed in demonstrating efficacy and safety for any product candidates in clinical trials or in obtaining marketing approval thereafter. We have no assurance that our PREDATOR platform will be able to produce product candidates that will successfully progress from preclinical studies into clinical development and ultimately marketing approval. We have invested substantially all of our efforts and financial resources in building our PREDATOR platform and developing our initial INDUKINE molecules by leveraging our PREDATOR platform, and our future success is highly dependent on the continued successful development of our platform and product candidates that we develop by leveraging our platform. Because all of our product candidates are based upon our PREDATOR platform, any development problems we may experience in the future related to any of our product candidates has the potential to impact the development of our other product candidates and any such development problems have the potential to cause significant delays or unanticipated costs and may ultimately not be able to be solved.

In addition, the clinical trial requirements of the FDA and other regulatory agencies and the criteria these regulators use to determine the safety and efficacy of a product candidate may vary according to the type, complexity, novelty and intended use and market of the potential products. The regulatory approval process for novel product candidates can be more expensive and take longer than for other, better known or extensively studied pharmaceutical or other product candidates. As a result, we may face a greater regulatory burden to initiate clinical trials or to obtain regulatory approval of our product candidates as compared to product candidates based on more established technology. In addition, any product candidates for which we may be able to obtain marketing approval 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.

Manufacturing INDUKINE molecules is subject to risk since they are a novel class of multi-domain biologics that include protease cleavable linkers, and they have never been produced on a clinical or commercial scale. We may be unable to manufacture INDUKINE molecules at the scale needed for clinical development and commercial production on a timely basis or at all, which would adversely affect our ability to conduct clinical trials and seek regulatory approvals or commercialize our programs, which would have an adverse effect on our business.

The manufacturing cell line currently in use to develop INDUKINE manufacturing processes has not been used to manufacture multi-domain proteins that include our protease cleavable linkers. The presence of these linkers presents a risk that unintended proteolysis may occur during the manufacture of INDUKINE molecules and that undesired fragments may not be able to be sufficiently removed by the purification process. The novel multi-domain composition of INDUKINE molecules may present a risk due to its complexity and challenges inherent to the manufacture of biologics. As a result, the risk of delays or failure in the manufacture of our INDUKINE molecules is high. Before we can commence clinical trials for a product candidate, the manufactured INDUKINE molecules must complete extensive analytical testing and be qualified for use in human studies. We cannot be certain of the timely completion or outcome of our analytical testing and suitability for human studies and cannot predict if the FDA or other regulatory authorities will accept our proposed clinical material or if the outcome of our analytical testing will ultimately support the further development of our programs. As a result, we cannot be sure that we will be able to submit INDs or similar applications for WTX-124, WTX-330, WTX-613 or any future preclinical programs on the timelines we expect, if at all, and we cannot be sure that the submission of INDs or similar applications will result in the FDA or other regulatory authorities allowing clinical trials to begin. In addition, we cannot be certain that we will be able to produce product candidates at the scale required for our clinical trials and, for any approved products, commercial production on a timely basis or at all, which could also have an adverse effect on our business.

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

We have chosen to initially develop our lead product candidate, WTX-124, for the treatment of advanced solid tumors. We plan to develop our second product candidate, WTX-330, for the treatment of relapsed or refractory advanced or metastatic tumors or lymphoma. Nevertheless, our development efforts will be limited to a small number of cancer types and we may forego or delay pursuit of opportunities

in other cancer types that may prove to have greater potential. Likewise, we may forego or delay the pursuit of opportunities with other potential product candidates that may prove to have greater commercial potential.

Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable product candidates. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other similar arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to the product candidate.

Preclinical development is uncertain. Our preclinical programs may experience delays or may never advance to clinical trials, which would adversely affect our ability to obtain regulatory approvals or commercialize these programs on a timely basis or at all, which would have an adverse effect on our business.

All of our product candidates are still in the preclinical stage, and their risk of failure is high. Before we can commence clinical trials for a product candidate, we must complete extensive preclinical testing and studies that support our planned INDs in the United States, or similar applications in other jurisdictions. We cannot be certain of the timely completion or outcome of our preclinical testing and studies and cannot predict if the FDA or other regulatory authorities will accept our proposed clinical programs or if the outcome of our preclinical testing and studies will ultimately support the further development of our programs. As a result, we cannot be sure that we will be able to submit INDs or similar applications for our preclinical programs on the timelines we expect, if at all, and we cannot be sure that submission of INDs or similar applications will result in the FDA or other regulatory authorities allowing clinical trials to begin.

Preclinical studies and clinical trials are expensive, time-consuming and difficult to design and implement, and involve uncertain outcomes. Furthermore, results of earlier preclinical studies and clinical trials may not be predictive of results of future preclinical studies or clinical trials.

The risk of failure for our current and any future product candidates is high. It is impossible to predict when or if any of our product candidates will successfully complete preclinical studies or clinical trials evaluating their safety and effectiveness in humans or will ultimately receive regulatory approval. To obtain the requisite regulatory approvals to market and sell any of our product candidates, we must demonstrate through extensive preclinical studies and clinical trials that our product candidates are safe and effective in humans for use in each target indication. To date, we have never advanced a product candidate into a clinical trial. Preclinical and clinical testing is expensive and can take many years to complete, and the outcome is inherently uncertain. Failure can occur at any time during the preclinical or clinical trial process. The outcome of preclinical testing and early clinical trials may not be predictive of the results of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. In particular, while we have conducted certain preclinical studies of WTX-124, WTX-330 and WTX-613, we do not know whether any of these product candidates will perform in our planned clinical trials as it has performed in these prior preclinical studies. Additionally, if we successfully commence clinical trials there can be no assurance that success in early clinical trials will lead to success in later clinical trials. Many companies in the biopharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development and we cannot be certain that we will not face similar setbacks. These setbacks have been caused by, among other things, preclinical findings made while clinical trials were underway, or safety or efficacy observations made in preclinical studies and clinical trials, including previously unreported adverse events. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in clinical trial procedures set forth in protocols, differences in the size and type of the patient populations, adherence to the dosing regimen and other clinical trial protocols, and the rate of dropout among clinical trial participants. If we fail to produce positive results in our planned preclinical studies or clinical trials of any of our product candidates, the development timeline and regulatory approval and commercialization prospects for our product candidates, and, correspondingly, our business and financial prospects, would be materially and adversely affected.

We may encounter substantial delays in the commencement or completion, or termination or suspension, of our clinical trials, which could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our commercial prospects.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidate for its intended indications. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. We may experience numerous unforeseen events during or as a result of clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- we may be unable to generate sufficient preclinical, toxicology, or other *in vivo* or *in vitro* data to obtain regulatory authorizations to commence a clinical trial;
- we may experience issues in reaching a consensus with regulatory authorities on trial design;
- regulators or institutional review boards, or IRBs, or ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable terms with prospective trial sites and prospective contract research organizations, or CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;

- clinical trial sites may deviate from a trial protocol or drop out of a trial or fail to conduct the trial in accordance with regulatory requirements;
- the number of subjects required for clinical trials of our product candidates may be larger than we anticipate or subjects may fail to enroll or remain in clinical trials at the rate we expect;
- subjects that enroll in our studies may misrepresent their eligibility or may otherwise not comply with the clinical trial protocol, resulting in the need to drop the subject from the trial, increase the needed enrollment size for the clinical trial or extend its duration;
- subjects may choose an alternative treatment for the indication for which we are developing our product candidates, or participate in competing clinical trials;
- subjects may experience severe or unexpected drug-related adverse effects;
- clinical trials of our product candidates may produce unfavorable, inconclusive, or clinically insignificant results;
- we may decide to, or regulators or IRBs or ethics committees may require us to, make changes to a clinical trial protocol or conduct additional preclinical studies or clinical trials, or we may decide to abandon product development programs;
- we may need to add new or additional clinical trial sites;
- our third-party contractors, including those manufacturing our product candidates or conducting clinical trials on our behalf, may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we may experience manufacturing delays, and any changes to manufacturing processes or third party contractors that may be necessary or desired could result in other delays;
- we or our third party contractors may experience delays due to complications associated with the continuing COVID-19 pandemic;
- the cost of preclinical testing and studies and clinical trials of any product candidates may be greater than we anticipate or greater than our available financial resources;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate or we may not be able to obtain sufficient quantities of combination therapies for use in clinical trials;
- reports may arise from preclinical or clinical testing of other cancer therapies that raise safety or efficacy concerns about our product candidates; and
- regulators may revise the requirements for approving our product candidates, or such requirements may not be as we anticipate.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond the clinical trials and testing that we contemplate, if we are unable to successfully complete clinical trials or other testing of our product candidates, if the results of these clinical trials or tests are unfavorable or are only modestly favorable or if there are safety concerns associated with any of product candidates, we may:

- incur additional unplanned costs;
- be required to suspend or terminate ongoing clinical trials;
- be delayed in obtaining marketing approval, if at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing or other requirements;
- be required to perform additional clinical trials to support approval;
- have regulatory authorities withdraw, or suspend, their approval of the drug or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation strategy, or REMS;
- be subject to the addition of labeling statements, such as warnings or contraindications;
- have the product removed from the market after obtaining marketing approval;
- be subject to lawsuits; or
- experience damage to our reputation.

Conducting clinical trials in foreign countries, as we may do for our product candidates, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocols as a result of

differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries.

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

In addition to the factors above, we may make formulation or manufacturing changes to our product candidates, in which case we may need to conduct additional preclinical studies to bridge our modified product candidates to earlier versions, which may be costly, time consuming and may not be successful at all.

Our failure to successfully initiate and complete clinical trials of our product candidates and to demonstrate the efficacy and safety necessary to obtain regulatory approval to market any of our product candidates would significantly harm our business. We cannot provide assurances that our clinical trials will begin as planned or be completed on schedule, if at all, or that we will not need to restructure our clinical trials. Significant preclinical study or clinical trial delays could also shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates, which may harm our business and results of operations. In addition, many of the factors that cause, or lead to, delays of clinical trials may ultimately lead to the denial of regulatory approval of our product candidates.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

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

- the severity of the disease under investigation;
- the patient eligibility and the inclusion and exclusion criteria defined in the protocol;
- the size and health of the patient population required for analysis of the trial's primary endpoints;
- the proximity of patients to trial sites;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- clinicians' and patients' perceptions as to the potential advantages of the drug candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating;
- our ability to obtain and maintain patient consents;
- our ability to monitor patients adequately during and after treatment;
- the risk that patients enrolled in clinical trials will drop out of the trials before completion; and
- factors we may not be able to control, including the impacts of the COVID-19 pandemic, that may limit the availability of patients, principal investigators or staff or clinical sites.

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 trials may instead opt to enroll in a trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials at such clinical trial site.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or might require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, slow down or halt our product candidate development and approval process and jeopardize our ability to seek and obtain the marketing approval required to commence product sales and generate revenue, which would cause the value of our company to decline and limit our ability to obtain additional financing, if needed.

Our product candidates may cause undesirable or unexpectedly severe side effects 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.

Undesirable or unexpectedly severe side effects caused by our product candidates could cause us to interrupt, delay or halt preclinical studies or could cause us 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. We have not yet initiated clinical trials for any of our

product candidates and it is likely that, as is the case with many treatments for cancer, there may be side effects associated with their use. Results of our trials could reveal a high and unacceptable severity and prevalence of these or other 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 trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Further, by design, clinical trials rely on a sample of the potential patient population. With a limited number of patients and limited duration of exposure, rare and severe side effects of our product candidates may only be uncovered when a significantly larger number of patients is exposed to the product candidate. If our product candidates receive marketing approval and we or others identify undesirable side effects caused by such product candidates after such approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may require the addition of labeling statements, such as a "black box" warning or a contraindication;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- regulatory authorities may require a REMS plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools;
- we may be required to change the way such product candidates are distributed or administered, conduct additional clinical trials or change the labeling of the product candidates;
- we may be subject to regulatory investigations and government enforcement actions;
- regulatory authorities may withdraw or limit their approval of such product candidates;
- we may decide to remove such product candidates from the marketplace;
- we could be sued and held liable for injury caused to individuals exposed to or taking our product candidates; and
- we may suffer reputational harm.

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

The COVID-19 pandemic, or a similar pandemic, epidemic, or outbreak of an infectious disease, may materially and adversely affect our business and our financial results and could cause a disruption to the development of our product candidates.

Public health crises such as the COVID-19 pandemic or similar outbreaks could adversely impact our business. In response to the COVID-19 pandemic, governments throughout the world have implemented a variety of quarantines, travel restrictions and other public health and safety measures that have impacted, and may continue to impact, our operations. The ultimate extent to which COVID-19 impacts our operations, including our preclinical testing, will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the duration of the outbreak and the actions taken to contain COVID-19 or treat its impact, among others. Any negative impact COVID-19 has on the execution of our product development plans could adversely affect our ability to timely submit INDs for product candidates, negatively affect our ability to obtain regulatory approval for and to commercialize our product candidates, increase our operating expenses, and have a material adverse effect on our financial results.

Effects of the COVID-19 pandemic that may delay or otherwise adversely affect our ongoing and planned preclinical activities, our planned clinical trials as well as our business generally, include:

- delays related to COVID-19 disruptions at CROs and contract manufacturers, or in the supply chain;
- delays in receiving approval from regulatory authorities to initiate our planned clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff who, as healthcare providers, may have heightened exposure to COVID-19;
- delays or difficulties in enrolling and retaining patients in clinical trials;
- delays in clinical sites receiving the supplies and materials needed to conduct our planned clinical trials;
- difficulties interpreting data from clinical trials due to the possible effects of COVID-19 on patients;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as clinical trial sites and hospital staff supporting the conduct of clinical trials;
- interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others;
- interruption or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines; and
- interruptions, difficulties or delays arising in our existing operations and company culture as a result of many of our employees working remotely, including those hired during the COVID-19 pandemic.

Any of these effects, and other effects of the COVID-19 pandemic, could have a material adverse effect on our business and our results of operation and financial condition. Further, uncertainty around these and related issues could lead to adverse effects on the economy of the United States and other economies, which could impact our ability to raise the necessary capital needed to develop and commercialize our programs and product candidates.

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

From time to time, we may publish interim top-line or preliminary data from our clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or "top-line" data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects.

We expect to develop WTX-124 and WTX-330, and potentially future product candidates, in combination with third-party drugs, some of which may still be in development, and we will have limited or no control over the safety, supply, regulatory status or regulatory approval of such drugs.

We intend to develop WTX-124 and WTX-330, and likely other future product candidates, in combination with third-party cancer drugs, which may be either approved or unapproved. For example, we plan to conduct clinical trials of WTX-124 and WTX-330 both as monotherapy and in combination with immune checkpoint inhibitors. Our ability to develop and ultimately commercialize our current product candidates, and any future product candidates, used in combination with third-party drugs will depend on our ability to access such drugs on commercially reasonable terms for clinical trials and their availability for use with our commercialized product, if approved. We cannot be certain that current or potential future commercial relationships will provide us with a steady supply of such drugs on commercially reasonable terms or at all. Any failure to maintain or enter into new successful commercial relationships, or the expense of purchasing such third-party drugs in the market, may delay our development timelines, increase our costs and jeopardize our ability to develop our current product candidates and any future product candidates as commercially viable therapies. If any of these occur, our business, financial condition, operating results, or prospects may be materially harmed.

Moreover, the development of product candidates for use in combination with another product or product candidate may present challenges that are not faced for single agent product candidates. For example, our planned clinical trials for WTX-124 and WTX-330 in combination with an immune checkpoint inhibitor may result in adverse events based on the combination therapy that may negatively impact the reported safety profile of the monotherapy in such clinical trials. Checkpoint inhibitors have been shown to have adverse events, including immune-related adverse events involving the lung, liver and other organ systems, which may limit the maximum dose in our clinical trials or otherwise negatively impact our combination clinical trials. In addition, the FDA or comparable foreign regulatory authorities may require us to use more complex clinical trial designs in order to evaluate the contribution of each product and product candidate to any observed effects. It is possible that the results of such trials could show that any positive previous trial results are attributable to the third-party drug and not our product candidate. Developments related to the third-party drug may also impact our clinical trials for the combination as well as our commercial prospects should we receive regulatory approval. Such developments may include changes to the third-party drug's safety or efficacy profile, changes to the availability of the third-party drug, quality, and manufacturing and supply issues with respect to the third-party drug.

If we are able to obtain marketing approval, the FDA or comparable foreign regulatory authorities may require that products used in conjunction with each other be cross labeled for combined use. To the extent that we do not have rights to the third-party drug, this may require us to work with such third party to satisfy such a requirement. We would also continue to be subject to the risks that the FDA or comparable foreign regulatory authorities could revoke approval of the third-party drug used in combination with our product candidate or that safety, efficacy, manufacturing or supply issues could arise with such drug. Similarly, if the third-party drugs we use in combination with our product candidates are replaced as the standard of care for the indications we choose for any of our product candidates, the FDA or comparable foreign regulatory authorities may require us to conduct additional clinical trials. The occurrence of any of these risks could result in our own products, if approved, being removed from the market or being less successful commercially.

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

Although we intend to explore other therapeutic opportunities in addition to the product candidates that we are currently developing, we may fail to identify or discover viable new product candidates for clinical development for a number of reasons. If we fail to identify additional potential product candidates, our business could be materially harmed.

Research programs to pursue the development of our existing and 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 will 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.

Accordingly, there can be no assurance that we will ever be able to identify additional therapeutic opportunities for our current product candidates or to develop suitable additional product candidates through internal research programs, which could materially adversely affect our future growth and prospects.

We may become exposed to costly and damaging liability claims, either when testing our product candidates in the clinic or following commercial sale, and any product liability insurance we may obtain may not cover all damages from such claims.

We are exposed to potential product liability risks that are inherent in the research, development, manufacturing, marketing and use of biopharmaceutical products. The use of product candidates by us in clinical trials, and any sale of approved products in the future, may expose us to liability claims. For example, we may be sued if our product candidates cause or are perceived to cause injury or are found to be otherwise unsuitable during clinical trials, 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.

Although the clinical trial process is designed to identify and assess potential side effects, it is always possible that a drug, even after regulatory approval, may exhibit unforeseen side effects. If any of our product candidates were to cause adverse side effects during clinical trials or after approval thereof, we may be exposed to substantial liabilities. Physicians and patients may not comply with any warnings that identify known potential adverse effects and patients who should not use our product candidates. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit or cease the development or commercialization of our product candidates or any products for which we may have received marketing approval. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- delay or termination of clinical trials;
- decreased demand for any product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants or difficulties in recruiting new trial participants;
- initiation of investigations by regulators;
- costs to defend or settle the related litigation;
- a diversion of management’s time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- significant negative financial impact; and
- the inability to commercialize any of our product candidates, if approved.

Although we will seek to procure and maintain product liability insurance coverage, such insurance may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage each time we commence a clinical trial and if we successfully commercialize any product candidate. As the expense of insurance coverage is increasing, we may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. If a successful product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be materially harmed.

We have never commercialized a product candidate and we may lack the necessary expertise, personnel and resources to successfully commercialize any products that receive regulatory approval, either on our own or together with collaborators.

We have never commercialized a product candidate. We currently have no sales force or marketing or distribution capabilities. To achieve commercial success of our product candidates, if any are approved, we will have to develop our own sales, marketing and supply capabilities or outsource these activities to one or more third parties.

Factors that may affect our ability to commercialize our product candidates on our own include our ability to recruit and retain adequate numbers of effective sales and marketing personnel and obtain access to or persuade adequate numbers of physicians to prescribe our product candidates, as well as any unforeseen costs we may incur in connection with creating an independent sales and marketing organization. Developing a sales and marketing organization requires significant investment, is time-consuming and could delay the launch of our product candidates. We may not be able to build an effective sales and marketing organization in the United States, the European Union or other key global markets. To the extent we need to rely upon one or more third parties, we may have little or no control over the marketing and sales efforts of those third parties and our revenue from product sales may be lower than if we had commercialized our product candidates ourselves. We will also face competition in any search for third parties to assist us with sales and marketing efforts for our product candidates. If we are unable to build our own distribution and marketing capabilities or to find suitable partners for the commercialization of our product candidates, we may have difficulties generating revenue from them.

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

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current product candidates and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical, specialty pharmaceutical and biotechnology companies among others. We compete in the segments of the pharmaceutical, biotechnology and other related markets that develop immunotherapies for the treatment of cancer. There are other companies working to develop immunotherapies for the treatment of cancer including divisions of pharmaceutical and biotechnology companies of various sizes. Some of these competitive therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. 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.

We are developing our initial product candidates for the treatment of cancer and have not commenced clinical trials of or received marketing approval for any of our product candidates. There are already a variety of available therapies marketed for cancer and some of the currently approved therapies are branded and subject to patent protection, and others are available on a generic basis. Many of these approved therapies are well-established and widely accepted by physicians, patients and third-party payors. Insurers and other third-party payors may also encourage the use of generic products. We expect that if our product candidates are approved, they will be priced at a significant premium over competitive generic products. This may make it difficult for us to achieve our business strategy of using our product candidates in combination with existing therapies or replacing existing therapies with our product candidates. Competition may further increase with advances in the commercial applicability of technologies and greater availability of capital for investment in these industries.

We are aware of a number of companies that are developing cytokines as immunotherapies, as well as different modalities, including monoclonal antibodies, cell therapies, oncolytic viruses and vaccines.

Our lead product candidate, WTX-124, if approved, may face competition from other Interleukin-2, or IL-2, based cancer therapies. Proleukin (aldesleukin), a synthetic protein very similar to IL-2, is approved and marketed for the treatment of metastatic renal cell carcinoma and melanoma. In addition, we are aware that a number of other companies have modified IL-2 programs in development for the treatment of cancer, including Alkermes Plc, BioNTech SE, Medicenna Therapeutics Corp., Nektar Therapeutics (Bristol-Myers Squibb Company), Neoleukin Therapeutics, Inc., F. Hoffmann-La Roche AG, or Roche, Synthorx, Inc. (Sanofi) and Xilio Therapeutics, Inc.

There are no approved IL-12 therapies currently on the market for the treatment of cancer. However, if approved, WTX-330 may face competition from other IL-12 cytokine programs in clinical and preclinical development for oncology indications, including programs from Sanofi S.A. (Amunix), DragonFly Therapeutics, Inc., Juno Therapeutics, Inc. (Bristol-Myers Squibb Company), Oncorus, Inc., Turnstone Biologics Corp. (partnered with Takeda Pharmaceutical Company Limited, or Takeda) and Oncosec Medical Incorporated.

If approved, WTX-613 may face competition from other Interferon alpha, or IFNα, cancer therapies. Intron-A, a recombinant IFNα-2b molecule marketed by Merck & Co., Inc., has been approved by the FDA for the treatment of several forms of cancer, including specific types of leukemia and lymphoma. We are aware of other IFNα programs targeting the treatment of cancer in development by Immunomedics (acquired by Gilead Sciences, Inc.) and Takeda. Roferon A, a recombinant IFNα-2a molecule developed and marketed by Roche for the treatment of specific types of leukemia, was discontinued globally in 2020.

Our competitors may succeed in developing, acquiring or licensing, on an exclusive basis, products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. We also compete with these organizations in establishing clinical trial sites and patient registration for clinical trials, as well as in recruiting and retaining qualified scientific and management personnel, which could negatively affect our level of expertise and our ability to execute our business plan.

Many of our competitors, either alone or with their collaborators, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical and clinical testing, obtaining regulatory approvals and reimbursement and marketing approved products than we do. Established pharmaceutical companies may invest heavily to accelerate discovery and development of novel product candidates or to in-license novel product candidates that could make our product candidates less competitive or obsolete. Smaller or early-stage companies may also prove to be significant competitors, including through collaborative arrangements with large and established companies. In addition, any new product that competes with an approved product must demonstrate compelling advantages in efficacy, convenience, tolerability and safety in order to overcome price competition and to be commercially successful. The availability of competing products could limit the demand and the price we are able to charge for product candidates we commercialize, if any. The inability to compete with existing or subsequently introduced drugs would harm our business, financial condition and results of operations.

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

The potential market opportunities for our product candidates are difficult to estimate and, if our product candidates are approved, will ultimately depend on, among other things, the indications for which our product candidates are approved for sale, any drugs with which our product candidates are co-administered, the success of competing therapies and therapeutic approaches, acceptance by the medical community, patient access, product pricing and reimbursement. Our estimates of the potential market opportunities for our product candidates are predicated on many assumptions, which may include industry knowledge and publications, third-party research reports and other surveys. Although we believe that our internal assumptions are reasonable, these assumptions involve the exercise of significant judgment on the part of our management, are inherently uncertain, and their reasonableness has not been assessed by an independent source. If any of the assumptions proves to be inaccurate, the actual markets for our product candidates could be smaller than our estimates of the potential market opportunities.

The successful commercialization of our product candidates will depend in part on the extent to which we obtain and maintain favorable coverage, adequate reimbursement levels and pricing policies with third party payors.

The availability and adequacy of coverage and reimbursement by third-party payors, including governmental healthcare programs such as Medicare and Medicaid, managed care organizations, and private health insurers, are essential for most patients to be able to afford prescription medications such as our product candidates, if approved. Our ability to achieve acceptable levels of coverage and reimbursement for products by third-party payors will have an effect on our ability to successfully commercialize our product candidates. We cannot be sure that coverage and reimbursement in the United States, the European Union or elsewhere will be available for our product candidates, if approved, or any product that we may develop, and any reimbursement that may become available may be decreased or eliminated in the future.

Third-party payors increasingly are challenging prices charged for pharmaceutical products and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs or biologics when an equivalent generic drug, biosimilar or a less expensive therapy is available. It is possible that a third-party payor may consider our product candidates as substitutable and only offer to reimburse patients for the less expensive product. Even if we show improved efficacy or improved convenience of administration with our product candidates, pricing of existing third-party therapeutics may limit the amount we will be able to charge for our product candidates. These payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in our product candidates, if approved. Even if our product candidates are approved and we obtain coverage for our product candidates by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Interim reimbursement levels for new medicines, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Net prices for medicines 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 medicines from countries where they may be sold at lower prices than in the United States. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates, if approved, and may not be able to obtain a satisfactory financial return on our product candidates.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. The regulations that govern marketing approvals, pricing and reimbursement for new medicines vary widely from country to country. In the United States, third-party payors play an important role in determining the extent to which new drugs and biologics will be covered. The Medicare and Medicaid programs increasingly are used as models in the United States for how third-party payors develop their coverage and reimbursement policies for drugs and biologics. Some third-party payors may require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers who use such therapies. We cannot predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates, if approved.

No uniform policy for coverage and reimbursement for products exists among third-party payors in the United States. Therefore, coverage and reimbursement for products can differ significantly from payor to payor and coverage and reimbursement by one payor does not guarantee coverage and reimbursement by another payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases on short notice, and we believe that changes in these rules and regulations are likely.

Even if a product candidate we develop receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, hospitals, cancer treatment centers, third-party payors and others in the medical community necessary for commercial success.

If any product candidate we develop receives marketing approval, whether as a single agent or in combination with other therapies, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, hospitals, cancer treatment centers, third-party payors, and others in the medical community. For example, cancer treatments like chemotherapy, radiation therapy and certain existing immunotherapies are well established in the medical community, and doctors may continue to rely on these therapies. If the product candidates we develop do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable.

The degree of market acceptance of any product, if approved for commercial sale, will depend on a number of factors, including:

- its efficacy, safety and potential advantages compared to alternative treatments;
- the prevalence and severity of any side effects;
- the product’s convenience and ease of administration compared to alternative treatments;
- the clinical indications for which the product is approved;
- the willingness of the target patient population to try a novel treatment and of physicians to prescribe such treatments;
- the recommendations with respect to the product in guidelines published by scientific organizations;
- the ability to obtain sufficient third-party insurance coverage and adequate reimbursement, including, if applicable, with respect to the use of the product as a combination therapy;
- the strength of marketing, sales and distribution support;
- the effectiveness of our sales and marketing efforts;

- the approval of other new products for the same indications; and
- our ability to offer the product for sale at competitive prices.

If we obtain marketing approval for a product but such product does not achieve an adequate level of market acceptance, we may not generate or derive significant revenue from that product and our business, financial condition and results of operations may be adversely affected.

We expect the product candidates we develop will be regulated as biological products, or biologics, and therefore they may be subject to competition sooner than anticipated.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or 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, a reference biological product is granted 12 years of non-patent exclusivity from the time of first licensure of the product, and the FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product. In addition, the 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 due to congressional action or otherwise, or that the FDA will not consider our investigational medicines to be reference products for competing products, potentially creating the opportunity for biosimilar competition sooner than anticipated. Moreover, the extent to which a biosimilar, once 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 regulatory approval for biosimilars referencing our product candidates, our product candidates may become subject to competition from such biosimilars, with the attendant competitive pressure and consequences.

Risks Related to Our Dependence on Third Parties

We rely, and expect to continue to rely, on third parties to conduct our preclinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines or comply with regulatory requirements, we may not be able to obtain regulatory approval of or commercialize any product candidates.

We depend, and expect to continue to depend, upon third parties, including independent investigators and CROs, to conduct preclinical studies and our planned clinical trials. We expect to have to negotiate budgets and contracts with CROs and trial sites, and any of these third parties may terminate their engagements with us at any time, any of which may result in delays to our development timelines and increased costs.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibility to ensure that each of our trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. We and these third parties are required to comply with current Good Clinical Practices, or cGCP, requirements for clinical trials, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for product candidates in clinical development. Regulatory authorities enforce these cGCP requirements through periodic inspections of trial sponsors, clinical investigators and trial sites. If we or any of these third parties fail to comply with applicable cGCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to suspend or terminate these trials or perform additional preclinical studies or clinical trials before approving our marketing applications. We cannot be certain that, upon inspection, such regulatory authorities will determine that any of our clinical trials comply with the cGCP requirements. In addition, our clinical trials must be conducted with biologic product produced under current Good Manufacturing Practice, or cGMP, requirements.

Our failure or any failure by these third parties to comply with the applicable regulations may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

Any third parties conducting our clinical trials will not be our employees and, except for remedies that may be available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our clinical trials. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other product development activities, which could affect their performance on our behalf. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced 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 other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to complete development of, obtain regulatory approval of or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed.

If any of our relationships with these third-party CROs or others terminate, we may not be able to enter into arrangements with alternative CROs or other third parties or to do so on commercially reasonable terms. Switching or adding additional CROs involves additional cost and

requires management time and focus. In addition, there is a natural transition period when a new CRO begins work. As a result, delays may occur, which could materially impact our ability to meet our desired clinical development timelines. Though we plan to carefully manage our relationships with CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

The manufacturing of biologics is complex and we do not have our own clinical manufacturing capabilities. We will rely on third parties to produce preclinical, clinical and commercial supplies of all current and any future product candidates.

To date, we have produced limited quantities of our product candidates at our own facilities for preclinical evaluation. However, going forward we will rely on third-party contract manufacturers to manufacture some of our preclinical supply and all of our clinical trial supply. We do not own manufacturing facilities capable producing drug products at clinical scale. We have in the past experienced delays in receiving preclinical product supplies from third-party manufacturers and there can be no assurance that our preclinical and clinical development product supplies from third parties will not in the future be limited or interrupted, or be of satisfactory quality or continue to be available at acceptable prices. Additionally, the process of manufacturing biologics is complex, highly regulated, and subject to multiple risks. Manufacturing biologics is highly susceptible to product loss due to contamination, equipment failure, improper installation or operation of equipment, vendor or operator error, inconsistency in yields, variability in product characteristics and difficulties in scaling the production process. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects, other supply disruptions and higher costs. If microbial, viral or other contaminations are discovered at the facilities of our contract manufacturing organizations, or CMOs, such facilities may need to be closed for an extended period of time to investigate and remedy the contamination, which could delay clinical trials, result in higher costs of drug product and adversely affect our business.

We have engaged CMOs to provide certain services to support our clinical and preclinical development. Pursuant to the terms of separate contract manufacturing services agreements, we have engaged one CMO to provide drug substance manufacturing process development and to manufacture WTX-124 and WTX-330 drug substance to cGMP specifications for use in the further manufacture of clinical supply, a second CMO to provide drug product manufacturing process development and to manufacture clinical supply of WTX-124 and WTX-330 vialled drug product to cGMP specifications and a third CMO to provide drug substance manufacturing for WTX-613. To support the manufacture of clinical vialled drug product, our CMO will conduct substantial analytical testing of WTX-124 and WTX-330 vialled drug product. If our CMOs are unable to supply us with sufficient clinical grade quantities of WTX-124 or WTX-330, and we are unable to timely establish an alternate supply from one or more third-party contract manufacturers, we will experience delays in our development efforts as we seek to locate and qualify new manufacturers. In particular, any replacement of our CMOs could require significant effort and expertise because there may be a limited number of qualified replacements or capacity could be limited at each of the qualified replacements. Additionally, contract manufacturers may rely on single source suppliers for certain of the raw materials for our preclinical and clinical product supplies. If current or future suppliers are delayed or unable to supply sufficient raw materials to manufacture product for our preclinical studies and clinical trials, we may experience delays in our development efforts as materials are obtained or we locate and qualify new raw material manufacturers. Further, for our planned combination clinical trials of WTX-124 or WTX-330 with immune checkpoint inhibitors, we will need to procure supply of the immune checkpoint inhibitors for use in the clinical trials. If we are unable to procure sufficient supply from third-party manufacturers or other sources, we may be required to purchase our supply of checkpoint inhibitors on the open market, which may result in significant additional expense.

The manufacturing process for a clinical candidate is subject to FDA and foreign regulatory authority review. Suppliers and manufacturers must meet applicable manufacturing requirements and undergo rigorous facility and process validation tests required by regulatory authorities in order to comply with their standards, such as cGMPs. In the event that any of our CMOs fail to comply with such requirements or to perform their obligations to us in relation to quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, we may be forced to manufacture the materials ourselves, for which we currently do not have the capabilities or resources, or enter into an agreement with another third-party, which we may not be able to do on reasonable terms, if at all. The transfer of the manufacturing of biologic products to a new CMO and any additional process development that may be necessary can be lengthy and involve significant additional costs. 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 and guidelines. The delays associated with the verification of a new CMO would negatively affect our ability to develop product candidates in a timely manner or within budget.

Further, our reliance on third-party manufacturers exposes us to risks beyond our control, including the:

- inability to meet our drug specifications and quality requirements consistently;
- inability to initiate or continue preclinical studies or clinical trials of product candidates under development;
- delay or inability to procure or expand sufficient manufacturing capacity;
- manufacturing and drug quality issues, including related to scale-up of manufacturing;
- failure to comply with cGMP and similar foreign standards;
- reliance on a limited number of sources, and in some cases, single sources for drug components and raw materials, such that if we are unable to secure a sufficient supply of these drug components and raw materials, we will be unable to manufacture and sell our future product candidate in a timely fashion, in sufficient quantities or under acceptable terms;
- lack of qualified backup suppliers for those components and raw materials that are purchased from a sole or single source supplier;
- inability to negotiate manufacturing agreements with third parties under commercially reasonable terms;

- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us;
- disruption of operations by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier or the issuance of an FDA Form 483 notice or warning letter, or as a result of the effects of the COVID-19 pandemic on third-party manufacturers;
- carrier disruptions or increased costs that are beyond our control;
- failure to deliver our drugs under specified storage conditions and in a timely manner; and
- the possible misappropriation of our proprietary information, including our trade secrets and know-how.

Some of these events could be the basis for FDA action, including injunction, recall, seizure or total or partial suspension of production, any of which could result in a failure to begin our clinical trials or having to stop ongoing clinical trials. In addition, our CMOs and suppliers are subject to FDA inspection from time to time. Failure by our CMOs and suppliers to pass such inspections and otherwise satisfactorily complete the FDA approval regimen with respect to our product candidate may result in regulatory actions such as the issuance of FDA Form 483 notices of observations, warning letters or injunctions or the loss of operating licenses. In addition, our CMOs and suppliers are subject to numerous environmental, health and safety laws and regulations, including those governing the handling, use, storage, treatment and disposal of waste products, and failure to comply with such laws and regulations could result in significant costs associated with civil or criminal fines and penalties for such third parties. Based on the severity of the regulatory action, our clinical or commercial supply of drug and packaging and other services could be interrupted or limited, which could harm our business.

In addition, our CMOs are or may be engaged with other companies to supply and manufacture materials or products for such companies, which also exposes our suppliers and CMOs to regulatory risks for the production of such materials and products. As a result, failure to meet the regulatory requirements for the production of those materials and products may also affect the regulatory clearance of a contract supplier's or CMO's facility, which could impact the contract supplier's or CMO's ability to manufacture drug product for us.

We may seek to enter into collaborations or other similar arrangements for our product candidates. If we are unable to enter into such collaborations, or if these collaborations are not successful, our business could be adversely affected.

A part of our strategy is to strategically evaluate and, as deemed appropriate, enter into collaborations in the future on an asset-by-asset basis to maximize the value of each of our programs. We may also enter into collaborations in connection with our platform technology in order to advance the development of programs beyond our initial focus in cytokines. Such collaborations may include the development and commercialization of any of our product candidates or the commercialization of any of our product candidates that are approved for marketing outside the United States. Our likely collaborators for any collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. We have limited capabilities for product development and do not yet have any capability for commercialization. Accordingly, we may enter into collaborations with other companies to provide us with important technologies and funding for our programs and platform technology. We will face significant competition in seeking appropriate collaborators. We may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for any product candidates because they may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view such product candidates as having the requisite potential to demonstrate safety and efficacy. We may also be restricted under future license agreements from entering into agreements on certain terms or at all with potential collaborators.

Collaborations involving our product candidates would pose significant risks to us, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- we could grant exclusive rights to our collaborators that would prevent us from collaborating with others;
- 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 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 clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- 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;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or drugs, which may cause collaborators to cease to devote resources to the 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 such products;
- a collaborator's sales and marketing activities or other operations may not be in compliance with applicable laws resulting in civil or criminal proceedings;

- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays in or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend our or their intellectual property rights or may use our or their proprietary information in such a way as to invite litigation that could jeopardize or invalidate such intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- collaborators may not provide us with timely and accurate information regarding development, regulatory or commercialization status or results, which could adversely impact our ability to manage our own development efforts, accurately forecast financial results or provide timely information to our stockholders regarding our out-licensed product candidates;
- 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; and
- collaborations may be terminated, including for the convenience of the collaborator, and, if terminated, we may find it more difficult to enter into future collaborations or be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

Any future collaborations that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. In addition, all of the risks relating to product development, regulatory approval and commercialization described in this Annual Report will apply to the activities of any of our collaborators.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent protection for any product candidates we develop or for our PREDATOR platform and other proprietary technologies we may develop, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize product candidates and technology similar or identical to our product candidates and technology, and our ability to successfully commercialize any product candidates we may develop, and our technology may be adversely affected.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our PREDATOR platform, our product candidates, their respective components, formulations, combination therapies, methods used to manufacture them and methods of treatment and development that are important to our business. If we do not adequately protect our intellectual property rights, competitors may be able to erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability. To protect our proprietary position, we file patent applications in the United States and abroad related to our PREDATOR platform and our product candidates that are important to our business; we also license and may in the future license or purchase additional patents and patent applications filed by others. If we are unable to secure or maintain patent protection with respect to our PREDATOR platform, our product candidates and any proprietary products and technology we develop, our business, financial condition, results of operations and prospects could be materially harmed.

If the scope of the patent protection we or our potential licensors obtain is not sufficiently broad, we may not be able to prevent others from developing and commercializing technology and products similar or identical to ours. The degree of patent protection we require to successfully compete in the marketplace may be unavailable or severely limited in some cases and may not adequately protect our rights or permit us to gain or keep any competitive advantage. We cannot provide any assurances that any of our patents have, or that any of our pending patent applications that mature into issued patents will include, claims with a scope sufficient to protect our current and future product candidates or otherwise provide any competitive advantage. In addition, to the extent that we license intellectual property in the future, we cannot provide assurances that those licenses will remain in force. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Furthermore, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized.

Our patents and pending patent applications, if issued, may not provide us with any meaningful protection or prevent competitors from designing around our patent claims to circumvent our patents by developing similar or alternative technologies or therapeutics in a non-infringing manner. For example, a third party may develop a competitive therapy that provides benefits similar to one or more of our product candidates but that uses a formulation and/or a device that falls outside the scope of our patent protection. If the patent protection provided by the patents and patent applications we hold or pursue with respect to our product candidates is not sufficiently broad to impede such competition, our ability to successfully commercialize our product candidates could be negatively affected, which would harm our business.

Patent positions of life sciences companies can be uncertain and involve complex factual and legal questions. No consistent policy governing the scope of claims allowable in the field of engineered therapeutic proteins has emerged in the United States. The scope of patent protection in jurisdictions outside of the United States is also uncertain. Changes in either the patent laws or their interpretation in any jurisdiction that we seek patent protection may diminish our ability to protect our inventions, maintain and enforce our intellectual property rights; and, more generally, may affect the value of our intellectual property, including the narrowing of the scope of our patents and any that we may license.

The patent prosecution process is complex, expensive, time-consuming and inconsistent across jurisdictions. We may not be able to file, prosecute, maintain, enforce, or license all necessary or desirable patent rights at a commercially reasonable cost or in a timely manner. In addition, we may not pursue or obtain patent protection in all relevant markets. It is possible that we will fail to identify important patentable aspects of our research and development efforts in time to obtain appropriate or any patent protection. While we enter into non-disclosure and confidentiality agreements with parties who have access to confidential or patentable aspects of our research and development efforts, including for example, our employees, external academic scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach the agreements and disclose our confidential or proprietary information before a patent application is filed, thereby endangering our ability to seek patent protection. In addition, publications of discoveries in the scientific and scholarly literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Consequently, we cannot be certain that we were the first to file for patent protection on the inventions claimed in our patents or pending patent applications.

The issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Pending patent applications cannot be enforced against third parties unless, and until, patents issue from such applications, and then only to the extent the issued claims cover the technology. There can be no assurance that our patent applications or any patent applications that we may license in the future will result in patents being issued. Further, the scope of the invention claimed in a patent application can be significantly reduced before the patent is issued, and this scope can be reinterpreted after issuance. Even if patent applications we currently own or that we may license in the future issue as patents, they may not issue in a form that will provide us with adequate protection to prevent competitors or other third parties from competing with us, or otherwise provide us with a competitive advantage. Any patents that eventually issue may be challenged, narrowed or invalidated by third parties. Consequently, we do not know whether our PREDATOR platform or any of our product candidates will be protectable or remain protected by valid and enforceable patent rights. Our competitors or other third parties may be able to evade our patent rights by developing new products that are similar to our product candidates, biosimilars of our product candidates, or alternative technologies or products in a non-infringing manner.

The issuance or grant of a patent is not irrefutable as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. There may be prior art of which we are not aware that may affect the validity or enforceability of a patent 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. We may in the future, become subject to a third-party pre-issuance submission of prior art or opposition, derivation, revocation, re-examination, post-grant and *inter partes* review, or interference proceeding and other similar proceedings challenging our patent rights or the patent rights of others in the U.S. Patent and Trademark Office, or USPTO, or other foreign patent office. An unfavorable determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or extinguish our ability to manufacture or commercialize products without infringing third-party patent rights.

In addition, 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 intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Moreover, some of our owned and in-licensed patents and patent applications may in the future be co-owned with third parties. If we are unable to obtain an exclusive license to any such third-party co-owners' interest in such patents or patent applications, such 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. In addition, we or our licensors may need the cooperation of any such co-owners of our owned and in-licensed patents in order to enforce such patents against third parties, and such cooperation may not be provided to us or our licensors. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects.

We rely on the Harpoon Agreement for patent rights with respect to our product candidates and may in the future acquire additional third-party intellectual property rights on which we may similarly rely. We face risks with respect to such reliance, including the risk that we could lose these rights that are important to our business if we fail to comply with our obligations under these licenses.

We rely on our Second Amended and Restated Assignment and License Agreement, or the Harpoon Agreement, with Harpoon, pursuant to which we have non-exclusive and exclusive rights to technology that is incorporated into our PREDATOR platform, development programs and product candidates. The Harpoon Agreement gives us non-exclusive, sublicensable, worldwide rights to develop, manufacture, and commercialize products containing certain of Harpoon's patented technology and exclusive, irrevocable rights to certain other Harpoon inventions that may be made during a limited collaboration period. The Harpoon Agreement imposes disclosure, royalty payment and other obligations on us.

Moreover, the growth of our business may depend in part on our ability to acquire, in-license or use additional third-party intellectual property rights. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. Licenses to additional third-party intellectual property, technology and materials that may be required for the development and commercialization of our product candidates or technology may not be available at all or on commercially reasonable terms. In that event, we may be required to expend significant time and resources to redesign our product candidates or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize our future product candidates or technologies, which could materially harm our business, financial condition, results of operations and growth prospects.

Under the Harpoon Agreement, Harpoon is responsible for prosecution and maintenance of the licensed patents and any future third party from whom we may license patent rights may similarly be responsible for prosecution and maintenance of such patents. We have limited control over the activities that are the responsibility of Harpoon, and would have limited control over the activities that are the responsibility of any future licensor, and it is possible that prosecution and maintenance of licensed patents by Harpoon or any future licensor may be less vigorous than had we conducted such activities ourselves. Furthermore, the Harpoon Agreement is subject to, and we expect our future license agreements may also be subject to, a reservation of rights by one or more third parties, including the licensor. 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 growth prospects.

Disputes may arise regarding intellectual property subject to the Harpoon Agreement or any future license agreements of ours, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- our or our licensor's ability to 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 any intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under the license agreement;
- 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 any partners of ours; and
- the priority of invention of patented technology.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates. We are generally also subject to all of the same risks described in this Annual Report with respect to protection of intellectual property that we license as we are for intellectual property that we own. If we or our licensors fail to adequately protect this intellectual property, our ability to commercialize products could suffer.

Harpoon and any potential future licensors might conclude that we have materially breached our license agreements and might therefore terminate the relevant license agreements, thereby removing our ability to develop and commercialize products and technology covered by such license agreements. If any of our current or future inbound license agreements are terminated, or if the underlying patents fail to provide the intended exclusivity, competitors would have the freedom to seek regulatory approval of, and to market, products that are covered by such license agreements and underlying patents, which might be identical to our products or product candidates. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations and growth prospects. Our business also would suffer if any current or future licensors fail to abide by the terms of the license or fail to enforce licensed patents against infringing third parties, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms. Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights.

Any licensor of ours may have relied on third-party consultants or collaborators or on funds from third parties, such as the United States government, such that such licensor is not the sole and exclusive owners of the patents we in-licensed. If other third parties have ownership rights or other rights to our in-licensed patents, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects.

In addition, while we cannot currently determine the amount of the royalty obligations we would be required to pay on sales of future products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in products that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize products, we may be unable to achieve or maintain profitability.

If our efforts to protect the proprietary nature of the intellectual property related to our technologies and product candidates are not adequate, we may not be able to compete effectively in our market.

Biotechnology and pharmaceutical companies generally, and we in particular, compete in a crowded competitive space characterized by rapidly evolving technologies and aggressive defense of intellectual property. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. Our or our licensor's failure to comply with all such provisions during the patent process could result in abandonment or lapse of a patent or patent application that we own or license, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market and compete with us earlier than would otherwise have been the case.

We rely upon a combination of patents, confidentiality agreements, trade secret protection and license agreements to protect the intellectual property related to our technologies and our product candidates. Any disclosure to or misappropriation by third parties of our confidential proprietary information could enable competitors to quickly duplicate or surpass our technological achievements and product candidates, thus eroding our competitive position in our market. 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 strengthen our patent position.

It is possible that defects of form in the preparation or filing of our patents or patent applications may exist, or may arise in the future, for example with respect to proper priority claims, inventorship, claim scope, or requests for patent term adjustments. If we or our partners, collaborators, licensees or licensors fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our partners, collaborators, licensees or licensors are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised. If there are material defects in the form, preparation, prosecution, or enforcement of our patents or patent applications, such patents may be invalid and/or unenforceable, and such applications may never result in valid, enforceable patents. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

We seek or plan to seek patent protection for our PREDATOR platform and product candidates by filing and prosecuting patent applications in the United States and other countries as appropriate. However, we cannot predict:

- if and when patents will issue;
- if patents will issue with claims that cover our product candidates;
- the degree and range of protection any issued patents will afford us against competitors including whether third parties will find ways to invalidate or otherwise circumvent our patents;
- whether any of our intellectual property will provide any competitive advantage;
- whether any of our patents that may be issued may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage;
- whether or not others will obtain patents claiming aspects similar to those covered by our patents and patent applications; or
- whether we will need to initiate or defend litigation or administrative proceedings which may be costly regardless of whether we win or lose.

Additionally, we cannot be certain that the claims in our pending patent applications covering our product candidates, PREDATOR platform and research programs will be considered patentable by the USPTO, or by patent offices in foreign countries, or that the claims in any of our issued patents will be considered valid by courts in the United States or foreign countries.

The strength of patents in the biotechnology and pharmaceutical 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 technology or uses thereof in the United States or in other foreign countries. Even if 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 intellectual property or prevent others from designing around our claims. If the breadth or strength of protection provided by the patents and patent applications we hold with respect to our product candidates or technology 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. Since patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we were the first to file any patent application related to our product candidates. Furthermore, for U.S. 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. We cannot be certain that we are the first to invent the inventions covered by pending patent applications and, if we are not, we may be subject to priority disputes. We may be required to disclaim part or all of the term of certain patents or all of the term of certain patent applications. Various post-grant review proceedings, such as *inter partes* review, post-grant review and derivation proceedings, are available and may be pursued by any interested third party in the USPTO to challenge the patentability of claims issued in patents to us or our licensors. No assurance can be given as to the outcome of any such post-grant review proceedings. 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, a competitor's technology or product would be found by a court to infringe our patents. 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 we have had issued that cover our products.

Recent or future 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. In March 2013, under the Leahy-Smith America Invents Act, or America Invents Act, 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 USPTO-administered post-grant review system that has affected patent litigation. The America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

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 polypeptides or nucleic acids that are similar to our product candidates or components of our product candidates but that are not covered by the claims of our patents;
- the active biological ingredients in our current product candidates will eventually become commercially available in biosimilar drug products, and no patent protection may be available with regard to formulation or method of use;
- we or our licensors, as the case may be, may fail to meet our obligations to the U.S. government in regards to any 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 or technology;
- our 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 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;
- 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, and 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 technology 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.

Our proprietary position in part depends upon patents that are manufacturing, formulation or method-of-use patents, which may not prevent a competitor or other third party from using the same product candidate for another use.

Composition of matter patents for biological and pharmaceutical products are generally considered to be the strongest form of intellectual property protection for those types of products, as such patents provide protection without regard to any method of making or method of use. Although we have two issued patents with certain composition of matter claims with respect to WTX-124 and IL-12 INDUKINE molecules, we also have pending patent applications with other composition of matter claims with respect to our product candidates. We cannot be certain, however, that the claims in our pending patent applications, including those claims covering the composition of matter of our product candidates, will be considered patentable by the USPTO or by patent offices in foreign countries, or that the claims in any of our patents that have issued or may issue will be considered valid and enforceable by courts in the United States or foreign countries. Furthermore, in some cases, we may not be able to obtain issued claims covering compositions of matter relating to our product candidates, and instead may need to rely on filing patent applications with claims covering a method of use and/or method of manufacture. Method of use patents protect a specified method of using a product, such as a method of use for treating a particular medical indication. This type of patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their products for our targeted indications, physicians may prescribe these products "off-label" for those uses that are covered by our method of use patents. Although off-label prescriptions may infringe or contribute to the infringement of method of use patents, the practice is common and such infringement is difficult to prevent by enforcing patent rights or otherwise. There can be no assurance that any such patent applications will issue as granted patents, and even if they do issue, such patent claims may be insufficient to prevent third parties, such as our competitors, from utilizing our technology. Any failure to obtain or maintain patent protection with respect to our product candidates could have a material adverse effect on our business, financial condition, results of operations, and prospects.

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

In addition to the protection afforded by patents, we seek to rely on trade secret protection, confidentiality agreements, and license and other agreements to protect proprietary know-how that is not patentable, processes for which patents are difficult to enforce and any other elements of our product discovery and development processes that involve proprietary know-how, information, or technology that is not covered by patents. We cannot be certain that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Furthermore, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, operating results and financial condition.

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. For example, significant elements of our product candidates and PREDATOR platform, including aspects of sample preparation, methods of manufacturing, cell culturing conditions, computational-biological algorithms and related processes are based on unpatented trade secrets that are not publicly disclosed. 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. However, we cannot provide assurance that these agreements and policies will not be breached by our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors and that our trade secrets and other proprietary and confidential information will not be disclosed to publicly or to competitors.

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 avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including interference, reexamination, and post-grant review 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 pharmaceutical 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
- redesigning our product candidates or processes so they do not infringe third party intellectual property rights, 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.

Third parties may assert that we are employing their proprietary technology without authorization. Generally, conducting preclinical and clinical trials and other development activities in the United States is not considered an act of infringement. If WTX-124, WTX-330, WTX-613 or another product candidate is approved by the FDA, a third party may then seek to enforce its patent by filing a patent infringement lawsuit against us. For example, we have received, and we may in the future receive, correspondence from third parties or their legal counsel disclosing that such third party owns patents that may encompass one or more of our product candidates. It is also possible that a third party may file a lawsuit against us alleging infringement of its patents. The outcome of any such proceeding is uncertain and would likely result in the expenditure of significant financial resources and the diversion of management's time and resources, which could harm our business. While we do not believe that any claims that could otherwise have a materially adverse effect on the commercialization of our product candidates are valid and enforceable, we may be incorrect in this belief, or we may not be able to prove it in litigation. In this regard, patents issued in the United States by law enjoy a presumption of validity that can be rebutted only with evidence that is "clear and convincing," a heightened standard of proof. There may be issued third-party patents of which we are currently unaware with claims to compositions, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Patent applications can take many years to issue. There may be currently pending patent applications which may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Moreover, we may fail to identify relevant patents or incorrectly conclude that a patent is invalid, not enforceable, exhausted, or not infringed by our activities. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of our product candidates, constructs or molecules used in or formed during the manufacturing process, or any final product itself, the holders of any such patents may be able to block our ability to commercialize the product candidate unless we obtained a license under the applicable patents, or until such patents expire or they are finally determined to be held invalid or unenforceable. Similarly, if any third-party patent were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, including combination therapy or patient selection methods, 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, could 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 on commercially reasonable terms or at all. Furthermore, even in the absence of litigation, we may need or may choose 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.

We may not be successful in obtaining or maintaining necessary rights to product components and processes for our development pipeline through acquisitions and in-licenses.

Presently we have certain intellectual property rights, under patents and patent applications that we own or will own and under the Harpoon Agreement, related to WTX-124, WTX-330, WTX-613 and other product candidates we may develop in the future. Our development of additional product candidates may require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in-license or use these proprietary rights. In addition, while we have patent rights directed to certain INDUKINE constructs we may not be able to obtain intellectual property to broad INDUKINE polypeptides or engineered INDUKINE constructs.

Our product candidates may also require specific formulations to work effectively and efficiently, and rights to such formulation technology may be held by others. Similarly, efficient production or delivery of our product candidates may also require specific compositions or methods, and the rights to these may be owned by third parties. 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. Moreover, the specific components, such as linkers and antibody fragments, that will be used with our product candidates may be covered by the intellectual property rights of others.

Additionally, we may collaborate with or sponsor research at academic institutions to accelerate our preclinical research or development under written agreements with these institutions. In certain cases, these institutions may provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration or sponsorship. 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.

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 licensors. To counter infringement or unauthorized use, we may be required to file lawsuits with 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. 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. 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.

Post-grant proceedings provoked by third parties or brought by the USPTO may be necessary to determine the validity or 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. Litigation or post-grant 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.

Some of our patent applications have been granted or may be granted or allowed in the future. We cannot be certain that an allowed patent application will become an issued patent. There may be events that can cause the allowance of a patent application to be withdrawn. For example, after a patent application has been allowed, but prior to being issued, material that could be relevant to patentability may be identified. In such circumstances, the applicant may pull the application from allowance in order for the USPTO to review the application in view of the new material. We cannot be certain that the USPTO will re-allow the application in view of the new material. Further, 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 similar provisions during the patent application process and following the issuance of a patent. We rely on our outside counsel and other professionals or our licensing partners to pay these fees due to the USPTO and non-U.S. government patent agencies and to help us comply with other procedural, documentary and other similar requirements and we are also dependent on our licensors to take the necessary action to comply with these requirements with respect to our licensed intellectual property. 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 such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

Issued patents covering our product candidates or technology 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 or our technology, the defendant could counterclaim that the patent covering our product candidate or technology, 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 (such as 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 or technology. 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 or technology. 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.

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

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain. In addition, the United States continues to adapt to wide-ranging patent reform legislation that became effective starting in 2012. Moreover, 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. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. For example, in the case *Assoc. for Molecular Pathology v. Myriad Genetics, Inc.*, the U.S. Supreme Court held that certain claims to DNA molecules are not patentable. While we do not believe that any of the patents owned or licensed by us will be found invalid based on this decision, we cannot predict how future decisions by the courts, Congress or the USPTO may impact the value of our patents. Similarly, changes in the patent laws of other jurisdictions could adversely affect our ability to obtain and effectively enforce our patent rights, which would have a material adverse effect on our business and financial condition.

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

We have obtained granted patents in the United States that we consider to be important for certain of our product candidates, however, we may have less robust intellectual property rights outside the United States, and, in particular, we may not be able to pursue generic coverage of our PREDATOR platform or of our INDUKINE molecules outside of 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 enforcement is not as strong as that in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Most of our patent portfolio is at the very early stage. We will need to decide whether and in which jurisdictions to pursue protection for the various inventions in our portfolio prior to applicable deadlines.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biopharmaceutical products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. 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.

In addition, many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. Many countries also limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business and financial condition may be adversely affected.

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

We generally enter into confidentiality and intellectual property assignment agreements with our employees, consultants, and contractors. These agreements generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, those agreements may not be honored and may not effectively assign intellectual property rights to us. Moreover, there may be some circumstances, where we are unable to negotiate for such ownership rights. Disputes regarding ownership or inventorship of intellectual property can also arise in other contexts, such as collaborations and sponsored research. If we are subject to a dispute challenging our rights in or to patents or other intellectual property, such a dispute could be expensive and time consuming. If we were unsuccessful, we could lose valuable rights in intellectual property that we regard as our own.

We may be subject to damages resulting from claims that we or our employees have wrongfully used or disclosed confidential information of our competitors or are in breach of non-competition or non-solicitation agreements with our competitors.

Many of our employees were previously employed at other pharmaceutical companies, including our competitors or potential competitors, in some cases until recently. We may be subject to claims that we or our employees have inadvertently or otherwise used or disclosed trade secrets or other confidential information of these former employers or competitors. In addition, we have been and may in the future be subject

to claims that we caused an employee to breach the terms of his or her non-competition or non-solicitation agreement. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and could be a distraction to management. If our defense to those claims fails, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Any litigation or the threat thereof may adversely affect our ability to hire employees. A loss of key personnel or their work product could hamper or prevent our ability to commercialize product candidates, which could have an adverse effect on our business, results of operations and financial condition.

If we do not obtain patent term extension and data exclusivity for any of our current or future product candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of any of our current or future product candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman 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 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 marks of interest and our business may be adversely affected.

Our trademarks or trade names may be challenged, infringed, circumvented, declared generic or determined to be infringing on other marks. We rely on both registration and common law protection for our trademarks. 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. During the trademark registration process, we may receive Office Actions from the USPTO objecting to the registration of our trademark. Although we would be given an opportunity to respond to those objections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and/or to seek the cancellation of registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. 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.

Numerous factors may limit any potential competitive advantage provided by our intellectual property rights.

The degree of future protection afforded by our intellectual property rights, whether owned or in-licensed, is uncertain because intellectual property rights have limitations, and may not adequately protect our business, provide a barrier to entry against our competitors or potential competitors, or permit us to maintain our competitive advantage. Moreover, if a third party has intellectual property rights that cover the practice of our technology, we may not be able to fully exercise or extract value from our intellectual property rights. The factors that may limit any potential competitive advantage provided by our intellectual property rights include:

- pending patent applications that we own or license may not lead to issued patents;
- patents, should they issue, that we own or license, may not provide us with any competitive advantages, or may be challenged and held invalid or unenforceable;
- others may be able to develop and/or practice technology that is similar to our technology or aspects of our technology but that is not covered by the claims of any of our owned or in-licensed patents, should any such patents issue;
- third parties may compete with us in jurisdictions where we do not pursue and obtain patent protection;
- we (or our licensors) might not have been the first to make the inventions covered by a pending patent application that we own or license;
- we (or our licensors) might not have been the first to file patent applications covering a particular invention;
- others may independently develop similar or alternative technologies without infringing our intellectual property rights;
- we may not be able to obtain and/or maintain necessary licenses on reasonable terms or at all;
- third parties may assert an ownership interest in our intellectual property and, if successful, such disputes may preclude us from exercising exclusive rights, or any rights at all, over that intellectual property;
- we may not be able to maintain the confidentiality of our trade secrets or other proprietary information;
- we may not develop or in-license additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

Should any of these events occur, they could significantly harm our business and results of operation.

Risks Related to Regulatory Approval and Marketing of Our Product Candidates and Other Legal Compliance Matters

Even if we complete the necessary preclinical studies and clinical trials, the regulatory approval process is expensive, time consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our product candidates. As a result, we cannot predict when or if, and in which territories, we will obtain marketing approval to commercialize a product candidate.

The research, testing, manufacturing, labeling, approval, selling, marketing, promotion and distribution of products are subject to extensive regulation by the FDA and comparable foreign regulatory authorities. We are not permitted to market our product candidates in the United States or in other countries until we receive approval of an NDA or BLA from the FDA or marketing approval from applicable regulatory authorities outside the United States. Our product candidates are in various stages of development and are subject to the risks of failure inherent in development. We have not submitted an application for or received marketing approval for any of our product candidates in the United States or in any other jurisdiction. We have no experience as a company in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party CROs to assist us in this process.

The process of obtaining marketing approvals, both in the United States and abroad, is lengthy, expensive and uncertain. It may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information, including manufacturing information, to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. The FDA or other regulatory authorities may determine that our product candidates are not safe and effective, only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining marketing approval or prevent or limit commercial use.

In addition, changes in marketing approval policies during the development period, changes in or the enactment or promulgation of additional statutes, regulations or guidance or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

Any delay in obtaining or failure to obtain required approvals could negatively affect our ability or that of any future collaborators to generate revenue from the particular product candidate, which likely would result in significant harm to our financial position and adversely impact our stock price.

Failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed abroad. Any approval we may be granted for our product candidates in the United States would not assure approval of our product candidates in foreign jurisdictions and any of our product candidates that may be approved for marketing in a foreign jurisdiction will be subject to risks associated with foreign operations.

In order to market and sell our products in the European Union and other foreign jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The marketing approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. We may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may file for marketing approvals but not receive necessary approvals to commercialize our products in any market.

In many countries outside the United States, a product candidate must also be approved for reimbursement before it can be sold in that country. In some cases, the price that we intend to charge for our products, if approved, is also subject to approval. Obtaining non-U.S. regulatory approvals and compliance with non-U.S. regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our product candidates in certain countries. In addition, if we fail to obtain the non-U.S. approvals required to market our product candidates outside the United States or if we fail to comply with applicable non-U.S. regulatory requirements, our target markets will be reduced and our ability to realize the full market potential of our product candidates will be harmed and our business, financial condition, results of operations and prospects may be adversely affected.

Additionally, we could face heightened risks with respect to seeking marketing approval in the United Kingdom as a result of the withdrawal of the United Kingdom from the EU, commonly referred to as Brexit. As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or the MHRA, became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law, whereas Northern Ireland will continue to be subject to European Union rules under the Northern Ireland Protocol. The MHRA will rely on the Human Medicines Regulations 2012 (SI 2012/1916) (as amended), or the HMR, as the basis for regulating medicines. The HMR has incorporated into the domestic law of the body of European Union law instruments governing medicinal products that pre-existed prior to the United Kingdom's withdrawal from the European Union. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may force us to restrict or delay efforts to seek regulatory approval in the United Kingdom for our product candidates, which could significantly and materially harm our business.

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

obligations incident to doing business in another country; and workforce uncertainty in countries where labor unrest is more common than in the United States.

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

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States. Generally, a product with orphan drug designation only becomes entitled to orphan drug exclusivity if it receives the first marketing approval for the indication for which it has such designation, in which case the FDA or the European Medicines Agency, or EMA, will be precluded from approving another marketing application for the same product for that indication for the applicable exclusivity period. The applicable exclusivity period is seven years in the United States and ten years in Europe. The European exclusivity period can be reduced to six years if a product no longer meets the criteria for orphan drug designation or if the product is sufficiently profitable so that market exclusivity is no longer justified.

We may seek orphan drug designations for our product candidates and may be unable to obtain such designations. Even if we do secure such designations and orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different products can be approved for the same condition. Further, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, to be more effective or to make a major contribution to patient care. Finally, orphan drug exclusivity may be lost if the FDA or the EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition.

The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. This may be particularly true in light of a decision from the Court of Appeals for the 11th Circuit in September 2021 finding that, for the purpose of determining the scope of exclusivity, the term “same disease or condition” means the designated “rare disease or condition” and could not be interpreted by the Agency to mean the “indication or use.” We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

Any product candidate for which we obtain marketing approval is subject to ongoing regulation and could be subject to restrictions or withdrawal from the market, and we may be subject to substantial penalties if we fail to comply with regulatory requirements, when and if any of our product candidates are approved.

Any product candidate for which we obtain marketing approval will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to quality control and manufacturing, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping. In addition, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the medicine, including the requirement to implement a risk evaluation and mitigation strategy. Accordingly, if we receive marketing approval for one or more of our product candidates, we will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control. If we fail to comply with these requirements, we could have the marketing approvals for our products withdrawn by regulatory authorities and our ability to market any products could be limited, which could adversely affect our ability to achieve or sustain profitability.

We must also comply with requirements concerning advertising and promotion for any of our product candidates for which we obtain marketing approval. Promotional communications with respect to prescription products are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product’s approved labeling. Thus, we will not be able to promote any products we develop for indications or uses for which they are not approved. The FDA and other agencies, including the Department of Justice, or the DOJ, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug or biologic. Violations of the Federal Food, Drug, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription products may lead to investigations and enforcement actions alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

Failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on distribution or use of a product;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;

- recall of products;
- damage to relationships with collaborators;
- unfavorable press coverage and damage to our reputation;
- 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;
- injunctions or the imposition of civil or criminal penalties; and
- litigation involving patients using our products.

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

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

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

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

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

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

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

In the EU, we may seek PRIME designation for our product candidates in the future. PRIME is a voluntary program aimed at enhancing the EMA's role to reinforce scientific and regulatory support in order to optimize development and enable accelerated assessment of new medicines that are of major public health interest with the potential to address unmet medical needs. The program focuses on medicines that target conditions for which there exists no satisfactory method of treatment in the EU or even if such a method exists, it may offer a major therapeutic advantage over existing treatments. PRIME is limited to medicines under development and not authorized in the EU and the applicant intends to apply for an initial marketing authorization application through the centralized procedure. To be accepted for PRIME, a product candidate must meet the eligibility criteria in respect of its major public health interest and therapeutic innovation based on information that is capable of substantiating the claims.

The benefits of a PRIME designation include the appointment of a CHMP rapporteur to provide continued support and help to build knowledge ahead of a marketing authorization application, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review, meaning reduction in the review time for an opinion on approvability to be issued earlier in the application process. PRIME enables an applicant to request parallel EMA scientific advice and health technology assessment advice to facilitate timely market access. Even if we receive PRIME designation for any of our product candidates, the designation may not result in a materially faster development process, review or approval compared to conventional EMA procedures. Further, obtaining PRIME designation does not assure or increase the likelihood of EMA's grant of a marketing authorization.

We and our contract manufacturers are subject to significant regulation. The manufacturing facilities on which we rely may not continue to meet regulatory requirements, which could materially harm our business.

All entities involved in the preparation of product candidates for clinical trials or commercial sale, including any contract manufacturers, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical trials must be manufactured in accordance with cGMP. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. 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 our product candidates that may not be detectable in final product testing.

We or our contract manufacturer must supply all necessary documentation in support of a BLA on a timely basis and must adhere to the FDA's current Good Laboratory Practice and cGMP regulations enforced through its facilities inspection program. Our facilities and quality systems and the facilities and quality systems of some or all of our third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of any product candidate. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our product candidates or the associated quality systems for compliance with the regulations applicable to the activities being conducted. If these facilities do not pass a pre-approval plant inspection, FDA approval of the products will not be granted.

The regulatory authorities also may, at any time following approval of a product for sale, audit our manufacturing facilities or those of our third-party contractors. If any such inspection or audit identifies failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may 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 commercial sales 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.

If we or any of our third-party manufacturers fail to maintain regulatory compliance, the FDA can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new product, or revocation of a pre-existing approval. Any such consequence would severely harm our business, financial condition and results of operations.

We are conducting, and intend in the future to conduct, clinical trials for certain of our product candidates at sites outside the United States. The FDA may not accept data from trials conducted in such locations and the conduct of trials outside the United States could subject us to additional delays and expense.

We are conducting, and intend in the future to conduct, one or more of our clinical trials with trial sites that are located outside the United States. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of these data is subject to certain conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted and performed by qualified investigators in accordance with good clinical practice. The FDA must be able to validate the data from the trial through an onsite inspection if necessary. The trial population must also have a similar profile to the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful, except to the extent the disease being studied does not typically occur in the United States. In addition, while these clinical trials are subject to the applicable local laws, the FDA acceptance of the data will be dependent upon its determination that the trials also complied with all applicable U.S. laws and regulations. There can be no assurance that the FDA will accept data from clinical trials conducted outside of the United States. If the FDA does not accept the data from any trial that we conduct outside the United States, it would likely result in the need for additional trials, which would be costly and time-consuming and delay or permanently halt our development of our product candidates.

In addition, the conduct of clinical trials outside the United States could have a significant adverse impact on us or the trial results. Risks inherent in conducting international clinical trials include:

- clinical practice patterns and standards of care that vary widely among countries;
- non-U.S. regulatory authority requirements that could restrict or limit our ability to conduct our clinical trials;
- administrative burdens of conducting clinical trials under multiple non-U.S. regulatory authority schema;
- foreign exchange rate fluctuations; and
- diminished protection of intellectual property in some countries.

Inadequate funding for the FDA, the SEC and other government agencies, including from government shut downs, or other disruptions to these agencies' operations, including from the COVID-19 pandemic, 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. Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA 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, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. As of May 26, 2021, the FDA noted it was continuing to ensure timely reviews of applications for medical products during the ongoing COVID-19 pandemic in line with its user fee performance goals and conducting mission critical domestic and foreign inspections to ensure compliance of manufacturing facilities with FDA quality standards. However, the FDA may not be able to continue its current pace and review timelines could be extended, including where a pre-approval inspection or an inspection of clinical sites is required and due to the ongoing COVID-19 pandemic and travel restrictions, the FDA is unable to complete such required inspections during the review period. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities.

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

Current and future legislation may increase the difficulty and cost for us to obtain reimbursement for any of our candidate products that do receive marketing approval.

In the United States and 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 product candidates 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. If reimbursement of our products is unavailable or limited in scope, our business could be materially harmed.

The ACA substantially changed the way healthcare is financed by both governmental and private insurers and continues to significantly impact the U.S. pharmaceutical industry. Since enactment of the ACA, there have been numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the TCJA in 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Further, in December 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the TCJA, the remaining provisions of the ACA are invalid as well. In June 2021, the U.S. Supreme Court dismissed this action after finding that the plaintiffs do not have standing to challenge the constitutionality of the ACA. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2031 under the CARES Act. These Medicare sequester reductions have been suspended through the end of March 2022. From April 2022 through June 2022 a 1% sequester cut will be in effect, with the full 2% cut resuming thereafter. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

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

Current and future legislative efforts may limit the costs for our products, if and when they are licensed for marketing, and that could materially impact our ability to generate revenues.

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

In addition, in October 2020, HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program, or SIP, to import certain prescription drugs from Canada into the United States. The final rule is currently the subject of ongoing litigation, but at least six states (Vermont, Colorado, Florida, Maine, New Mexico, and New Hampshire) have passed laws allowing for the importation of drugs from Canada with the intent of developing SIPs for review and approval by the FDA. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed by the Biden administration until January 1, 2023.

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

At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care 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 health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Finally, outside the United States, in some nations, including those of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control and access. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we or our collaborators may be required to conduct a clinical trial that compares the cost-effectiveness of our product to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

We may be subject to certain healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, fines, disgorgement, exclusion from participation in government healthcare programs, curtailment or restricting of our operations, and diminished profits and future earnings.

Healthcare providers, third-party payors and others will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our current and future arrangements with healthcare providers and third-party payors will 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 research as well as market, sell and distribute any products for which we obtain marketing approval. Potentially applicable U.S. federal and state healthcare laws and regulations include the following:

Anti-Kickback Statute. The federal Anti-Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal healthcare programs such as Medicare and Medicaid.

False Claims Laws. The federal false claims laws, including the civil False Claims Act, impose criminal and civil penalties, including those from civil whistleblower or qui tam actions against individuals or entities for knowingly presenting, or causing to be presented to the federal

government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government.

HIPAA. The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for, among other things, executing or attempting to execute a scheme to defraud any healthcare benefit program.

HIPAA and HITECH. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or the HITECH Act, also imposes obligations on certain types of individuals and entities, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information.

False Statements Statute. The federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services.

Transparency Requirements. The federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to report annually to HHS information related to payments and other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists, and chiropractors) and ownership and investment interests by physicians and their immediate family members. As of January 1, 2022, applicable manufacturers also will be required to report such information regarding its payments and other transfers of value to physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists and certified nurse midwives during the previous year.

Analogous State and Foreign Laws. Analogous state laws and regulations, such as state anti-kickback and false claims laws, and transparency laws, may apply to sales or marketing arrangements, and claims involving healthcare items or services reimbursed by non-governmental third party payors, including private insurers, and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, in addition to requiring manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures. Many state laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. Foreign laws also govern the privacy and security of health information in many circumstances.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is prohibited in the European Union. Payments made to physicians in certain European Union Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual European Union Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Efforts to ensure that our business arrangements with third parties, and our business generally, will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, and reputational harm, any of which could substantially disrupt our operations. If any of the physicians or other providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Compliance with state, national and international privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could subject us to a variety of harms, including significant fines and penalties, litigation and reputational damage, any of which may have a material adverse effect on our business, financial condition or results of operations.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate or are likely to operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the European Union, including personal health data, is subject to the EU General Data Protection Regulation, or the GDPR, which took effect across all member states of the European Economic Area, or EEA, in May 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including strict rules on the transfer of personal data to countries outside the European Union, including the United States.

Brexit has complicated data protection regulation in the United Kingdom because, as of January 1, 2021, the GDPR has been converted into United Kingdom law and the United Kingdom is now a "third country" under the GDPR, subject to a transition period. Unless the European Commission makes an 'adequacy finding' in respect of the United Kingdom before the expiration of the transition period, the United Kingdom will become an 'inadequate third country' under the GDPR and transfers of data from the EEA to the United Kingdom will require a 'transfer mechanism,' such as the standard contractual clauses. Furthermore, following the expiration of the specified period, there will be increasing scope for divergence in application, interpretation and enforcement of the data protection law as between the United Kingdom and EEA.

As a result, there is increased scrutiny on the extent to which clinical trial sites located in the EEA should apply the GDPR to transfers of personal data from such sites to countries that are considered to lack an adequate level of data protection, such as the United States. The GDPR also permits data protection authorities to require destruction of improperly gathered or used personal information and/or impose substantial fines for violations of the GDPR, which can be up to four percent of global revenues or 20 million Euros, whichever is greater, and it also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR provides that European Union member states may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric or health data.

Actions are either in place or under way in the United States to enact similar legislation. There are a broad variety of data protection laws that are applicable to our activities, and a wide range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns based on general consumer protection laws. The Federal Trade Commission and state Attorneys General all are aggressive in reviewing privacy and data security protections for consumers. New laws also are being considered at both the state and federal levels. For example, the California Consumer Privacy Act, or CCPA, which went into effect on January 1, 2020, is creating similar risks and obligations as those created by GDPR, though the Act does exempt certain information collected as part of a clinical trial subject to the Federal Policy for the Protection of Human Subjects (the Common Rule). Many other states are considering similar legislation. A broad range of legislative measures also have been introduced at the federal level. Accordingly, failure to comply with federal and state laws (both those currently in effect and future legislation) regarding privacy and security of personal information could expose us to fines and penalties under such laws. There also is the threat of consumer class actions related to these laws and the overall protection of personal data. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business.

Additionally, California voters approved a new privacy law, the California Privacy Rights Act, or CPRA, in the November 3, 2020 election. Effective starting on January 1, 2023, the CPRA 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.

In addition to the foregoing, any breach of privacy laws or data security laws, particularly resulting in a significant security incident or breach involving the misappropriation, loss or other unauthorized use or disclosure of sensitive or confidential patient or consumer information, could have a material adverse effect on our business, reputation and financial condition. As a data controller, we will be accountable for any third-party service providers we engage to process personal data on our behalf, including our CROs. There is no assurance that privacy and security-related safeguards we implement will protect us from all risks associated with the third-party processing, storage and transmission of such information.

New legislation proposed or enacted in Colorado, Illinois, Massachusetts, Nevada, New Jersey, New York, Rhode Island, Virginia, Washington and other states, and a proposed right to privacy amendment to the Vermont Constitution, imposes, or has the potential to impose, additional obligations on companies that collect, store, use, retain, disclose, transfer and otherwise process confidential, sensitive and personal information, and will continue to shape the data privacy environment nationally. State laws are changing rapidly and there is discussion in Congress of a new federal data protection and privacy law to which we would become subject if it is enacted. All of these evolving compliance and operational requirements impose significant costs that are likely to increase over time, may require us to modify our data processing practices and policies, divert resources from other initiatives and projects, and could restrict the way products and services involving data are offered, all of which could significantly harm our business, financial condition, results of operations and prospects. Further, certain state laws may be more stringent or broader in scope, or offer greater individual rights, with respect to confidential, sensitive and personal information than federal, international or other state laws, and such laws may differ from each other, which may complicate compliance efforts.

Given the breadth and depth of changes in data protection obligations, preparing for and complying with such requirements is rigorous and time intensive and requires significant resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities and increase our cost of doing business, and could lead to government enforcement actions, private litigation and significant fines and penalties against us and could have a material adverse effect on our business, financial condition or results of operations.

We are subject to U.S. and certain foreign export control, import, sanctions, anti-corruption, and anti-money laundering laws with respect to our operations and non-compliance with such laws can subject us to criminal and/or civil liability and harm our business.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Control, the U.S. Foreign Corrupt Practices Act of 1977, as amended, or the FCPA, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and other state and national anti-bribery and anti-money laundering laws in countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, third-party intermediaries, joint venture partners and collaborators from authorizing, promising, offering or providing, directly or indirectly, improper payments or benefits to recipients in the public or private sector. We may have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities and other organizations. In addition, we may engage third party intermediaries to promote our clinical research activities abroad and/or to obtain necessary permits, licenses, and other regulatory approvals.

We can be held liable for the corrupt or other illegal activities of these third-party intermediaries, our employees, representatives, contractors, partners and agents, even if we do not explicitly authorize or have actual knowledge of such activities.

Noncompliance with the laws and regulations described above could subject us to whistleblower complaints, investigations, sanctions, settlements, prosecution, other enforcement actions, disgorgement of profits, significant fines, damages, other civil and criminal penalties or injunctions, suspension and/or debarment from contracting with certain persons, the loss of export privileges, reputational harm, adverse media coverage and other collateral consequences. If any subpoenas, investigations or other enforcement actions are launched, or governmental or other sanctions are imposed, or if we do not prevail in any possible civil or criminal litigation, our business, results of operations and financial condition could be materially harmed. In addition, responding to any action will likely result in a materially significant diversion of management's attention and resources and significant defense and compliance costs and other professional fees. In certain cases, enforcement authorities may even cause us to appoint an independent compliance monitor which can result in added costs and administrative burdens.

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 harm 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. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

We maintain 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, however this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Current or future environmental laws and regulations may impair our research, development or production efforts. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

Our employees, independent contractors, CROs, consultants, commercial partners, vendors and principal investigators may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements.

We are exposed to the risk of fraud or other misconduct by our employees, independent contractors, CROs, consultants, commercial partners, vendors and, if we commence clinical trials, our principal investigators. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in the European Union and other jurisdictions, provide accurate information to the FDA, the European Commission and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately, or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements.

Such misconduct also could involve the improper use of information obtained in the course of clinical trials or interactions with the FDA or other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our reputation. Even with appropriate policies and procedures, it is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent such activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. 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 and prospects, including the imposition of significant fines or other sanctions.

Risks Related to Our Business Operations, Employee Matters and Managing Growth

Our future success depends on our ability to retain key employees, consultants and advisors and to attract, retain and motivate qualified personnel.

We are highly dependent on the management, research and development, clinical, financial and business development expertise of our executive officers, as well as the other members of our scientific and clinical teams. Although we have employment offer letters which outline the terms of employment with each of our executive officers, each of them may terminate their employment with us at any time. As such, these employment offer letters do not guarantee our retention of our executive officers for any period of time. We do not maintain "key person" insurance for any of our employees.

Recruiting and retaining qualified scientific and clinical personnel and, if we are successful in obtaining marketing approval for our product candidates, sales and marketing personnel, is 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 other 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 regulatory approval for and commercialize our product candidates. We are based in the Cambridge area of Boston, a region that is home to many other biopharmaceutical companies as well as many academic and research institutions, resulting in fierce

competition for qualified personnel. Furthermore, to the extent we hire personnel from competitors, we may be subject to allegations that they have been improperly solicited or that they have divulged proprietary or other confidential information, or that their former employers own their research output. 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 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. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited, and could harm our business, prospects, financial condition and results of operations.

We expect to grow our organization, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

As of December 31, 2021, we had 39 employees. We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of clinical development, regulatory affairs, finance and, if any of our product candidates receive marketing approval, sales, marketing and distribution. Our management may need to divert a disproportionate amount of its attention away from our day-to-day activities to devote time to managing these growth activities. To manage these growth activities, 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. Our inability to effectively manage the expansion of our operations may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If our management is unable to effectively manage our expected growth, our expenses may increase more than expected, our potential ability to generate revenue could be reduced and we may not be able to implement our business strategy.

We depend on our information technology systems, and any failure of these systems could harm our business. Security breaches, loss of data, inability to access systems, and other disruptions could compromise sensitive information related to our business or prevent us from accessing critical information and expose us to liability, which could adversely affect our business, results of operations and financial condition.

We collect and maintain information in digital and other forms that is necessary to conduct our business, and we are increasingly dependent on information technology systems and infrastructure to operate our business. In the ordinary course of our business, we collect, store and transmit large amounts of confidential information, including intellectual property, proprietary business information and personal information. It is critical that we do so in a secure manner to maintain the privacy, security, confidentiality, availability and integrity of such confidential information. Our internal information technology systems and infrastructure, and those of our contractors, consultants, vendors and other third parties on which we rely, are vulnerable to damage or unauthorized access or use resulting from computer viruses, malware, natural disasters, terrorism, war, telecommunication and electrical failures, cyber-attacks or cyber-intrusions over the Internet, denial or degradation of service attacks, ransomware, hacking, phishing and other social engineering attacks, attachments to emails, intentional or accidental actions or inactions by persons inside our organization or by persons with access to systems inside our organization.

The risk of a security breach or disruption or data loss, particularly through cyber-attacks or cyber intrusion, including by computer hackers, supply chain attacks foreign governments and cyber terrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. In addition, the prevalent use of mobile devices that access confidential information increases the risk of lost or stolen devices, security incidents and data security breaches, which could lead to the loss of confidential information or other intellectual property. As a result of the COVID-19 pandemic, we may face increased risks of a security breach or disruption due to our reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. The costs to us to mitigate network security problems, bugs, viruses, worms, malicious software programs and security vulnerabilities could be significant, and while we have implemented security measures to protect our data security and information technology systems, our efforts to address these problems may not be successful, and these problems could result in unexpected interruptions, delays, cessation of service, negative publicity and other harm to our business and our competitive position. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our product development programs.

Any security compromise affecting us, our partners or our industry, whether real or perceived, could harm our reputation, erode confidence in the effectiveness of our security measures and lead to regulatory scrutiny. If such an event were to occur and cause interruptions in our operations or result in the unauthorized acquisition of or access to personally identifiable information or individually identifiable health information (violating certain privacy laws, as applicable, such as HIPAA, CCPA, HITECH and GDPR), it could result in a material disruption of our discovery and development programs and our business operations, whether due to a loss of our trade secrets or other similar disruptions. Some of the federal, state and foreign government requirements include obligations of companies to notify individuals of security breaches involving particular personally identifiable information, which could result from breaches experienced by us or by our vendors, contractors, or organizations with which we have formed strategic relationships. Notifications and follow-up actions related to a security breach could impact our reputation, cause us to incur significant costs, including legal expenses and remediation costs. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the lost data. We would also be exposed to a risk of loss, governmental investigations or enforcement, or litigation and potential liability, any of which could materially adversely affect our business, results of operations and financial condition.

Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

We depend on our employees, consultants, contract manufacturers, and CROs, and other parties, for the continued operation of our business. Our or their operations could be significantly disrupted by earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, ice and snowstorms, extreme weather conditions, medical epidemics or pandemics, terrorist attacks, and other natural or manmade disasters or business interruptions, for which we are, and they may be, predominantly self-insured. Because we rely on third-party contract manufacturers to produce our product candidates, our ability to obtain clinical supplies of our product candidates could be disrupted if the operations of these suppliers were affected by a man-made or natural disaster or other business interruption. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.

A variety of risks associated with marketing our product candidates internationally, if approved, could materially adversely affect our business.

We plan to seek regulatory approval of our product candidates outside of the United States and, accordingly, we expect that we will be subject to additional risks related to operating in foreign countries if we obtain the necessary approvals, including:

- regulatory requirements in foreign countries that differ from those in the United States;
- unexpected changes in tariffs, trade barriers, price and exchange controls and other regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- complexities associated with managing multiple payor reimbursement regimes, government payors or patient self-pay systems;
- difficulties staffing and managing foreign operations;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- potential liability under the FCPA or comparable foreign regulations;
- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism.

Any of these factors could harm our future international expansion and operations and, consequently, our results of operations.

We may engage in strategic transactions that could impact our liquidity, increase our expenses and present significant distractions to our management.

From time to time, we may consider strategic transactions, such as acquisitions of companies, asset purchases and out-licensing or in-licensing of intellectual property, products or technologies. Additional potential transactions that we may consider in the future include a variety of business arrangements, including spin-offs, strategic partnerships, joint ventures, restructurings, divestitures, business combinations and investments. Any future transactions could increase our near and long-term expenditures, result in potentially dilutive issuances of our equity securities, including our common stock, or the incurrence of debt, contingent liabilities, amortization expenses or acquired in-process research and development expenses, any of which could affect our financial condition, liquidity and results of operations. Future acquisitions may also require us to obtain additional financing, which may not be available on favorable terms or at all. These transactions may never be successful and may require significant time and attention of management. In addition, the integration of any business that we may acquire in the future may disrupt our existing business and may be a complex, risky and costly endeavor for which we may never realize the full benefits of the acquisition. Accordingly, although there can be no assurance that we will undertake or successfully complete any additional transactions of the nature described above, any additional transactions that we do complete could have a material adverse effect on our business, results of operations, financial condition and prospects.

Risks Related to Ownership of Our Common Stock and Our Status as a Public Company

An active trading market for our common stock may not continue to develop or be sustained and our stockholders may not be able to resell their shares of our common stock.

Our common stock began trading on the Nasdaq Global Select Market on April 30, 2021. Prior to April 30, 2021, there was no public market for our common stock. We cannot predict the extent to which an active market for our common stock will continue to develop or be sustained, or how the development of such a market might affect the market price for our common stock. As a result, it may be difficult for our stockholders to sell their shares of our common stock at an attractive price or at all.

The price of our common stock could be subject to volatility related or unrelated to our operations.

Our stock price is likely be volatile. For example, from April 30, 2021, when our stock first began trading on Nasdaq until February 28, 2022, our stock price has ranged from $6.53 to $21.67. The stock market in general and the market for biotechnology and pharmaceutical 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, investors may not be able to sell their common stock at an attractive price or at all. The market price for our common stock may be influenced by many factors, including:

- adverse results from preclinical studies;
- the commencement, enrollment or results of any future clinical trials we may conduct, or changes in the development status of our product candidates;
- adverse results from, delays in initiating or completing, or termination of clinical trials;
- unanticipated serious safety concerns related to the use of our product candidates;
- clinical trial results from, or regulatory approval of, a competitor's product candidate;
- adverse regulatory decisions, including failure to receive regulatory approval of our product candidates;
- any delay in our regulatory filings for our product candidates and any adverse development or perceived adverse development with respect to the applicable regulatory authority's review of such filings, including without limitation the FDA's issuance of a "refusal to file" letter or a request for additional information;
- lower than expected market acceptance of our product candidates following approval for commercialization;
- adverse developments concerning our manufacturers;
- our inability to obtain adequate product supply for any approved product or inability to do so at acceptable prices;
- introduction of new products or services by our competitors;
- changes in financial estimates by us or by any securities analysts who might cover our stock;
- conditions or trends in our industry;
- our cash position;
- sales of our common stock by us or our stockholders in the future;
- adoption of new accounting standards;
- ineffectiveness of our internal controls;
- changes in the market valuations of similar companies;
- stock market price and volume fluctuations of comparable companies and, in particular, those that operate in the biotechnology and pharmaceutical industry;
- publication of research reports about us or our industry or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- announcements by us or our competitors of significant acquisitions, strategic partnerships or divestitures;
- announcements of investigations or regulatory scrutiny of our operations or lawsuits filed against us;
- investors' general perception of our company and our business;
- recruitment or departure of key personnel;
- overall performance of the equity markets;
- trading volume of our common stock;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies and product candidates;
- significant lawsuits, including patent or stockholder litigation;
- proposed changes to healthcare laws or pharmaceutical pricing in the United States or foreign jurisdictions, or speculation regarding such changes;
- developments with respect to the COVID-19 pandemic;
- general political and economic conditions; and
- other events or factors, many of which are beyond our control.

In addition, in the past, stockholders have initiated class action lawsuits against pharmaceutical and biotechnology companies following periods of volatility in the market prices of these companies' stock. This risk is especially relevant for us because biopharmaceutical companies have experienced significant stock price volatility in recent years. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management's attention and resources from our business.

If securities or industry analysts do not publish or cease publishing research or reports about our company, or if they issue unfavorable or inaccurate research regarding our business, our share price and trading volume could decline.

The trading market for our common stock relies, in part, on the research and reports that securities or industry analysts publish about us or our business. We do not have research control over these analysts. There can be no assurance that existing analysts will continue to cover us or that new analysts will begin to cover us. There is also no assurance that any covering analysts with provide favorable coverage. Although we have obtained coverage, if one or more of the analysts covering us downgrades our stock or publishes unfavorable or inaccurate research about our business, our stock price may decline. If one or more of these analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

Our principal stockholders and management own a significant percentage of our common stock and will be able to exert significant control over matters subject to stockholder approval.

As of March 18, 2022, our executive officers, directors, holders of 5% or more of our common stock and their respective affiliates beneficially owned in the aggregate approximately 51.4% of our outstanding common stock.

As a result of their share ownership, these stockholders, if they act together, have the ability to influence our management and policies and are able to significantly affect the outcome of matters requiring stockholder approval such as elections of directors, amendments of our organizational documents or approvals of any merger, sale of assets or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that our stockholders may feel are in their best interest.

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.

We have broad discretion regarding use of our cash and cash equivalents, and we may use them in ways that do not enhance our operating results or the market price of our common stock.

Our management has broad discretion in the application of our cash and cash equivalents. We could utilize our cash and cash equivalents in ways our stockholders may not agree with or that do not yield a favorable return, if any, and our management might not apply our cash and cash equivalents in ways that ultimately increase the value of our stockholders' investments. If we do not utilize our cash and cash equivalents in ways that enhance stockholder value, we may fail to achieve expected financial results, which could cause our stock price to decline.

We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.

We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. In addition, the terms of any future debt agreements may preclude us from paying dividends. Any return to stockholders will therefore be limited in the foreseeable future to the appreciation of their stock.

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

As a public company, we incur significant legal, accounting and other expenses that we did not previously incur as a private company. The Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, Nasdaq listing requirements, and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel have and will need to continue to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs, particularly as we hire additional financial and accounting employees to meet public company internal control and financial reporting requirements and will make some activities more time-consuming and costly compared to when we were a private company.

We are evaluating these rules and regulations and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. We intend to invest resources to comply with evolving laws, regulations and standards, and this investment may result in increased general and administrative expenses and a diversion of management's time and attention from revenue-generating activities to compliance activities. If notwithstanding our efforts to comply with new laws, regulations and standards, we fail to comply, regulatory authorities may initiate legal proceedings against us and our business may be harmed.

Pursuant to Section 404 of the Sarbanes-Oxley Act, or Section 404, we will be required to furnish a report by our management on our internal control over financial reporting beginning with our filing of an Annual Report on Form 10-K with the SEC for the year ending December 31, 2022. However, while we remain an emerging growth company or a smaller reporting company with less than $100.0 million in annual

revenue, 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 are engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, including through hiring additional financial and accounting personnel, 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 we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses in our internal control over financial reporting, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

In the past, we have identified material weaknesses in our internal control over financial reporting, and if we are unable to implement and maintain effective internal control over financial reporting in the future, investors may lose confidence in the accuracy and completeness of our financial reports, and the market price of our common stock may be materially adversely affected.

In the past, we identified material weaknesses in our internal control over financial reporting, all of which have since been remediated. We did not identify any material weakness as of December 31, 2021.

Furthermore, if in the future, we have a material weakness in our internal controls over financial reporting, we may not detect errors on a timely basis and our consolidated financial statements may be materially misstated. We or our independent registered public accounting firm may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall. In addition, as a public company we are required to file accurate and timely quarterly and annual reports with the Securities and Exchange Commission, or SEC, under the Securities Exchange Act of 1934, as amended, or the Exchange Act. Any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from the Nasdaq Global Select Market or other adverse consequences that would materially harm our business. In addition, we could become subject to investigations by the stock exchange on which our securities are listed, the SEC, and other regulatory authorities, and become subject to litigation from investors and stockholders, which could harm our reputation and our financial condition, or divert financial and management resources from our core business.

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. As discussed above, we have identified material weaknesses in the past which have since been remediated. However, our remediation of previous material weaknesses may not prevent any future deficiency in our internal control over financial reporting. 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 will be required to disclose changes made in our internal controls and procedures on a quarterly basis and our management will be required to assess the effectiveness of these controls annually. However, for as long as we are an emerging growth company under the Jumpstart Our Business Startups Act, or the JOBS Act, enacted in April 2012 or a smaller reporting company with less than $100.0 million in annual revenue, 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 emerging growth company for up to five years. An independent assessment of the effectiveness of our internal control over financial reporting could detect problems that our management’s assessment might not. Undetected material weaknesses in our internal control over financial reporting 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.

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

We are subject to certain reporting requirements of the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, 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 control over financial reporting, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements or insufficient disclosures due to error or fraud may occur and not be detected.

Provisions in our corporate charter documents and under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current directors and members of management.

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

- establish a classified board of directors such that only one of three classes of directors is elected each year;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from our board of directors;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least two-thirds of the votes that all our stockholders would be entitled to cast to amend or repeal specified provisions of our certificate of incorporation or bylaws.

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

Our restated certificate of incorporation designates the Court of Chancery of the State of Delaware and the federal district courts of the United States of America 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 and employees and increase the costs to our stockholders of bringing such claims.

Our restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Court of Chancery of the State of Delaware does not have jurisdiction, the federal district court for the District of Delaware) will be the sole and exclusive forum for the following types of actions or proceedings under Delaware statutory or common law:

- any derivative action or proceeding brought on our behalf;
- any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, employees or stockholders to our company or our stockholders;
- any action asserting a claim arising pursuant to any provision of the DGCL or as to which the DGCL confers jurisdiction on the Court of Chancery of the State of Delaware; or
- any action asserting a claim arising pursuant to any provision of our certificate of incorporation or bylaws (in each case, as they may be amended from time to time) or governed by the internal affairs doctrine.

These choice of forum provisions will not apply to suits brought to enforce a duty or liability created by the Exchange Act. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all such Securities Act actions, and investors cannot waive compliance with the federal securities laws and the rules and regulations thereunder. Accordingly, both state and federal courts have jurisdiction to entertain such claims. To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States of America shall, to the fullest extent permitted by law, be the sole and exclusive forum for the resolution of any claims arising under the Securities Act. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our restated certificate of incorporation. This may require significant additional costs associated with resolving such action in other jurisdictions and there can be no assurance that the provisions will be enforced by a court in those other jurisdictions.

These exclusive forum provisions may limit the ability of our stockholders to bring a claim in a judicial forum that such stockholders find favorable for disputes with us or our directors, officers or employees, and increase the costs to such stockholders of bringing such a claim, either of which may discourage such lawsuits against us and our directors, officers and employees. If a court were to find the either exclusive forum provision contained in our restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with resolving such action in other jurisdictions, all of which could materially adversely affect our business, financial condition and operating results.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Our principal facilities consist of office and laboratory space. We currently occupy 9,949 square feet of office and laboratory space in Cambridge, Massachusetts under a lease that expires in March 2024, and 7,500 square feet of office and laboratory space in Watertown, Massachusetts that expires in May 2022. In addition, in June 2021, we entered into an operating lease for an approximately eight-year term for 25,778 square feet of laboratory and office space in Watertown, Massachusetts, which will serve as our future headquarters. We believe that our existing and planned facilities will be adequate and suitable for our needs for the foreseeable future.

Item 3. Legal Proceedings

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

Item 4. Mine Safety Disclosures

Not applicable.

PART II

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

Market Information and Holders

Our common stock trades on the Nasdaq Global Select Market under the symbol "HOWL". As of March 18, 2022, we had approximately 33 holders of record of our common stock. This number does not include beneficial owners whose shares were held by nominees in street name.

Dividend Policy

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings, 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 and will depend on various factors, including applicable laws, our results of operations, financial condition, future prospects, then applicable contractual restrictions and any other factors deemed relevant by our board of directors. Investors should not purchase our common stock with the expectation of receiving cash dividends.

Recent Sales of Unregistered Securities

None.

Purchase of Equity Securities

We did not purchase any of our registered equity securities during the period covered by this Annual Report.

Use of Proceeds from Registered Securities

On May 4, 2021, we closed our initial public offering, or IPO, of common stock under a registration statement on Form S-1 (File No. 333-255132) that was declared effective on April 29, 2021. Information related to our intended use of the proceeds from our IPO is included in the "Use of Proceeds" section of the final prospectus dated April 29, 2021, filed with the SEC pursuant to Rule 424(b)(4) under the Securities Act. There has been no material change in the planned use of proceeds from our IPO as described in the final prospectus.

As of December 31, 2021, we have used approximately $32.5 million of the net proceeds from the IPO.

Item 6. [Reserved]

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

The following discussion and analysis is meant to provide material information relevant to an assessment of the financial condition and results of operations of our company, including an evaluation of the amounts and uncertainties of cash flows from operations and from outside resources, so as to allow investors to better view our company from management's perspective. The following discussion and analysis of our financial condition and results of operations should be read together with our consolidated financial statements and related notes appearing elsewhere in this Annual Report. In addition to historical information, this discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of certain factors. We discuss factors that we believe could cause or contribute to these differences below and elsewhere in this Annual Report, including those factors set forth in the section entitled "Cautionary Note Regarding Forward-Looking Statements and Industry Data" and in the section entitled "Risk Factors" in Part I, Item 1A of this Annual Report.

Overview

We are an innovative biopharmaceutical company pioneering the development of therapeutics engineered to stimulate the body's immune system for the treatment of cancer. We are leveraging our proprietary PREDATOR platform to design conditionally activated molecules that stimulate both adaptive and innate immunity with the goal of addressing the limitations of conventional proinflammatory immune therapies. Our molecules, which we refer to as INDUKINE molecules, are intended to activate selectively in the tumor microenvironment. Our most advanced product candidates, WTX-124 and WTX-330, are systemically delivered, conditionally activated Interleukin-2 and Interleukin-12, respectively, INDUKINE molecules for the treatment of multiple tumor types. We plan to submit an investigational new drug application, or IND, to the U.S. Food and Drug Administration for WTX-124 in the second quarter of 2022 and WTX-330 in the third quarter of 2022, and thereafter initiate first in-human clinical trials for each candidate.

We were incorporated and commenced operations in 2017. Since inception, we have devoted substantially all of our time and efforts to performing research and development activities, raising capital and recruiting management and technical staff to support these operations. To date, we have financed our operations primarily with proceeds from the sales of our convertible promissory notes and equity securities. From December 2017 to August 2018, we issued convertible promissory notes for aggregate gross cash proceeds of $11.0 million. From August 2019 to June 2020, we issued an aggregate of 80,246,565 shares of Series A preferred stock for aggregate gross cash proceeds of $44.2 million, together with conversion of all of our previously issued convertible promissory notes. In December 2020, we issued 78,222,173 shares of Series B preferred stock at a price of $0.92 per share, resulting in gross cash proceeds of $72.1 million. On May 4, 2021, we completed our IPO, pursuant to which we issued and sold 7,500,000 shares of our common stock at a public offering price of $16.00 per share. We received net proceeds of approximately $109.2 million, after deducting underwriting discounts and commissions and other offering expenses payable by us.

Due to our significant research and development expenditures, we have accumulated substantial net losses since our inception. As of December 31, 2021, we had an accumulated deficit of $252.9 million. We expect to continue to incur substantial and increasing expenses and net losses for the foreseeable future, as we continue to advance our current and future product candidates through preclinical and clinical development, manufacture drug product and drug supply, seek regulatory approval for our current and future product candidates, maintain and expand our intellectual property portfolio, hire additional research and development and business personnel and operate as a public company.

As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of public or private equity offerings and debt financings or other sources, such as potential collaboration agreements, strategic alliances and licensing arrangements. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on acceptable terms, or at all. Our failure to raise capital or enter into such agreements as and when needed could have a material adverse effect on our business, results of operations and financial condition.

Because of the numerous risks and uncertainties associated with product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to raise capital, maintain our research and development efforts, expand our business or continue our operations at planned levels, and as a result we may be forced to substantially reduce or terminate our operations.

Impact of COVID-19 on Our Business

The worldwide COVID-19 pandemic continues to evolve, and we will continue to monitor the COVID-19 pandemic closely. To date, we have not experienced a material financial statement impact or material business disruptions, including with our vendors, or impairments of any of our assets as a result of the pandemic. However, we cannot, at this time, predict the specific extent, duration or full impact that the COVID-19 pandemic will have on our financial statements and operations, including our ongoing and planned preclinical activities and future clinical trials. The extent of the impact of the COVID-19 pandemic on our business, operations and clinical development timelines and plans remains uncertain and will depend on certain developments, including the duration and spread of the pandemic and its impact on our contract research organizations, or CROs, third-party manufacturers, and other third parties with which we do business, as well as its impact on regulatory authorities and our key scientific and management personnel. To the extent possible, we are conducting business as usual, with necessary or advisable modifications to employee travel. We will continue to actively monitor the rapidly evolving situation related to COVID-19 and may take further actions that alter our operations, including those that may be required by federal, state or local authorities, or that we determine are in the best interests of our employees and other third parties with which we do business.

Furthermore, the COVID-19 pandemic could affect our employees or the employees of research sites and service providers on which we rely, including CROs, as well as those of companies with which we do business, including our suppliers and contract manufacturing organizations,

thereby disrupting our business operations. Quarantines and travel restrictions imposed by governments in the jurisdictions in which we and the companies with which we do business operate could materially impact the ability of employees to access preclinical and clinical sites, laboratories, manufacturing site and office. These and other events resulting from the COVID-19 pandemic could disrupt, delay, or otherwise adversely impact our business. Further information relating to the risks and uncertainties related to the ongoing COVID-19 pandemic is contained in the section titled "Risk Factors" in Part I, Item 1A of this Annual Report.

Financial Operations Overview

Revenue

To date, we have not generated any revenue from any sources, including from product sales, and we do not expect to generate any revenue from the sale of products in the foreseeable future.

Operating Expenses

Research and Development Expenses

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

- salaries, benefits and other related costs, including stock-based compensation expense, for personnel engaged in research and development functions;
- expenses incurred under agreements with third parties that conduct research and preclinical activities on our behalf;
- costs of outside consultants, including their fees, stock-based compensation and related travel expenses;
- costs of laboratory supplies and acquiring, developing and manufacturing preclinical study and future clinical trial materials; and
- facility-related expenses, which include direct depreciation costs and allocated expenses for rent and maintenance of facilities and other operating costs.

We expense research and development costs as incurred. Costs for external development activities are recognized based on an evaluation of the progress to completion of specific tasks using information provided to us by our vendors. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of performance of the individual arrangements, which may differ from the pattern of billings incurred, and are reflected in our consolidated financial statements as prepaid or accrued research and development expenses.

We typically use our employee and infrastructure resources across our development programs. We track external development costs by product candidate or development program, but we do not allocate personnel costs, license payments made under our licensing arrangements or other internal costs to specific development programs or product candidates.

Our external development costs for the year ended December 31, 2021 and 2020 were as follows:

	Year Ended December 31,	
	2021	2020
WTX-124	$ 8,928	$ 4,420
WTX-330	8,168	3,904
WTX-613	3,401	1,122
Pre-development candidates	1,102	303
Total external development costs	$ 21,599	$ 9,749

Research and development activities are central to our business model. We expect that our research and development expenses will continue to increase substantially for the foreseeable future as we initiate clinical trials of WTX-124 and WTX-330, continue preclinical studies of WTX-613 and continue to discover and develop additional product candidates.

The process of conducting the necessary clinical research to obtain regulatory approval is costly and time-consuming. We cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete development of our current or future product candidates. The actual probability of success for our product candidates will depend on a variety of factors, including:

- the scope, rate of progress and expenses of our ongoing research activities as well as any preclinical studies and clinical trials and other research and development activities;
- establishing an appropriate safety profile;
- successful enrollment in and completion of clinical trials;
- whether our product candidates show safety and efficacy in our clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;

- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- commercializing product candidates, if and when approved, whether alone or in collaboration with others; and
- continued acceptable safety profile of the products following any regulatory approval.

A change in the outcome of any of these variables with respect to the development of our current and future product candidates would significantly change the costs and timing associated with the development of those product candidates and we may never succeed in achieving regulatory approval for any of our product candidates. As a result of the uncertainties discussed above, we are unable to determine the duration and completion costs of our research and development activities.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries, benefits 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; travel expenses; and facility-related expenses, which include direct depreciation costs and allocated expenses for rent and maintenance of facilities and other operating costs.

We expect that our general and administrative expenses will increase in the future as we increase our personnel headcount to support our continued research and development activities, manufacturing activities and expansion of our operations in connection with our anticipated commencement of clinical trials. We also anticipate increased expenses associated with operating as a public company, including costs for audit, legal, regulatory and tax-related services related to compliance with the rules and regulations of the SEC and listing standards applicable to companies listed on a national securities exchange, director and officer insurance premiums and investor relations costs.

Other Income

Change in fair value of preferred stock tranche liability

Change in fair value of our preferred stock tranche liability consists primarily of remeasurement gains or losses attributable to changes in the fair value of the tranche rights associated with our Series A preferred stock. The tranche liability was settled in June 2020 upon the closing of the second tranche of our Series A preferred stock financing. All obligations have been met by December 31, 2020 and therefore there will be no further remeasurement.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States. The preparation of these consolidated 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 and accompanying notes. On an ongoing basis, we evaluate our estimates which include, but are not limited to, accrued expenses, stock-based compensation expense and income taxes. We base our estimates on historical experience, known trends and events and various other factors that we believe to be reasonable under the circumstances. Actual results could differ from those estimates under different assumptions and conditions.

While our significant accounting policies are described in more detail in Note 2, *"Basis of Presentation and Summary of Significant Accounting Policies"* to our consolidated financial statements included within Part IV, Item 15 in this Annual Report, we believe the following accounting policies to be most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Leases

At the inception of a contract, we assess whether the contract is, or contains, a lease. The assessment is based on: (1) whether the contract involves the use of a distinct identified asset, (2) whether we obtain the right to substantially all the economic benefit from the use of the asset throughout the period, and (3) whether we have the right to direct the use of the asset. Leases with a term greater than one year are recognized on the balance sheet as right-of-use assets and short-term and long-term lease liabilities, as applicable. We do not recognize leases with terms of one year or less on the balance sheet.

Operating lease liabilities and their corresponding right-of-use assets are recorded based on the present value of lease payments over the expected remaining lease term. Certain adjustments to the right-of-use asset may be required for items such as incentives received. The interest rate implicit in lease contracts is typically not readily determinable. As a result, we utilize our incremental borrowing rate ("IBR"), which reflects the fixed rate at which we could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, and in a similar economic environment.

The Company subsequently measures its lease liability at the present value of remaining lease payments, discounted using the IBR for the lease. The right-of-use asset is subsequently measured at the amount of the lease liability, adjusted for prepaid or accrued lease payments and the remaining balance of lease incentives received. The Company recognizes operating lease expense on a straight-line basis over the lease term.

Accrued Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses as of each balance sheet date. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. This process involves reviewing open contracts and purchase orders, communicating with

internal personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. We periodically confirm the accuracy of our estimates with our service providers and make adjustments if necessary. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. The financial terms of agreements with these service providers are subject to negotiation, vary from contract to contract and may result in uneven payment flows. In circumstances where amounts have been paid in excess of costs incurred, we record a prepaid expense.

Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts actually incurred.

Stock-based Compensation

We account for stock-based payments in accordance with Accounting Standards Update ("ASU") No. 2018-07, *Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting* ("ASC 718"). This guidance requires all stock-based payments to employees, including grants of employee stock options, restricted stock awards and restricted stock units, to be recognized as expense in the consolidated statements of operations and comprehensive income (loss) based on their grant date fair values. For stock options granted to employees and to members of our board of directors for their services on the board of directors, we estimate the grant date fair value of each stock option using the Black-Scholes option-pricing model. For restricted stock awards and restricted stock units granted to employees, we estimate the grant date fair value of each award using intrinsic value, which is based on the value of the underlying common stock less any purchase price. For stock-based payments subject to service-based vesting conditions, we recognize stock-based compensation expense equal to the grant date fair value of stock-based payment on a straight-line basis over the requisite service period.

The Black-Scholes option pricing model requires the input of certain subjective assumptions, including (i) the calculation of expected term of the stock-based payment, (ii) the risk-free interest rate, (iii) the expected stock price volatility and (iv) the expected dividend yield. We use the simplified method as prescribed by SEC Staff Accounting Bulletin No. 107 to calculate the expected term for stock options granted to employees as we do not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. We determine the risk-free interest rate based on a treasury instrument whose term is consistent with the expected term of the stock options. Because there had been no public market for our common stock prior to our IPO, there is a lack of historical and implied volatility data. Accordingly, we base our estimates of expected volatility on the historical volatility of a group of publicly-traded companies with similar characteristics to us, including stage of product development and therapeutic focus within the life sciences industry. Historical volatility is calculated over a period of time commensurate with the expected term of the stock-based payment. We use an assumed dividend yield of zero as we have never paid dividends on our common stock, nor do we expect to pay dividends on our common stock in the foreseeable future.

We account for forfeitures of all stock-based payments when such forfeitures occur.

Recent Accounting Pronouncements

See Note 2, *"Basis of Presentation and Summary of Significant Accounting Policies,"* to our consolidated financial statements included within Part IV, Item 15 of this Annual Report for a description of recent accounting pronouncements applicable to our business.

JOBS Act Accounting Election and Smaller Reporting Company Implications

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012, as amended, or JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended, or Sarbanes-Oxley Act. Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period, and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

Even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company," which would allow us to continue to take advantage of reduced disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act if we are a smaller reporting company with less than $100.0 million in annual revenue.

Results of Operations

Comparison of the Years Ended December 31, 2021 and 2020

The following table summarizes our results of operations for the years ended December 31, 2021 and 2020:

	Year Ended December 31,		
(in thousands)	**2021**	**2020**	**$ Change**
Operating expenses:			
Research and development	$ 35,269	$ 16,641	$ 18,628
General and administrative	14,818	5,763	9,055
Total operating expenses	50,087	22,404	27,683
Operating loss	(50,087)	(22,404)	(27,683)
Other income:			
Change in fair value of preferred stock tranche liability	—	7,301	(7,301)
Interest income, net	104	63	41
Total other income	104	7,364	(7,260)
Net loss	$ (49,983)	$ (15,040)	$ (34,943)

Research and Development Expenses

The following table summarizes our research and development expenses for the years ended December 31, 2021 and 2020:

	Year Ended December 31,		
(in thousands)	**2021**	**2020**	**$ Change**
Manufacturing	13,797	6,528	7,269
Personnel	$ 8,939	$ 3,913	$ 5,026
Contract research organization	7,802	3,221	4,581
Lab consumables	3,250	2,416	834
Facilities	1,294	543	751
Other	187	20	167
Total research and development expenses	$ 35,269	$ 16,641	$ 18,628

Research and development expenses for the year ended December 31, 2021 were $35.3 million, compared to $16.6 million for the year ended December 31, 2020. The increase of approximately $18.6 million was primarily due to:

- $7.3 million of increased manufacturing expense related to costs incurred with contract manufacturing organizations to support the production of preclinical and future clinical trial materials associated with our product candidates WTX-124, WTX-330 and WTX-613;
- $5.0 million of increased personnel costs, including $1.3 million of increased stock-based compensation expense, primarily due to increased headcount associated with expanded discovery efforts as well as the hiring of a clinical development team;
- $4.6 million of increased contract research organization expense, primarily driven by preclinical studies to support upcoming IND submissions for WTX-124 and WTX-330;
- $0.8 million of increased lab consumables costs, primarily driven by expanded discovery efforts; and
- $0.8 million of increased facilities costs, primarily driven by our short-term lease and lease for our new corporate headquarters, signed in March 2021 and June 2021, respectively.

General and Administrative Expenses

The following table summarizes our general and administrative expenses for the years ended December 31, 2021 and 2020:

	Year Ended December 31,		
(in thousands)	**2021**	**2020**	**$ Change**
Personnel	$ 6,192	$ 2,216	$ 3,976
Professional services	4,280	2,357	1,923
Facilities	1,443	941	502
Other	2,903	249	2,654
Total general and administrative expenses	$ 14,818	$ 5,763	$ 9,055

General and administrative expenses were $14.8 million for the year ended December 31, 2021, compared to $5.8 million for the year ended December 31, 2020. The increase of approximately $9.1 million was primarily due to:

- $4.0 million of increased personnel costs incurred due to the requirements of operating as a public company, which included $2.1 million of increased stock-based compensation expense;
- $1.9 million of increased professional costs to support our operations as a public company; and
- $2.7 million of increased other costs, primarily driven by $1.9 million of increased insurance costs associated with public company management liability insurance.

Other Income

Changes in the fair value of the preferred stock tranche liability resulted in a gain of $7.3 million for the year ended December 31, 2020. The tranche liability was settled in June 2020 upon the closing of the second tranche of our Series A preferred stock financing.

Liquidity and Capital Resources

Sources of Liquidity

We have funded our operations through December 31, 2021 primarily through the issuance of convertible promissory notes for aggregate cash proceeds of $11.0 million, the issuance and sale of shares of our Series A and Series B preferred stock for aggregate cash proceeds of $116.3 million and the issuance and sale of shares of our common stock in our IPO in May 2021 for net proceeds of approximately $109.2 million, after deducting underwriting discounts and commissions and other offering expenses payable by us.

Plan of Operation and Future Funding Requirements

We use our capital resources primarily to fund operating expenses, primarily research and development expenditures. We plan to increase our research and development expenses for the foreseeable future as we continue the preclinical development and move into clinical development of our product candidates. At this time, due to the inherently unpredictable nature of preclinical and clinical development and given the early stage of our product candidates, we cannot reasonably estimate the costs we will incur and the timelines that will be required to complete development, obtain marketing approval and commercialize our current product candidates or any future product candidates, if at all. For the same reasons, we are also unable to predict when, if ever, we will generate revenue from product sales or whether, or when, if ever, we may achieve profitability. Clinical and preclinical development timelines, the probability of success, and development costs can differ materially from expectations. In addition, we cannot forecast which product candidates may be subject to future collaborations, when such arrangements will be secured, if at all, and to what degree such arrangements would affect our development plans and capital requirements. Further, inflation generally affects us by increasing our cost of labor and certain services. We do not believe that inflation had a material effect on our financial statements included elsewhere in this Annual Report; however, our operations may be adversely affected by inflation in the future.

Due to our significant research and development expenditures, we have accumulated substantial net losses in each period since inception. We have incurred an accumulated deficit of $252.9 million through December 31, 2021. We expect to continue to incur substantial and increasing expenses and net losses for the foreseeable future, as we continue to advance our current and future product candidates through preclinical and clinical development, manufacture drug product and drug supply, seek regulatory approval for our current and future product candidates, maintain and expand our intellectual property portfolio, hire additional research and development and business personnel and operate as a public company. Based on our current research and development plans, we expect that our existing cash and cash equivalents of $157.5 million, will be sufficient to fund our operations through at least the second quarter of 2023. We have based this estimate on assumptions that may prove to be wrong, however, and we could use our capital resources sooner than we expect.

The timing and amount of our operating expenditures will depend largely on:

- the scope, progress, timing, costs and results of researching and developing our current product candidates or any future product candidates, including with respect to our planned clinical trials of WTX-124 and WTX-330; the costs associated with attracting, hiring and retaining skilled personnel and consultants as our preclinical and clinical activities increase;
- the cost of manufacturing our product candidates WTX-124, WTX-330, WTX-613 and any future product candidates for clinical trials and, if we are able to obtain marketing approval, for commercial sale;
- the costs of any third-party products used in our planned combination clinical trials that are not covered by such third parties or other sources;

- the potential additional expenses attributable to adjusting our development plans (including any supply related matters) as a result of the COVID-19 pandemic;
- the timing of, and the cost involved in, obtaining marketing approval for WTX-124, WTX-330, WTX-613 or any future product candidates, and our ability to obtain marketing approval and generate revenue from any potential commercial sales of such product candidates;
- the cost of building a sales force in anticipation of product commercialization and the cost of commercialization activities for WTX-124, WTX-330, WTX-613 or any future product candidates if we receive marketing approval, including marketing, sales and distribution costs;
- the potential emergence of competing therapies and other adverse market developments;
- the amount and timing of any payments we may be required to make pursuant to our license agreement with Harpoon Therapeutics, Inc., or Harpoon, or other future license agreements or collaboration agreements;
- our ability to establish future collaborations, licensing or other arrangements and the financial terms of any such agreements, including the timing and amount of any future milestone, royalty or other payments due under any such agreement;
- the costs involved in preparing, filing, prosecuting, maintaining, expanding, defending and enforcing patent claims, including litigation costs and the outcome of such litigation;
- any product liability or other lawsuits related to our product candidates;
- the extent to which we in-license or acquire other products and technologies; and
- the costs of operating as a public company.

Our existing cash and cash equivalents will not be sufficient to complete development of WTX-124, WTX-330, WTX-613 or any other product candidate. Accordingly, we will be required to obtain further funding to achieve our business objectives.

Until such time, if ever, as we can generate substantial revenue from product sales, we expect to fund our operations and capital funding needs through equity and/or debt financing. We may also consider entering into collaboration arrangements or selectively partnering for clinical development and commercialization. The sale of additional equity may result in additional dilution to our stockholders. The incurrence of debt financing would result in debt service obligations and the instruments governing such debt could provide for operating and financing covenants that would restrict our operations or our ability to incur additional indebtedness or pay dividends, among other items. If we raise additional funds through governmental funding, collaborations, strategic partnerships and alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are not able to secure adequate additional funding, we may be forced to make reductions in spending, extend payment terms with suppliers, liquidate assets where possible, and/or suspend or curtail planned programs. Any of these actions could materially and adversely affect our business, financial condition, results of operations, cash flows and prospects.

Cash Flows

The following table provides information regarding our cash flows for the years ended December 31, 2021 and 2020:

	Year Ended December 31,	
(in thousands)	**2021**	**2020**
Net cash (used in) provided by:		
Operating activities	$ (42,876)	$ (18,624)
Investing activities	(498)	(560)
Financing activities	109,427	93,857
Net increase in cash, cash equivalents and restricted cash	$ 66,053	$ 74,673

Operating Activities

Net cash used in operating activities for the year ended December 31, 2021 was $42.9 million, compared to $18.6 million for the year ended December 31, 2020. This increase of approximately $24.3 million was primarily attributable to an increase in net loss of $34.9 million for the year ended December 31, 2021 compared to the year ended December 31, 2020. Included in the aforementioned increase in net loss is an increase in non-cash stock-based compensation expense of $3.4 million and a decrease in gain on change in fair value of preferred stock tranche liability of $7.3 million for the year ended December 31, 2021, compared to the year ended December 31, 2021.

Investing Activities

Net cash used in investing activities for the year ended December 31, 2021 was $0.5 million, compared to $0.6 million for the year ended December 31, 2020. This decrease of approximately $0.1 million was primarily attributable to a decrease in purchases of property and equipment for the year ended December 31, 2021 compared to the year ended December 31, 2020.

Financing Activities

Net cash provided by financing activities for the year ended December 31, 2021 was $109.4 million, compared to $93.9 million for the year ended December 31, 2020. This increase of $15.6 million was primarily attributable to the proceeds from the issuance of common stock at the closing of the IPO during the year ended December 31, 2021, compared to the proceeds from the issuance of Series A redeemable convertible preferred stock during the year ended December 31, 2020.

Contractual Obligations

Overview

In the normal course of business, we enter into agreements with CROs, contact manufacturers, vendors and other third parties for preclinical studies, manufacturing services and other services and products for operating purposes. These contracts do not contain minimum purchase commitments and are cancelable by us upon prior written notice. Payments due upon cancellation consist only of payments for services provided or expenses incurred, including noncancelable obligations of our service providers, up to the date of cancellation.

Clinical Trial Collaboration and Supply Agreement

In August 2021, we entered into a Clinical Trial Collaboration and Supply Agreement, or Clinical Supply Agreement, with Merck & Co., Inc., or Merck, to evaluate WTX-124 in combination with KEYTRUDA® (pembrolizumab), Merck's anti-PD-1 therapy. The planned clinical trial will be conducted by Werewolf and is designed to evaluate the safety and preliminary efficacy of WTX-124 as a monotherapy and in combination with pembrolizumab in patients with solid tumors. Under the terms of the Clinical Supply Agreement, Werewolf will sponsor the study and Merck will supply Werewolf with pembrolizumab in exchange for jointly owning any inventions or discoveries relative to the combined use of WTX-124 and pembrolizumab. Each party is responsible for its own internal costs and expenses to support the trial.

Lease Agreements

In April 2019, we entered into an operating lease for approximately 9,949 square feet of office and laboratory space which commenced in April 2019 and terminates in March 2024. Total estimated base rent payments over the remaining term of the lease are approximately $2.1 million.

In March 2021, we entered into a short-term lease for approximately 7,500 square feet of office and laboratory space which commenced in April 2021 and terminates in May 2022. Total estimated base rent payments over the remaining term of the lease are approximately $0.2 million.

In June 2021, we entered into an operating lease for approximately 25,778 square feet of office and laboratory space in Watertown, Massachusetts, which will serve as the Company's future headquarters. The lease term is targeted to commence in April 2022 and has an approximate eight-year term. Total estimated base rent payments over the term of the lease are approximately $19.1 million.

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, or the Exchange Act, and are not required to provide the information under this item.

Item 8. Financial Statements and Supplementary Data

The financial statements required to be filed pursuant to this Item 8 are appended to this Annual Report. An index of those financial statements is found in Part IV, Item 15.

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

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Securities and Exchange Act of 1934 is (1) recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms and (2) accumulated and communicated to our management, including our President and Chief Executive Officer, who is our principal executive officer, and Chief Financial Officer, who is also our principal financial and accounting officer, 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 management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

As of December 31, 2021, our management, with the participation of our principal executive officer and principal financial and accounting officer, evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities and Exchange Act of 1934). Our principal executive officer and principal financial and accounting officer have concluded based upon the evaluation described above that, as of December 31, 2021, our disclosure controls and procedures were effective at the reasonable assurance level.

Remediation of Material Weaknesses

Based on our prior assessment as of December 31, 2020, management concluded that our internal control over financial reporting was not effective due to material weaknesses relating to the lack of maintaining a sufficient complement of personnel commensurate with the accounting and financial reporting requirements in order to have adequate segregation of key duties and responsibilities. There were no changes to any of our previously released financial statements. Based on these material weaknesses, our management concluded that at December 31, 2020, our internal control over financial reporting was not effective.

During the year ended December 31, 2021, we have implemented measures designed to improve internal control over financial reporting to remediate the control deficiencies that led to our material weaknesses. Among other things, we have hired qualified personnel with appropriate expertise to perform specific functions and ensure adequate segregation of key duties and responsibilities. We hired a full-time chief financial officer in early February 2021, and additional finance personnel during 2021. We continue to utilize financial consultants to assist with the financial statement close process and the evaluation and documentation of technical accounting matters. Additionally, we engaged third-party internal control specialists to assist in our design and implementation of improved processes and internal controls, including ongoing senior management review and audit committee oversight, and implemented financial systems with sufficient reporting and internal control capabilities to support our operations as a public company.

We tested the effectiveness of the procedures and controls related to our remediation. As a result, management has concluded that, as of December 31, 2021, we had remediated the previously reported material weaknesses.

Management's Annual Report on Internal Control over Financial Reporting

This Annual Report does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of our independent registered public accounting firm due to a transition period established by rules of the SEC for newly public companies, outside of the conclusion noted in the section above regarding the remediation of the material weaknesses identified during the fiscal year 2020.

Changes in Internal Control over Financial Reporting

Except for changes made in connection with our remediation of the material weaknesses mentioned above, there have been no changes 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 period covered by this Annual Report 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 Inspections

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

Except to the extent provided below, the information required by this Item 10 will be included in the section captioned “Corporate Governance” and “Proposal No. 1” in our definitive proxy statement to be filed with the Securities and Exchange Commission, or the SEC, with respect to our 2022 Annual Meeting of Stockholders within 120 days of December 31, 2021, which information is incorporated herein by reference.

Board of Directors

Board Composition and Structure

The Board of Directors is currently comprised of eight members. Below is a list of the names, ages as of March 18, 2022, and classification of the individuals who currently serve as our directors.

Name	Age	Position
Luke Evnin, Ph.D.	58	Chair of the Board of Directors
Sakae Asanuma, C.F.A.	56	Director
Meeta Chatterjee, Ph.D.	67	Director
Derek DiRocco, Ph.D.	41	Director
Daniel J. Hicklin, Ph.D. (1)	58	President, Chief Executive Officer and Director
Alon Lazarus, Ph.D.	47	Director
Briggs W. Morrison, M.D.	63	Director
Mike Sherman, M.B.A.	55	Director

(1) Daniel J. Hicklin, Ph.D. is also an executive officer and his biographical information appears below.

Director Biographies

Luke Evnin, Ph.D., is a co-founder of our company, served as our President and Chief Executive Officer from December 2017 until August 2019 and has served on our board of directors since October 2017 and as chairman of the board of directors since August 2019. Dr. Evnin serves on the board of directors of Oncorus, Inc., a publicly traded biotechnology company, and is Chief Executive Officer of Turmeric Acquisition Corp., a publicly traded special purpose acquisition company formed by MPM Capital. In 2015, Dr. Evnin co-founded Harpoon Therapeutics, Inc., a publicly held immunotherapy company, and served as chairman of its board of directors until July 2020. Dr. Evnin served on the board of directors of Syndax Pharmaceuticals, Inc., a publicly traded biotechnology company, from May 2012 until September 2018. Over the past eight years, as a component of his MPM activities, Dr. Evnin has been a co-founder and served as chairman of the board for seven MPM portfolio companies. Dr. Evnin has also served on the board of directors of a number of public and private companies over his 28-year venture capital career and currently serves, on behalf of MPM Capital, as a director for seven private companies. Dr. Evnin co-founded MPM Capital, an early-stage life sciences venture investing firm, in 1997, where he currently serves as Managing Director. Prior to co-founding MPM Capital, Dr. Evnin spent seven years as a venture capitalist at Accel Partners. Dr. Evnin also serves as chairman of the board of directors of the Scleroderma Research Foundation, a not-for-profit entity. Dr. Evnin holds an A.B. in molecular biology from Princeton University and a Ph.D. in biochemistry from the University of California, San Francisco. We believe that Dr. Evnin’s depth and expertise in the life sciences and venture capital industries including significant experience serving on boards of directors and his educational background provide him with the qualifications and skills to serve on our board of directors.

Sakae Asanuma, C.F.A., has served on our board of directors since August 2019. Mr. Asanuma established and has served since April 2016 as President of Taiho Ventures, LLC, the corporate venture arm of Taiho Pharmaceutical Co., Ltd., a Japanese specialty pharmaceutical company focusing on oncology, allergy and immunology and urology. Previously, Mr. Asanuma was President and Chief Executive Officer at Astellas Venture Management LLC, the corporate venture capital arm of Astellas Pharma, Inc., from April 2012 until January 2016, and U.S. Head of Astellas Innovation Management from 2013 to 2015. Before joining Astellas, he worked for Yasuda Enterprise, a Japan/US-based venture capital firm. Mr. Asanuma has served on the boards of directors of many private biotechnology companies and has been involved in numerous biotechnology and pharmaceutical partnering transactions. Mr. Asanuma holds a Master of Science in Industrial Administration (MBA) from Carnegie Mellon University. We believe Mr. Asanuma’s experience working with and serving on the boards of directors of life sciences companies and his experience working in the venture capital industry qualifies him to serve on our board of directors.

Meeta Chatterjee, Ph.D., has served on our board of directors since October 2021. She has served as the Senior Vice President of Global Business Development of Legend Biotech Corporation since March 2019. From November 2007 to May 2018, she served in roles of increasing seniority and responsibility at Merck Research Laboratories, a division of Merck & Co., Inc., a multinational pharmaceutical company, most recently as Head of Strategy, Transactions, and Operations within the Business Development and Licensing (BD&L) group. Dr. Chatterjee oversaw discovery and late-stage transactions worldwide, as well as early-stage transactions in key geographies. She also was responsible for Merck’s BD&L governance, oversight, and control as well as out-licensing efforts. Dr. Chaterjee has served on the board of directors of Editas Medicine, a publicly traded clinical stage biotechnology company, since December 2020. Dr. Chatterjee has over 30 years of broad strategic and operational experience in pharmaceutical research and development, mergers and acquisition evaluation, in-licensing,

and externalization activities. Over the course of her extensive career, Dr. Chatterjee has led or contributed to a number of transactions or collaborations, has led research efforts in the areas of hypertension, atherosclerosis, and obesity, and was an integral contributor to the discovery of ZETIA® and ZONTIVITY®. Dr. Chatterjee received her undergraduate education at St. Xavier's University in Ahmedabad, India, and Rutgers University (B.A., Hons Physics). Dr. Chatterjee received her Doctor of Philosophy in Physiology from Rutgers University and completed a postdoctoral fellowship in the Department of Physiology at the University of Virginia School of Medicine. Dr. Chatterjee is also active in industry and licensing focused organizations. We believe Dr. Chatterjee's extensive business development experience in the biotechnology industry and serving on the board of directors of a biotechnology company qualifies her to serve on our board of directors.

Derek DiRocco, Ph.D., has served on our board of directors since December 2020. Dr. DiRocco has been a partner at RA Capital Management, L.P. since December 2020 and was previously a principal from December 2017 until December 2020, an analyst from June 2015 to December 2017 and an associate from July 2013 to June 2015. Dr. DiRocco has served on the board of directors of iTeos Therapeutics, Inc. since March 2020 and 89bio, Inc. since April 2018, each of which is a publicly traded biotechnology company. Dr. DiRocco also serves on the board of directors of several privately held biotechnology companies. Dr. DiRocco holds a B.A. in biology from College of the Holy Cross and a Ph.D. in pharmacology from the University of Washington. He conducted his postdoctoral research at Brigham and Women's Hospital/Harvard Medical School. We believe that Dr. DiRocco is qualified to serve as a member of our board of directors because of his experience as an investor in biotechnology companies and role in early-stage companies.

Alon Lazarus, Ph.D., has served as a member of our board of directors since August 2019. Dr. Lazarus has held the position of Biotech Investment Manager of the Pharma Division of Arkin Holdings, Ltd., an investment firm, focused in the healthcare and pharmaceutical sectors, since August 2013. Prior to joining Arkin Holdings, Ltd., Dr. Lazarus worked for the Healthcare Business Development Department of Yissum Research Development Company of the Hebrew University of Jerusalem from January 2012 until August 2013, and as an Analyst for Integra Holdings, Ltd., an Israel-based healthcare investment company. Dr. Lazarus served as a member of the board of directors of Keros Therapeutics, Inc, a publicly traded biotechnology company, from April 2016 to December 2020. Dr. Lazarus also serves as a member of the board of directors of several private life science companies. Dr. Lazarus holds a Ph.D. in Molecular Biology from the Hadassah Medical School of Hebrew University of Jerusalem in Israel, an M.B.A. from the School of Business Administration of Hebrew University of Jerusalem in Israel and a B.Sc. in Biology from Hebrew University of Jerusalem in Israel. We believe that Dr. Arkin's extensive experience in the biotechnology industry and his service on numerous life sciences board of directors qualify him to serve on our board of directors.

Briggs W. Morrison, M.D., has served as a member of our board of directors since November 2019. He has served as Executive Partner at MPM Capital, Inc. since June 2015 and as President, Head of Research and Development since February 2022, and a member of the board of directors of Syndax Pharmaceuticals, Inc., a publicly traded biopharmaceutical company, since June 2015. Dr. Morrison was previously the Chief Executive Officer of Syndax Pharmaceuticals, Inc., from June 2015 to February 2022. Dr. Morrison has also served as a member of the board of directors of NextCure Inc. since April 2019, Arvinas Holding Company, LLC since June 2018, Repare Therapeutics Inc. since June 2017, and Codiak BioSciences, Inc. since February 2018, all of which are publicly traded biopharmaceutical companies. Before that, Dr. Morrison was the Chief Medical Officer and Head of Global Medicines Development at AstraZeneca plc from 2012 to 2015. Before joining AstraZeneca, he held several positions at Pfizer Inc., including Head, Medical Affairs, Safety and Regulatory Affairs for Pfizer's human health business. Dr. Morrison also previously held several positions at Merck Research Laboratories, a division of Merck & Co., Inc., including Vice President, Clinical Sciences, Oncology. He was a member of the executive committee of the Clinical Trials Transformation Initiative sponsored by the FDA and is on the board of the Alliance for Clinical Research Excellence and Safety. Dr. Morrison also serves on the board of directors for multiple private pharmaceutical companies. Dr. Morrison has a B.S. in biology from Georgetown University and an M.D. from the University of Connecticut Medical School. He completed residency training in internal medicine at Massachusetts General Hospital and a fellowship in medical oncology at the Dana-Farber Cancer Institute. We believe Dr. Morrison is qualified to serve as a member of our board of directors due to his extensive executive leadership experience, his medical background and training and his service on the boards of other public and private biopharmaceutical and biotechnology companies.

Mike Sherman, M.B.A. has served as a member of our board of directors since May 2021. He has served as the Chief Executive Officer of Chimerix Inc. ("Chimerix"), a publicly traded biotechnology company, since April 2019. Before joining Chimerix, Mr. Sherman served as Chief Executive Officer of Endocyte, Inc., or Endocyte, a biopharmaceutical company, beginning in 2016, and led it to its $2.1 billion acquisition by Novartis in 2018. Mr. Sherman joined Endocyte in 2006 and served as its Chief Financial Officer and Chief Operating Officer prior to becoming Chief Executive Officer. Prior to joining Endocyte, Mr. Sherman served in various executive roles, including as vice president of finance and strategic planning for Guidant Corporation, which was acquired by Boston Scientific Corporation. Mr. Sherman holds a BA in economics from DePauw University and an MBA from the Tuck School of Business at Dartmouth, graduating as a Tuck Scholar. Mr. Sherman currently serves on the Board of Trustees for the Children's Museum of Indianapolis, a nonprofit organization, as past chairman. He also served on the Boards of Directors at Biospecifics Technologies, Inc. until its acquisition by Endo Pharmaceuticals and Mead Johnson Nutrition until its acquisition by Reckitt Benckiser. We believe that Mr. Sherman's 30 years' experience advancing therapeutics to commercial launch and driving companies to successful operations and strategic transactions in the biotechnology and medical technology industries qualifies him to serve as a member of our board of directors.

Executive Officers

The following table sets forth our executive officers as of March 18, 2022.

Name	Age	Position
Daniel J. Hicklin, Ph.D.	58	President, Chief Executive Officer and Director
Randi Isaacs, M.D.	66	Chief Medical Officer
Chulani Karunatilake, Ph.D.	63	Chief Technology Officer
Reid Leonard, Ph.D.	63	Chief Operating Officer
Ellen Lubman, M.B.A.	46	Chief Business Officer
Cynthia Seidel-Dugan, Ph.D.	63	Chief Scientific Officer
Tim Trost	64	Chief Financial Officer and Treasurer

Executive Biographies

Daniel J. Hicklin, Ph.D., has served as our President and Chief Executive Officer since August 2019. Dr. Hicklin founded Werewolf Therapeutics in October 2017 and served as a consultant until his appointment as our President and Chief Executive Officer. Previously, Dr. Hicklin was a founder of Potenza Therapeutics, Inc., a privately held biotechnology company, and served as its President and Chief Executive Officer from April 2014 until its acquisition by Astellas Pharma Inc. in December 2018. From August 2013 until February 2014, Dr. Hicklin was President and Chief Scientific Officer of CoStim Pharmaceuticals, Inc., a privately held biotechnology company that was acquired by Novartis in February 2014. Dr. Hicklin has also served as an Executive Partner from 2014 to December 2019 and an advisor at MPM Capital since January 2020. Prior to joining CoStim Pharmaceuticals, Dr. Hicklin held several positions at Merck Research Laboratories (formerly the Schering-Plough Research Institute prior to its acquisition by Merck), including leading its Biologics Strategy for Oncology and the Immuno-Modulation Discovery team. Dr. Hicklin also previously held several positions at Imclone Systems Incorporated, including Vice President, Experimental Therapeutics. Dr. Hicklin has served as a member of the board of directors of several private biotechnology companies. Dr. Hicklin also currently serves on the Industry Advisory Committee for The Mark Foundation for Cancer Research. Dr. Hicklin holds an M.S. and Ph.D. in Microbiology and Immunology from New York Medical College, where he trained with Dr. Soldano Ferrone, and a B.S. from the University of Iowa. We believe that Dr. Hicklin's operational and historical experience with our company gained from being a founder and serving as our President and Chief Executive Officer and member of our board of directors, combined with his extensive experience in oncology drug discovery, qualifies him to serve as a member of our board of directors.

Randi Isaacs, M.D., has served as our Chief Medical Officer since November 2020. Previously, from May 2010 until November 2020, Dr. Isaacs held roles of increasing responsibility as Clinical Program Leader, Deputy Site Head, and, from August 2015 to November 2020, Executive Director and Clinical Site Head of Translational Clinical Oncology at the Novartis Institutes for Biomedical Research. She previously held executive leadership roles in oncology and clinical development at Merck, Schering Plough and Sandoz. Prior to transitioning to the biopharmaceutical industry, Dr. Isaacs held various academic appointments, including Assistant Professor of Medicine in the Division of Hematology/Oncology at the State University of New York Health Sciences Center and Clinical Assistant Professor of Hematology/Oncology at the University of Medicine and Dentistry of New Jersey. Dr. Isaacs has served on the board of directors of C4 Therapeutics, Inc., a publicly traded biotechnology company, since May 2021. Dr. Isaacs also serves on the Scientific Advisory Board of MMF Investment Fund, a not-for-profit entity, and Tornado Therapeutics, a subsidiary of Cambrian Biopharma, Inc., a privately held entity. Dr. Isaacs earned her B.A. in Chemistry from Wellesley College and holds an M.D. with honors from Dartmouth Medical School. She completed her residency and postdoctoral training at the University of California San Francisco and University of Pennsylvania and hematology/medical oncology fellowship training at the Memorial Sloan-Kettering Cancer Center.

Chulani Karunatilake, Ph.D., has served as our Chief Technology Officer since June 2021. Previously, from July 2019 to June 2021, Dr. Karunatilake served as Senior Vice President of Technical Operations for Maverick Therapeutics (acquired by Takeda), where he was responsible for all aspects of Chemistry and Manufacturing Controls (CMC). Prior to Maverick, Dr. Karunatilake was Senior Vice President of Biologics CMC and initially Vice President of Pharmaceutical Development and Manufacturing at Nektar Therapeutics, from May 2011 to May 2019. He has also held numerous leadership positions at Amgen, Chiron/Novartis, Genentech, and Eli Lilly. Dr. Karunatilake earned his Ph.D. in Chemistry/Biochemistry from the University of Illinois and holds a B.S. in Chemistry from the University of Colombo in Sri Lanka.

Reid Leonard, Ph.D., has served as our Chief Operating Officer since April 2019. From July 2014 until December 2018, Dr. Leonard served in various roles at Potenza Therapeutics, including Chief Operating Officer from January 2018 to December 2018, Senior Vice President of Corporate Development from January 2016 to December 2017 and Vice President of Corporate Development from July 2014 to December 2015. Dr. Leonard served as a venture partner at MPM Capital from September 2016 until September 2017 and has also served as a consultant to several private biotechnology companies. Dr. Leonard began his career with Merck & Co., where he served for over 25 years. Dr. Leonard graduated from Brandeis University with an A.B. in Biology and Psychology, holds a Ph.D. in Biology from Purdue University and completed a postdoctoral fellowship in molecular pharmacology at Caltech with Profs. Henry Lester and Norman Davidson.

Ellen Lubman, M.B.A., has served as our Chief Business Officer since August 2020. From October 2018 to July 2020, Ms. Lubman served as the Chief Business Officer at Impel NeuroPharma, Inc., a privately held biotechnology company focused on neurological diseases. Prior to Impel, she was the Vice President of External Science & Innovation at Forest Labs, from February 2014 until its acquisition by Actavis plc in July 2014, and served in the same role at Actavis through June 2018 during which time Actavis merged with and renamed itself Allergan plc. Prior to Allergan, Ms. Lubman held numerous executive and leadership roles at Kadmon Pharmaceuticals, Bristol Myers Squibb, Celtic

Pharma Management, L.P., Robertson Stephens Investment Bank and Abbott Labs. Ms. Lubman has been a member of the board of directors at Field Trip Health, a publicly traded developer of therapeutics, since June 2021. She serves on the Advisory Board of TMRW.org. Ms. Lubman also currently serves on the Scientific Advisory Board of the Daedalus Innovation Fund of Weill-Cornell, the board of directors of Gilda's Club of NYC, and is the Southern California Chairwoman of Executive Women in BIO. Ms. Lubman earned her M.B.A. from Stanford Graduate School of Business with a focus on Global Management and her B.A. in Biology from Rutgers College.

Cynthia Seidel-Dugan, Ph.D., has served as our Chief Scientific Officer since April 2019. From May 2014 until December 2018, Dr. Seidel-Dugan served in several positions at Potenza Therapeutics, including most recently Chief Scientific Officer from January 2018 to December 2018, and previously Senior Vice President of Research from January 2016 to December 2017 and Vice President of Research from May 2014 to December 2015. Prior to joining Potenza Therapeutics, Dr. Seidel-Dugan served as Vice President, Biology for CoStim Pharmaceuticals from May 2013 until February 2014. Early in her career, Dr. Seidel-Dugan served in various roles at Ariad Pharmaceuticals, Exelixis Pharmaceuticals, Schering-Plough Research Institute and (upon merger) Merck Research Laboratories. Dr. Seidel-Dugan earned a B.S. in Biology from the College of William and Mary and holds a Ph.D. in Microbiology and Molecular Biology from the University of Pennsylvania. She also completed a postdoctoral fellowship with Dr. Joan Brugge at the University of Pennsylvania.

Timothy W. Trost has served as our Chief Financial Officer and Treasurer since February 2021. Previously, Mr. Trost served as Chief Financial Officer of Asklepios Biopharmaceutical, Inc., or AskBio, a biotechnology company, from May 2020 until it was acquired by Bayer AG in December 2020. Prior to joining AskBio, from March 2011 until May 2019, Mr. Trost served as Senior Vice President, Chief Financial Officer, of Chimerix, Inc., a biopharmaceutical company, and also served as its Corporate Secretary from February 2012 until May 2019. Previously, Mr. Trost served as Vice President and Chief Financial Officer at Argos Therapeutics, Inc., a venture-backed immunotherapy company; Senior Vice President and Chief Financial Officer at InteCardia, Inc., a venture-backed cardiac imaging company that was acquired by Syncor International Corporation; and as Executive Vice President and Chief Financial Officer of Coastal Physician Group, Inc., a contract provider of emergency room physicians, having joined as Vice President of Corporate Development. Mr. Trost previously served with PricewaterhouseCoopers LLP, last serving as a Senior Manager in the Research Triangle practice. Mr. Trost holds a B.S. in accounting from the University of Illinois at Urbana-Champaign and is a Certified Public Accountant.

Code of Ethics

We have adopted a written code of business conduct and ethics that applies to our directors, officers, and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. A copy of the code is posted on the Corporate Governance section of our website, which is located at www.werewolftx.com. If we make any substantive amendments to, or grant any waivers from, the code of business conduct and ethics for any officer or director, we will disclose the nature of such amendment or waiver on our website or in a current report on Form 8-K. We will provide any person, without charge, a copy of such Code of Business Conduct and Ethics upon written request, which may be mailed to 1030 Massachusetts Ave, Ste. 210, Cambridge, MA 02138, Attn: Corporate Secretary.

Item 11. Executive Compensation

The information required by this Item 11 will be included in the section captioned "Executive Compensation" in our definitive Proxy Statement for our 2022 Annual Meeting of Stockholders to be filed with the SEC within 120 days of December 31, 2021, which information is incorporated herein by reference.

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

Except to the extent provided below, the information required by this Item 12 will be included in the section captioned "Principal Stockholders" in our definitive Proxy Statement for our 2022 Annual Meeting of Stockholders to be filed with the SEC within 120 days of December 31, 2021, which information is incorporated herein by reference.

Equity Compensation Plan Information

The following table contains information about our 2017 Stock Incentive Plan, or the 2017 Plan, our 2021 Stock Incentive Plan, or the 2021 Plan, and our 2021 Employee Stock Purchase Plan, or 2021 ESPP, as of December 31, 2021.

Plan Category	As of December 31, 2021 Number of Securities to be Issued upon Exercise of Outstanding Options, Warrants and Rights	Weighted Average Exercise Price of Outstanding Options, Warrants and Rights	Number of Securities Remaining Available for Future Issuance under Equity Compensation Plans (Excluding Securities Reflected in Column (a))
	(a)	(b)	(c)
Equity compensation plans approved by security holders [(1)(2)(3)]	3,265,694	$ 8.24	2,182,895
Equity compensation plans not approved by security holders	—	—	—
Total	3,265,694	$ 8.24	2,182,895

(1) Includes the 2017 Plan, the 2021 Plan and the 2021 ESPP.

(2) As of December 31, 2021, 1,938,895 shares of our common stock were available for issuance under the 2021 Plan. The number of shares reserved for issuance under the 2021 Plan will be increased on each January 1 through January 1, 2031 by the lesser of (i) 5% of the number of shares of our common stock outstanding on the first day of such year and (ii) an amount determined by our board of directors. The shares of common stock underlying any awards that are expired, forfeited, canceled, held back upon exercise or settlement of an award to satisfy the exercise price or tax withholding, repurchased or are otherwise terminated by us under the 2021 Plan or the 2017 Plan are added back to the shares of common stock available for issuance under the 2021 Plan. On January 1, 2022, the shares under the 2021 Plan were increased by 1,380,397 shares pursuant to the annual increase described above.

(3) As of December 31, 2021, 244,000 shares of our common stock were reserved for issuance under the 2021 ESPP. The number of shares reserved for issuance under the 2021 ESPP will be increased on each January 1 through January 1, 2032 by the least of (i) 488,000 shares, (ii) 1% of the number of shares of our common stock outstanding on the first day of such year and (iii) an amount determined by our board of directors.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this Item 13 will be included in the sections captioned “Corporate Governance” and “Transactions with Related Persons” in our definitive Proxy Statement for our 2022 Annual Meeting of Stockholders to be filed with the SEC within 120 days of December 31, 2021, which information is incorporated herein by reference.

Item 14. Principal Accountant Fees and Services

The information required by this Item 14 will be included in the section captioned “Ratification of the Appointment of Deloitte & Touche LLP As Our Independent Registered Public Accounting Firm For The Fiscal Year Ending December 31, 2022” in our definitive Proxy Statement for our 2022 Annual Meeting of Stockholders to be filed with the SEC within 120 days of December 31, 2021, which information is incorporated herein by reference.

PART IV

Item 15. Exhibit and Financial Statement Schedules

(1) Financial Statements

The following documents are attached hereto and are filed as part of this Annual Report.

(2) Financial Statement Schedules

Schedules have been omitted since they are either not required or not applicable or the information is otherwise included herein.

(3) Exhibits

The exhibits filed or furnished as part of this Annual Report are listed in the Exhibit Index immediately preceding the signatures, which Exhibit Index is incorporated herein by reference.

Item 16. Form 10-K Summary

None.

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Werewolf Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Werewolf Therapeutics, Inc. and its subsidiary (the "Company") as of December 31, 2021 and 2020, the related consolidated statements of operations, redeemable convertible preferred stock and stockholders' (deficit) equity, and cash flows, for each of the two years in the period ended December 31, 2021, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2021, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
March 24, 2022

We have served as the Company's auditor since 2020.

Werewolf Therapeutics, Inc.
Consolidated Balance Sheets
(amounts in thousands, except par value amounts)

	December 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 157,531	$ 92,570
Prepaid expenses and other current assets	3,537	344
Total current assets	161,068	92,914
Property and equipment, net	2,913	651
Restricted cash	1,208	207
Operating lease right of use asset	13,412	2,471
Deferred financing costs	—	155
Other non-current assets	649	—
Total assets	$ 179,250	$ 96,398
Liabilities, Redeemable Convertible Preferred Stock, and Stockholders' Equity (Deficit):		
Current liabilities:		
Accounts payable	$ 2,037	$ 1,021
Accrued expenses and other current liabilities	8,765	3,586
Operating lease liability, current	1,072	677
Total current liabilities	11,874	5,284
Operating lease liability, net of current portion	14,589	1,864
Other liabilities	—	31
Total liabilities	26,463	7,179
Commitments and contingencies		
Redeemable convertible preferred stock:		
Series A redeemable convertible preferred stock, par value $0.0001 per share, no shares and 80,247 shares authorized, issued and outstanding at December 31, 2021 and December 31, 2020, respectively; liquidation preference of $69,012 at December 31, 2020	—	69,012
Series B redeemable convertible preferred stock, par value $0.0001 per share, no shares and 78,222 shares authorized, issued and outstanding at December 31, 2021 and December 31, 2020, respectively; liquidation preference of $72,070 at December 31, 2020	—	72,070
Stockholders' equity (deficit):		
Preferred stock, $0.0001 par value, 5,000 shares and no shares authorized at December 31, 2021 and December 31, 2020, respectively; no shares issued or outstanding as of December 31, 2021 or December 31, 2020	—	—
Common stock, $0.0001 par value, 200,000 shares and 193,500 shares authorized as of December 31, 2021 and December 31, 2020, respectively; 27,608 and 1,746 shares issued as of December 31, 2021 and December 31, 2020, respectively; 27,313 and 1,184 shares outstanding as of December 31, 2021 and December 31, 2020, respectively	2	2
Additional paid-in capital	405,680	—
Accumulated deficit	(252,895)	(51,865)
Total stockholders' equity (deficit)	152,787	(51,863)
Total liabilities, redeemable convertible preferred stock, and stockholders' equity (deficit)	$ 179,250	$ 96,398

The accompanying notes are an integral part of these consolidated financial statements.

Werewolf Therapeutics, Inc.
Consolidated Statements of Operations
(amounts in thousands, except per share amounts)

	Year Ended December 31,	
	2021	**2020**
Operating expenses:		
Research and development	$ 35,269	$ 16,641
General and administrative	14,818	5,763
Total operating expenses	50,087	22,404
Operating loss	(50,087)	(22,404)
Other income:		
Change in fair value of preferred stock tranche liability	—	7,301
Interest income, net	104	63
Total other income	104	7,364
Net loss	(49,983)	(15,040)
Accretion of redeemable convertible preferred stock to redemption value	(151,942)	(13,177)
Net loss attributable to common stockholders	$ (201,925)	$ (28,217)
Net loss per share attributable to common stockholders, basic and diluted	$ (10.94)	$ (28.08)
Weighted-average common shares outstanding, basic and diluted	18,455	1,005

The accompanying notes are an integral part of these consolidated financial statements.

Werewolf Therapeutics, Inc.
Consolidated Statements of Redeemable Convertible Preferred Stock and Stockholders' (Deficit) Equity
(amounts in thousands)

	Series A Redeemable Convertible Preferred Stock		Series B Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Deficit	Total Stockholders' (Deficit) Equity
	Shares	Amount	Shares	Amount	Shares	Amount			
Balance at December 31, 2019	48,675	$ 34,073	—	$ —	1,737	$ 2	$ 102	$ (24,408)	$ (24,304)
Issuance of Series A Preferred Stock, net of issuance costs of $31	31,572	22,069	—	—	—	—	—	—	—
Issuance of Series B Preferred Stock, net of issuance costs of $307	—	—	78,222	71,763	—	—	—	—	—
Accretion of redeemable convertible preferred stock to redemption value	—	12,870	—	307	—	—	(760)	(12,417)	(13,177)
Stock-based compensation expense	—	—	—	—	—	—	632	—	632
Stock option exercises	—	—	—	—	16	—	26	—	26
Repurchases of restricted stock	—	—	—	—	(7)	—	—	—	—
Net loss	—	—	—	—	—	—	—	(15,040)	(15,040)
Balance at December 31, 2020	80,247	$ 69,012	78,222	$ 72,070	1,746	$ 2	$ —	$ (51,865)	$ (51,863)
Issuance of common stock from initial public offering, net of issuance costs of $2,379	—	—	—	—	7,500	—	109,221	—	109,221
Accretion of redeemable convertible preferred stock to redemption value	—	79,372	—	72,570	—	—	(895)	(151,047)	(151,942)
Conversion of redeemable convertible preferred stock to common stock upon closing of initial public offering	(80,247)	(148,384)	(78,222)	(144,640)	18,280	—	293,024	—	293,024
Stock-based compensation expense	—	—	—	—	—	—	4,095	—	4,095
Stock option exercises	—	—	—	—	82	—	235	—	235
Net loss	—	—	—	—	—	—	—	(49,983)	(49,983)
Balance at December 31, 2021	—	$ —	—	$ —	27,608	$ 2	$ 405,680	$ (252,895)	$ 152,787

The accompanying notes are an integral part of these consolidated financial statements.

Werewolf Therapeutics, Inc.
Consolidated Statements of Cash Flows
(amounts in thousands)

	Year Ended December 31,	
	2021	**2020**
Operating activities:		
Net loss	$ (49,983)	$ (15,040)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	4,095	632
Depreciation expense	216	150
Non-cash lease expense	519	627
Change in fair value of preferred stock tranche liability	—	(7,301)
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(3,072)	(177)
Other non-current assets	(649)	—
Accounts payable	1,007	388
Accrued expenses and other current liabilities	5,263	2,616
Right of use assets and operating lease liability	(241)	(527)
Other liabilities	(31)	8
Net cash used in operating activities	(42,876)	(18,624)
Investing activities:		
Purchases of property and equipment	(498)	(560)
Net cash used in investing activities	(498)	(560)
Financing activities:		
Deferred financing costs	—	(155)
Proceeds from issuance of Series A redeemable convertible preferred stock	—	22,100
Proceeds from issuance of Series B redeemable convertible preferred stock	—	72,070
Proceeds from initial public offering of common stock	111,600	—
Payment of equity issuance costs	(2,378)	(184)
Proceeds from stock option exercises	205	26
Net cash provided by financing activities	109,427	93,857
Net increase in cash and cash equivalents	66,053	74,673
Cash, cash equivalents and restricted cash—beginning of period	92,777	18,104
Cash, cash equivalents and restricted cash—end of period	$ 158,830	$ 92,777
Supplemental disclosure of cash flow information:		
Cash paid for lease liabilities	$ 1,035	$ 844
Supplemental disclosure of non-cash investing and financing activities:		
Stock option exercise receivables in prepaid expenses and other current assets	$ 30	$ —
Purchases of property and equipment in accounts payable and accrued expenses	$ 79	$ —
Issuance costs in accounts payable and accrued expenses	$ —	$ 154
Right of use assets obtained in exchange for lease liabilities	$ 13,658	$ —
Non-cash accretion of Series A and Series B redeemable convertible preferred stock	$ 151,942	$ 13,177

The accompanying notes are an integral part of these consolidated financial statements.

1. Nature of Business

Werewolf Therapeutics, Inc. ("Werewolf" or the "Company") was incorporated in the state of Delaware in October 2017. The Company is an innovative biopharmaceutical company pioneering the development of therapeutics engineered to stimulate the body's immune system for the treatment of cancer. The Company's headquarters are located in Cambridge, Massachusetts.

Since inception, the Company has devoted substantially all of its time and efforts to performing research and development activities, raising capital and recruiting management and technical staff to support these operations. The Company is subject to risks and uncertainties common to early-stage companies in the biotechnology industry including, but not limited to, technical risks associated with the successful research, development and manufacturing of product candidates, 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. Current and future programs will require significant research and development efforts, including extensive preclinical and clinical testing and regulatory approval prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel and infrastructure. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will realize significant revenue from product sales.

On May 4, 2021, the Company closed its initial public offering ("IPO") of 7,500,000 shares of the Company's common stock at a public offering price of $16.00 per share. The gross proceeds from the IPO were $120.0 million and the net proceeds were approximately $109.2 million, after deducting underwriting discounts and commissions and other offering expenses payable by the Company. Upon completion of the Company's IPO, all of the Company's then outstanding preferred stock was automatically converted into an aggregate of 18,279,712 shares of common stock.

The Company had cash and cash equivalents of $157.5 million at December 31, 2021. The Company expects that its cash and cash equivalents will enable it to fund its operating expenses and capital expenditure requirements for at least twelve months from the filing date of this Annual Report on Form 10-K. However, additional funding will be necessary beyond this point to fund future preclinical and clinical activities. The Company expects to finance its future cash needs through a combination of equity or debt financings, collaboration agreements, strategic alliances and licensing arrangements.

2. Basis of Presentation and Summary of Significant Accounting Policies

Basis of Presentation and Consolidation

The accompanying consolidated financial statements have been prepared in accordance with the rules and regulations of the Securities and Exchange Commission (the "SEC") and generally accepted accounting principles in the United States of America ("GAAP") as found in the Accounting Standards Codification ("ASC") and Accounting Standards Updates ("ASU") of the Financial Accounting Standards Board ("FASB"). The accompanying consolidated financial statements include the accounts of Werewolf Therapeutics, Inc. and its wholly-owned subsidiary, Werewolf Therapeutics Mass Securities, Inc. All intercompany transactions and balances have been eliminated in consolidation.

Segment Information

Operating segments are identified as components of an enterprise for which separate discrete financial information is available for evaluation by the Company's Chief Operating Decision Maker ("CODM") to make decisions with respect to resource allocation and assessment of performance. The CODM is the Company's Chief Executive Officer. The CODM manages the Company's operations as a single segment for the purposes of assessing performance and making operating decisions. The Company's singular concentration is focused on the discovery and development of cancer therapeutics by advancing a novel class of conditionally activated proinflammatory immune modulators.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. On an ongoing basis, the Company's management evaluates its estimates which include, but are not limited to, the fair values of common stock and redeemable convertible preferred stock and the fair value of the preferred stock tranche rights. Actual results could differ from those estimates.

Fair Value of Financial Instruments

ASU No. 2018-13, *Fair Value Measurement (Topic 820): Disclosure for Fair Value Measurement* ("ASC 820"), establishes a fair value hierarchy for instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company's own assumptions (unobservable inputs). Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability and are developed based on the best information available in the circumstances.

ASC 820 identifies fair value as the exchange price, or exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As a basis for considering market participant assumptions in fair value measurements, ASC 820 establishes a three-tier fair value hierarchy that distinguishes between the following:

- Level 1 inputs are quoted prices (unadjusted) in active markets for identical assets or liabilities.
- Level 2 inputs are inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly.

- Level 3 inputs are unobservable inputs that reflect the Company's own assumptions about the assumptions market participants would use in pricing the asset or liability. Financial assets and liabilities are classified in their entirety based on the lowest level of input that is significant to the fair value measurement.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

Cash and Cash Equivalents

The Company's cash and cash equivalents consist of cash maintained within a standard checking account. The Company also maintains a cash sweep account in which cash from its main operating cash account is invested overnight in highly liquid, short-term investments. The Company considers all highly liquid investments with a maturity date of 90 days or less at the date of purchase to be cash equivalents.

Property and Equipment

Property and equipment is recorded at cost and consists of laboratory equipment, furniture and office equipment, computer equipment, and leasehold improvements. The Company capitalizes property and equipment that is acquired for research and development activities and that has alternate future use. Expenditures for maintenance and repairs are recorded to expense as incurred, whereas major betterments are capitalized as additions to property and equipment. Leasehold improvements are depreciated over the lesser of their useful life or the term of the lease. Depreciation is calculated over the estimated useful lives of the assets using the straight-line method.

Impairment of Long-lived Assets

Long-lived assets consist of property and equipment. The Company reviews its property and equipment whenever events or changes in circumstances indicate that the carrying value of certain assets might not be recoverable and recognizes an impairment loss when it is probable that an asset's realizable value is less than the carrying value.

Leases

At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the unique facts and circumstances present in the arrangement. Leases with a term greater than one year are recognized on the balance sheet as right-of-use assets and short-term and long-term lease liabilities, as applicable. The Company does not recognize leases with terms of one year or less on the balance sheet. Options to renew a lease are not included in the Company's initial lease term assessment unless there is reasonable certainty that the Company will renew. The Company monitors its plans to renew its material leases on a quarterly basis.

Operating lease liabilities and their corresponding right-of-use assets are recorded based on the present value of lease payments over the expected remaining lease term. Certain adjustments to the right-of-use asset may be required for items such as incentives received. The interest rate implicit in lease contracts is typically not readily determinable. As a result, the Company utilizes its incremental borrowing rate ("IBR"), which reflects the fixed rate at which the Company could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, and in a similar economic environment.

The Company subsequently measures its lease liability at the present value of remaining lease payments, discounted using the IBR for the lease. The right-of-use asset is subsequently measured at the amount of the lease liability, adjusted for prepaid or accrued lease payments and the remaining balance of lease incentives received. The Company recognizes operating lease expense on a straight-line basis over the lease term.

Revenue Recognition

The Company analyzes its collaborations to assess whether such arrangements involve joint operating activities performed by parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities and therefore within the scope of ASC Topic 808, *Collaborative Arrangements* ("ASC 808"). This assessment is performed throughout the life of the arrangement based on changes in the responsibilities of all parties in the arrangement. For arrangements within the scope of ASC 808 that contain multiple elements, the Company first determines which elements of the collaboration are deemed to be within the scope of ASC 808 and which elements of the collaboration are more reflective of a vendor-customer relationship and therefore within the scope of ASC Topic 606, *Revenue from Contracts with Customers* ("ASC 606"). For elements of collaboration arrangements that are accounted for pursuant to Topic 808, an appropriate recognition method is determined and applied consistently, either by analogy to authoritative accounting literature or by applying a reasonable and rational policy election.

For those elements of the arrangement that are accounted for pursuant to ASC 606, the Company recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. In applying ASC 606, the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the promises and 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 Company satisfies the performance obligations. The Company only applies the five-step model to contracts when it is probable that it will collect the consideration to which it is entitled 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, determines those that are performance obligations and assesses whether 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. As part of the assessment, the Company must develop assumptions that require judgment to determine the standalone selling price for each performance obligation

identified in the contract. The Company uses key assumptions to determine the standalone selling price, which may include reimbursement rates for personnel costs, development timelines and probabilities of regulatory success. The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is that the period between payment by the customer and the transfer of promised goods or services to the customer will be one year or less.

Arrangements that include upfront payments may require deferral of revenue recognition to a future period until obligations under these arrangements are fulfilled. The event-based milestone payments represent variable consideration, and the Company uses the "most likely amount" method to estimate this variable consideration. Given the high degree of uncertainty around the occurrence of these events, the Company determined the milestone and other contingent amounts to be fully constrained until the uncertainty associated with these payments is resolved. Revenue will be recognized from sales-based royalty payments when or as the sales occur. The Company will re-evaluate the transaction price in each reporting period as uncertain events are resolved and other changes in circumstances occur.

Research and Development Expenses

Expenditures relating to research and development are expensed as incurred. Research and development expenses include external expenses incurred under arrangements with third parties, academic and non-profit institutions and consultants; salaries and personnel-related costs, including non-cash stock-based compensation expense; license fees to acquire in-process technology and other expenses, which include direct and allocated expenses for laboratory, facilities and other costs. Non-refundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

As part of the process of preparing the consolidated financial statements, the Company is required to estimate its accrued research and development expenses as of each balance sheet date. In accruing service fees, the Company estimates the time period over which services will be performed and the level of effort to be expended in each period. This process involves reviewing open contracts and purchase orders, communicating with internal personnel to identify services that have been performed on the Company's behalf and estimating the level of service performed and the associated cost incurred for the service when the Company has not yet been invoiced or otherwise notified of the actual cost. The Company periodically confirms the accuracy of its estimates with its service providers and makes adjustments if necessary. The majority of the Company's service providers invoice monthly in arrears for services performed or when contractual milestones are met. The financial terms of agreements with these service providers are subject to negotiation, vary from contract to contract and may result in uneven payment flows. In circumstances where amounts have been paid in excess of costs incurred, the Company records a prepaid expense.

Intellectual Property Expenses

The Company expenses costs associated with intellectual property-related matters as incurred and classifies such costs as general and administrative expenses within the consolidated statements of operations.

Stock-based Compensation

The Company accounts for stock-based payments in accordance with ASU No. 2018-07, *Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting* ("ASC 718"). This guidance requires all stock-based payments to employees, including grants of employee stock options and restricted stock awards ("RSAs"), to be recognized as expense in the consolidated statements of operations and comprehensive (loss) income based on their grant date fair values. For stock options granted to employees and to members of the Company's board of directors for their services on the board of directors, the Company estimates the grant date fair value of each stock option using the Black-Scholes option-pricing model. For restricted stock units ("RSUs") and RSAs granted to employees, the Company estimates the grant date fair value of each award using intrinsic value, which is based on the value of the underlying common stock less any purchase price. For stock-based payments subject to service-based vesting conditions, the Company recognizes stock-based compensation expense equal to the grant date fair value of stock-based payment on a straight-line basis over the requisite service period.

The Black-Scholes option pricing model requires the input of certain subjective assumptions, including (i) the calculation of expected term of the stock-based payment, (ii) the risk-free interest rate, (iii) the expected stock price volatility and (iv) the expected dividend yield. The Company uses the simplified method as proscribed by SEC Staff Accounting Bulletin No. 107 to calculate the expected term for stock options granted to employees as the Company does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. The Company determines the risk-free interest rate based on a treasury instrument whose term is consistent with the expected term of the stock options. Because there had been no public market for the Company's common stock prior to the Company's IPO, there is a lack of Company-specific historical and implied volatility data. Accordingly, the Company bases its estimates of expected volatility on the historical volatility of a group of publicly-traded companies with similar characteristics to itself, including stage of product development and therapeutic focus within the life sciences industry. Historical volatility is calculated over a period of time commensurate with the expected term of the stock-based payment. The Company uses an assumed dividend yield of zero as the Company has never paid dividends on its common stock, nor does it expect to pay dividends on its common stock in the foreseeable future. The Company accounts for forfeitures of all stock-based payments when such forfeitures occur.

Income Taxes

Income taxes are recorded in accordance with ASU No. 2019-12, *Income Taxes (Topic 740)* ("ASC 740") which provides for deferred taxes using an asset and liability approach. The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the consolidated financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. A valuation allowance against deferred tax assets is recorded if, based on the weight of the available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

The Company accounts for uncertain tax positions using a more-likely-than-not threshold for recognizing and resolving uncertain tax positions. The evaluation of uncertain tax positions is based on factors, including, but not limited to, changes in the law, the measurement of tax positions taken or expected to be taken in tax returns, the effective settlement of matters subject to audit, new audit activity and changes in facts or circumstances related to a tax position.

Comprehensive Loss

The Company does not have items of other comprehensive loss for the years ended December 31, 2021 and 2020, and therefore does not present a consolidated statement of comprehensive loss. The Company's comprehensive loss equals its net loss.

Net Loss per Common Share

Basic net loss per share is computed using the "two-class" method, which includes the weighted average number of shares of common stock outstanding during the period and other securities that participate in undistributed earnings (a participating security). The Company's redeemable convertible preferred stock and restricted stock awards are participating securities as defined by ASU No. 2017-10, *Earnings per Share (Topic 260)* ("ASC 260-10"). During the periods where the Company incurs net losses, the Company allocates no loss to participating securities because these securities have no contractual obligation to share in the losses of the Company. Under the two-class method, basic net loss per share applicable to common stockholders is computed by dividing the net loss applicable to common stockholders by the weighted average number of common shares outstanding for the period. Diluted net loss per share is computed similar to basic net loss per share except that the denominator is increased to include the number of additional shares for the potential dilutive effects of warrants, redeemable convertible preferred stock and stock options outstanding during the period calculated in accordance with the treasury stock method, or the two-class method, whichever is more dilutive. The Company allocates net earnings on a *pari passu* (equal) basis to both common and preferred stockholders. Net losses are not allocated to preferred stockholders as they do not have an obligation to share in the Company's net losses. For all periods presented, basic and diluted net loss per share are the same, as any additional share equivalents would be anti-dilutive.

Concentration of Credit Risk and Off-Balance Sheet Risk

Financial instruments that potentially subject the Company to significant concentrations of credit risk consist of cash and cash equivalents. Cash is held in a checking account at two financial institutions. At times, such deposits may be in excess of insured limits. The Company has not experienced any losses on its deposits of cash and cash equivalents. The Company has no significant off-balance sheet concentrations of credit risk, such as foreign currency exchange contracts, option contracts or other hedging arrangements.

Recent Accounting Pronouncements

In October 2020, the FASB issued ASU No. 2020-10, *Codification Improvements* ("ASU 2020-10"), which updates various codification topics by clarifying or improving disclosure requirements to align with the SEC's regulations. The Company adopted ASU 2020-10 as of the reporting period beginning January 1, 2021 and the adoption did not have material impact on the Company's consolidated balance sheets, consolidated statements of operations or related disclosures.

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments—Credit Losses (Topic 326), Measurement of Credit Losses on Financial Instruments*. This guidance amends the impairment model by requiring entities to use a forward-looking approach based on expected losses to estimate credit losses for most financial assets and certain other instruments that aren't measured at fair value through net income. The Company has adopted the new guidance effective January 1, 2021 and the adoption did not have any material impact on the Company's consolidated balance sheets, consolidated statements of operations or related disclosures.

In December 2019, the FASB issued ASU No. 2019-12, *Income Taxes (Topic 740), Simplifying the Accounting for Income Taxes* ("ASU 2019-12"), which is intended to simplify various areas related to accounting for income taxes. ASU 2019-12 removes certain exceptions to the general principles in ASC 740 and also clarifies and amends existing guidance to improve consistent application. For public business entities, the guidance is effective for annual reporting periods beginning after December 15, 2020 and for interim periods within those fiscal years. The Company adopted the standard effective January 1, 2021 and the adoption did not have a material impact on the Company's consolidated financial statements.

Subsequent Events

The Company has evaluated subsequent events and transactions that occurred after the balance sheet date up to the date that the financial statements were issued. Other than as described in these financial statements, the Company did not identify any subsequent events that would have required adjustment to or disclosure in the financial statements.

3. Financial Instruments and Fair Value Measurements

The Company measures the fair value of money market funds based on quoted prices in active markets for identical securities.

The carrying amounts reflected in the consolidated balance sheets for cash, prepaid expenses and other current assets, accounts payable and accrued expenses approximate their fair values, due to their short-term nature.

Assets measured at fair value on a recurring basis as of December 31, 2021 were as follows (in thousands):

	Quoted Price in Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total
Assets:				
Money market funds	$ 157,531	$ —	$ —	$ 157,531
Total assets	$ 157,531	$ —	$ —	$ 157,531

Assets measured at fair value on a recurring basis as of December 31, 2020 were as follows (in thousands):

	Quoted Price in Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total
Assets:				
Money market funds	$ 92,570	$ —	$ —	$ 92,570
Total assets	$ 92,570	$ —	$ —	$ 92,570

There were no changes in valuation techniques during the years ended December 31, 2021 and 2020. There were no liabilities measured at fair value on a recurring basis as of December 31, 2021 or 2020.

Preferred Stock Tranche Liability—During 2019, the Company issued 48,675,140 shares of Series A redeemable convertible preferred stock ("Series A Preferred Stock") which contained the preferred stock tranche liability. The fair value of the preferred stock tranche liability was $7.8 million upon issuance and was remeasured to $7.3 million as of December 31, 2019. The preferred stock tranche liability was settled in June 2020 upon the closing of the second tranche of the Series A Preferred Stock.

4. Restricted Cash

The Company maintained restricted cash of $1.3 million and $0.2 million at December 31, 2021 and December 31, 2020, respectively. At December 31, 2021, $0.1 million of the Company's restricted cash balance is included within "Prepaid expenses and other current assets" in the accompanying consolidated balance sheets. These amounts are comprised solely of letters of credit required pursuant to the Company's leased office spaces.

5. Property and Equipment, Net

Property and equipment, net as of December 31, 2021 and 2020 was comprised as follows (in thousands):

	Estimated Useful Life (in years)	December 31, 2021	December 31, 2020
Laboratory equipment	5	$ 839	$ 606
Furniture and office equipment	5	9	13
Computer equipment	3	221	19
Leasehold improvements	Shorter of 7 years or remaining lease term	274	188
Construction in progress		1,961	—
Total property and equipment, gross		3,304	826
Less: accumulated depreciation		(391)	(175)
Total property and equipment, net		$ 2,913	$ 651

Depreciation expense for the years ended December 31, 2021 and 2020 was $216,000 and $150,000, respectively.

6. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities as of December 31, 2021 and 2020 were comprised as follows (in thousands):

	December 31, 2021	December 31, 2020
Manufacturing	$ 3,427	$ 1,741
Employee compensation and benefits	2,200	990
Professional fees	433	654
Contract research	2,542	107
Other	163	94
Total accrued expenses and other current liabilities	$ 8,765	$ 3,586

7. Term Loan

In May 2020, the Company entered into a Loan and Security Agreement (the "Loan Agreement") with Pacific Western Bank ("PWB"). Under the terms of the Loan Agreement, PWB made available a term loan up to $6.0 million ("Term Loan A"). Based on the satisfaction of certain conditions defined in the Loan Agreement, PWB was also obligated to make available an additional term loan in the amount of up to $8.0 million until November 29, 2021 ("Term Loan B", or collectively with Term Loan A, the "Term Loans"). The Company satisfied the conditions to draw Term Loan B in June 2020. Although Term Loan A was made available to the Company at the closing date, the Company elected to forgo making a draw, thereby incurring a delayed draw fee of $25,000 with PWB.

The Term Loans would have borne interest on the outstanding daily balance at a floating annual rate equal to greater of: (i) 1.75% above the prime rate then in effect or (ii) 5.00%. If the prime rate changed throughout the term, the interest rate would have been adjusted effective on the date of the prime rate change. All interest chargeable under the Loan Agreement would have been computed on a 360-day year for the actual number of days elapsed, with interest payable monthly.

The Company would have been obligated to pay PWB a fee of 5.00% of the amount drawn under the Term Loans upon the occurrence of the Company achieving certain conditions defined in the Loan Agreement (the "Success Fee"). The Success Fee would have survived ten years from the date of payment of the Term Loan in full, such that, if the Loan Agreement was terminated prior to the payment of the Success Fee, the Company would have remained obligated to pay the Success Fee upon the occurrence of a Success Fee Event (as described in the Loan Agreement).

The Company determined that the Success Fee constituted a freestanding financial instrument that should be accounted for as a liability in connection with ASC 480—*Distinguishing Liabilities from Equity.* The Company determined that the fair value of the Success Fee was immaterial at both issuance and through the expiration of the Loan Agreement.

Borrowings under the Loan Agreement would have been secured by the Company's personal property (exclusive of any intellectual property) and were subject to acceleration in the event of default. In the event of a late payment or default, the Company would have been obligated to pay a fee equal to 5.0% of such unpaid amounts. In connection with the Loan Agreement, the Company was required to comply with certain covenants, which among other things, restricted the Company from (i) effectuating a merger or consolidation with or into any other business organization, (ii) paying dividends or making certain other distributions and (iii) making investments in any entities or instruments other than certain investments specified in the Loan Agreement. In addition, the Loan Agreement contained standard affirmative covenants, including with respect to the issuance of audited consolidated financial statements, insurance, and maintenance of good standing and government compliance in the Company's state of formation. The Company was also required to maintain unrestricted cash balances of at least 2.5 times its monthly cash burn, and had covenanted not to make any capital expenditures in excess of $0.4 million in the aggregate in any fiscal year without the prior written consent of PWB. In December 2020, the Loan Agreement was amended to allow the Company to make investments in its subsidiary, Werewolf Therapeutics Mass Securities, Inc., subject to certain conditions described in the Loan Agreement. In February 2021, the Loan Agreement was amended such that the Company may not make any capital expenditures in excess of $2.0 million in the aggregate in 2021 and $0.5 million in the aggregate in any fiscal year thereafter without the prior written consent of PWB.

PWB would have had the right to accelerate all obligations of the Company in the event of a material adverse effect on (i) the operations, business or financial condition of the Company, (ii) the Company's ability to repay any portion of the Term Loans or perform any of its other obligations under the Loan Agreement and (iii) the Company's interest in, or the value, perfection or priority of PWB's security interest in the collateral. The Company did not draw down any Term Loans, and as a result, the Loan Agreement expired on November 29, 2021.

8. Common and Preferred Stock

Common Stock

The Company is authorized to issue 200.0 million shares of common stock. Common stockholders are entitled to dividends if and when declared by the Company's board of directors. As of December 31, 2021, no dividends on common stock had been declared by the Company.

The Company had reserved shares of common stock for issuance as follows (in thousands):

	As of December 31,	
	2021	**2020**
Redeemable convertible preferred stock outstanding	—	18,280
Options issued and outstanding	3,266	2,059
Warrants issued and outstanding	59	59
Total	3,325	20,398

Redeemable Convertible Preferred Stock

The Company's Series A and Series B redeemable convertible preferred stock, together referred to as "Preferred Stock," was classified as temporary equity on the accompanying consolidated balance sheets in accordance with authoritative guidance for the classification and measurement of redeemable securities as the preferred stock was redeemable upon the occurrence of a deemed liquidation event. Upon completion of the Company's IPO, all of the Company's then outstanding preferred stock was automatically converted into an aggregate of 18.3 million shares of common stock.

Series A Preferred Stock

The Series A Preferred Stock shares were issued at various closing dates between 2019 and 2020 for a purchase price of $0.70 per share. The shares were issued in exchange for cash proceeds of $44.0 million, net of issuance costs of $0.2 million, and the exchange of approximately $12.0 million in outstanding convertible notes, including accrued interest.

Tranche Rights Issued with Series A Preferred Stock

Included in the terms of the Series A Preferred Stock purchase agreement (the "Series A Stock Purchase Agreement") were certain tranche rights (the "Tranche Rights"). The Tranche Rights obligated the Series A Preferred Stock investors to purchase, and the Company to sell, an additional 31,571,425 shares of Series A Preferred Stock for a purchase price of $0.70 per share (the "Second Closing") on November 1, 2020 or based on the election of each investor prior to the Second Closing. On May 12, 2020, the Series A Stock Purchase Agreement was amended such that the Second Closing would occur on June 1, 2020 or on an earlier date at the election of each investor.

The Company concluded that the Tranche Rights met the definition of a freestanding financial instrument, as the Tranche Rights were legally detachable and separately exercisable from the Series A Preferred Stock. Therefore, the Company allocated the net proceeds between the Tranche Rights and the Series A Preferred Stock. The trigger for the Second Closing was based on the passage of time or the election of the holders of Series A Preferred Stock. Based on the contractual terms, and the fact that the issuance was based on an event that was not within the control of the Company (i.e., written consent or passage of time), the Tranche Rights imposed an obligation on the Company to issue shares. Since the Series A Preferred Stock was contingently redeemable, the Tranche Rights were classified as a liability under ASC 480, *Distinguishing Liabilities from Equity*, and were initially recorded at fair value. The Tranche Rights were measured at fair value at each reporting period. Since the Tranche Rights were subject to fair value accounting, the Company allocated the proceeds to the Tranche Rights based on the fair value at the date of issuance with the remaining proceeds being allocated to the Series A Preferred Stock.

The estimated fair value of the Tranche Rights was determined using a probability-weighted present value model that considered the probability of closing a tranche, the estimated future value of Series A redeemable convertible preferred stock at each closing and the investment required at each closing. Future values were converted to present value using a discount rate appropriate for probability-adjusted cash flows. The Tranche Rights were initially recorded as a liability of $7.8 million. The Company remeasured the liability on each subsequent balance sheet date and prior to settlement and issuance of shares in connection with the Second Closing, which occurred on June 1, 2020.

Series B Preferred Stock

The Series B Preferred Stock shares were issued for a purchase price of $0.92 per share. The issuance resulted in cash proceeds of $71.8 million, net of issuance costs of $0.3 million.

Redemption

Upon certain change in control events that are outside of the Company's control, including liquidation, sale or transfer of control of the Company, the Preferred Stock was contingently redeemable. In addition, the Preferred Stock was redeemable at any time on or after the fifth anniversary of the original issue date. The Preferred Stock was redeemable at a price equal to the greater of (i) the original issue price of $0.70 per share for Series A Preferred stock and the original issue price of $0.92 per share for Series B Preferred Stock, respectively, or (ii) the fair market value of the Series A Preferred Stock and Series B Preferred Stock, as applicable, as of the redemption request date. As the Preferred Stock approached becoming redeemable due to the passage of time, the Company recorded changes in the redemption value and accreted the Preferred Stock immediately to redemption value as it occurred.

Preferred Stock

The Company is authorized to issue 5.0 million shares of undesignated preferred stock in one or more series. As of December 31, 2021, no shares of preferred stock were issued or outstanding.

9. Stock-based Compensation

2017 Stock Incentive Plan

In December 2017, the Company adopted the 2017 Stock Incentive Plan (the "2017 Plan"), as amended and restated, under which it could grant incentive stock options ("ISOs"), non-qualified stock options, RSAs, RSUs, stock appreciation rights and other stock-based awards to eligible employees, officers, directors and consultants. The terms of stock options and restricted stock awards, including vesting requirements, are determined by the board of directors, subject to the provisions of the Plan.

2021 Stock Incentive Plan

In April 2021, the board of directors adopted and the Company's stockholders approved the 2021 Stock Incentive Plan (the "2021 Plan"), which became effective immediately prior to the effectiveness of the Company's IPO. As a result of the adoption of the 2021 Plan, no further awards will be made under the 2017 Plan.

The 2021 Plan provides for the grant of ISOs, non-qualified stock options, RSAs, RSUs, stock appreciation rights and other stock-based awards. The Company's employees, officers, directors, consultants and advisors are eligible to receive awards under the 2021 Plan. The terms of awards, including vesting requirements, are determined by the board of directors, subject to the provisions of the 2021 Plan.

The Company initially registered 3,352,725 shares of common stock under the 2021 Plan, pursuant to a Registration Statement on Form S-8 filed with the SEC on April 30, 2021, which was comprised of (i) 2,843,116 shares of common stock reserved for issuance under the 2021 Plan, (ii) 31,884 shares of common stock originally reserved for issuance under the 2017 Plan that became available for issuance under the

2021 Plan upon the completion of the Company's IPO, and (iii) 477,725 shares of unvested restricted stock subject to repurchase by us that may become issuable under the 2021 Stock Incentive Plan following such repurchase. The 2021 Plan also provides that an additional number of shares will be added annually to the shares authorized for issuance under the 2021 Plan on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2022 and continuing until, and including, the fiscal year ended December 31, 2031. The number of shares added each year will be equal to the lesser of (i) 5% of the number of outstanding common stock on such date and (ii) such amount as determined by the board of directors.

As of December 31, 2021, there were 1,938,895 shares available for future issuance under the 2021 Plan.

2021 Employee Stock Purchase Plan

In April 2021, the board of directors adopted and the Company's stockholders approved the 2021 Employee Stock Purchase Plan (the "2021 ESPP"), which became effective immediately prior to the effectiveness of the Company's IPO. The Company initially reserved 244,000 shares of common stock for future issuance under the 2021 ESPP. The 2021 ESPP provides that an additional number of shares will automatically be added to the shares reserved for issuance on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2022 and continuing for each fiscal year until, and including, the fiscal year ending on December 31, 2032. The number of shares added each year will be equal to the lowest of (i) 488,000 shares of common stock, (ii) 1% of the number of shares of outstanding common stock on such date, and (iii) such amount as determined by the board of directors. The Company had not initiated any offering periods under the 2021 ESPP as of December 31, 2021.

Stock-Based Compensation Expense

Total stock-based compensation expense recognized in the consolidated statements of operations for the years ended December 31, 2021 and 2020 was as follows (in thousands):

	Year Ended December 31,	
	2021	**2020**
Research and development	$ 1,524	$ 192
General and administrative	2,571	440
Total stock-based compensation	$ 4,095	$ 632

Restricted Stock Activity

The Company may, at its discretion, repurchase unvested shares of restricted stock issued pursuant to the 2017 Plan at the initial purchase price if the employees or non-employees terminate their service relationship with the Company. The shares are recorded in stockholders' deficit as they vest.

The following table summarizes restricted stock award activity during the year ended December 31, 2021 (in thousands, except per share amounts):

	Shares/Units	**Weighted-Average Grant Date Fair Value Per Share**
Unvested at December 31, 2020	562	$ 1.54
Granted	—	$ —
Vested	(267)	$ 1.87
Forfeited	—	$ —
Unvested at December 31, 2021	295	$ 1.35

As of December 31, 2021, there was unrecognized stock-based compensation expense related to unvested restricted stock awards of $0.4 million, which the Company expects to recognize over a weighted-average period of approximately 1.3 years.

The aggregate fair value of restricted stock awards that vested during the years ended December 31, 2021 and 2020, based upon the fair values of the stock underlying the restricted stock awards on the day of vesting, was $3.6 million and $0.6 million, respectively.

Stock Option Activity

The fair value of stock options granted during the years ended December 31, 2021 and 2020 was calculated on the date of grant using the following weighted-average assumptions:

	Year Ended December 31,	
	2021	**2020**
Risk-free interest rate	1.0 %	0.5 %
Expected term (in years)	6.0	6.1
Dividend yield	— %	— %
Expected volatility	78.7 %	82.8 %

Using the Black-Scholes option pricing model, the weighted-average grant date fair value of stock options granted during the years ended December 31, 2021 and 2020 was $9.72 and $2.73 per share, respectively.

The following table summarizes stock option activity during the year ended December 31, 2021 (in thousands, except per share amounts):

	Options Outstanding		
	Number of Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Life (in years)
Outstanding at December 31, 2020	2,059	$ 3.79	9.76
Granted	1,383	$ 14.38	
Exercised	(82)	$ 2.86	
Cancelled	(94)	$ 5.58	
Outstanding, December 31, 2021	3,266	$ 8.24	9.02
Exercisable at December 31, 2021	593	$ 5.07	8.76

The aggregate intrinsic fair value of stock options exercised during the years ended December 31, 2021 and 2020 was $0.8 million and less than $0.1 million, respectively.

As of December 31, 2021, there was unrecognized stock-based compensation expense related to unvested stock options of $14.8 million, which the Company expects to recognize over a weighted-average period of approximately 2.9 years.

10. Commitments and Contingencies

Leases

The Company's leases are as follows:

- An April 2019 operating lease for approximately 9,949 square feet of office and laboratory space which commenced in April 2019 and terminates in March 2024. The lease is subject to fixed-rate rent escalations and provided for a term extension option, which was not reasonably certain of exercise.
- A March 2021 short-term lease for approximately 7,500 square feet of office and laboratory space which commenced in April 2021 and terminates in May 2022. The Company did not recognize an operating lease right of use asset or a lease liability upon lease commencement. Rent expense for our short-term lease is recognized as incurred.
- A June 2021 operating lease for approximately 25,778 square feet of office and laboratory space which is targeted for occupancy in April 2022 and terminates in April 2030. The lease is subject to fixed-rate rent escalations and provided for $5.7 million in tenant improvements and a term extension option, which was not reasonably certain of exercise. The Company provided the landlord with a security deposit in the form of a letter of credit in the amount of $1.0 million upon signing, which is included in restricted cash as of December 31, 2021.

Accounting under ASC 842:

- Expected lease term: The expected lease term includes noncancelable lease periods and, when applicable, periods covered by an option to extend the lease if the Company is reasonably certain to exercise that option, as well as periods covered by an option to terminate the lease if the Company is reasonably certain not to exercise that option.
- Incremental borrowing rate: As the discount rates in the Company's lease are not implicit, management estimated the incremental borrowing rate based on the rate of interest the Company would have to pay to borrow a similar amount on a collateralized basis over a similar term.
- Lease and non-lease components: The Company is required to pay fees for operating expenses in addition to monthly base rent for certain operating leases (non-lease components). The Company has elected the practical expedient which allows non-lease components to be combined with lease components for all asset classes. Variable non-lease components are not included within the lease right-of-use asset and lease liability on the consolidated balance sheet, and instead are reflected as expense in the period they are paid.

The following table summarizes operating lease costs (in thousands):

	Year Ended December 31,	
	2021	2020
Operating lease costs	$ 1,312	$ 877
Variable lease costs	398	208
Short-term lease costs	411	—
Total	$ 2,121	$ 1,085

The following table summarizes the lease term and discount rate for operating leases:

	As of December 31,	
	2021	2020
Weighted-average remaining lease term (years)	7.6	3.3
Weighted-average discount rate	8.1 %	9.3 %

As of December 31, 2021, the future minimum lease payments due under the Company's leases are as follows (in thousands):

	Amount
2022	$ 2,494
2023	3,138
2024	2,511
2025	2,343
2026	2,409
Thereafter	8,527
Total remaining minimum rental payments	21,422
Less: effect of discounting	(5,761)
Total lease liability	$ 15,661

License Agreements

Harpoon License

In March 2018, the Company entered into a Patent Assignment and License Agreement (the "Harpoon Agreement") with Harpoon Therapeutics, Inc. ("Harpoon"), a clinical-stage immune-oncology company developing a novel class of T-cell engagers to fight cancer and other diseases. Under the terms of the Harpoon Agreement, Harpoon granted the Company a license to use its intellectual property, solely to make, have made, use, sell, offer for sale and import covered products in the licensed field and Harpoon sold, assigned and transferred other specific patents to the Company (the "Harpoon License").

On October 19, 2018, the Company and Harpoon entered into the First Amended and Restated Assignment and License Agreement which amended certain terms of the original agreement, but did not change the terms of the license to the Company, patent assignments between the parties or payments due to Harpoon. Further, on December 20, 2019, the companies entered into the Second Amended and Restated Assignment and License Agreement, which also amended certain terms of the original agreement to expand the licenses and assignments for specific patents granted to the Company or by the Company to Harpoon. In exchange for these additional terms, Harpoon agreed to reimburse up to $75,000 of the Company's legal costs. Additionally, the Company agreed to pay to Harpoon royalties on future net sales and pay minimum annual royalties of $250,000 upon achievement of its first commercial sale.

Under the terms of the Harpoon License, the Company paid an upfront fee of $500,000 in 2018 and is obligated to reimburse Harpoon for certain legal costs incurred by Harpoon. In addition, the Company is obligated to pay Harpoon royalties based on future net sales and has agreed to pay a minimum annual royalty payment at an amount in the low hundreds of thousands of dollars upon achievement of its first commercial sale. In 2018, the Company recorded the upfront fee as research and development expense upon payment as the intellectual property was acquired prior to regulatory approval and does not have an alternative future use. The royalty payments are contingent upon sales and, as such, the royalty payments made to Harpoon will be considered probable and estimable and treated as cost of sales when incurred. Accordingly, at the commencement of sales, the Company will account for the royalty payments as cost of sales equal to the greater of a percentage in the low-single digits of the net sales of the patent-covered products or a minimum annual royalty payment at an amount in the low hundreds of thousands of dollars. Any legal fees incurred in connection with the Harpoon Agreement will be expensed as incurred.

The Harpoon License will expire on a country-by-country basis upon the expiration of the last to expire patent or patent application included in the licensed patents within the applicable country. The Company has the right to terminate the Harpoon License upon 30 days prior written notice to Harpoon, and either party may terminate for a material breach if such breach is not cured within a specified number of days.

Adimab License

In March 2018, the Company entered into a Development and Option Agreement (the "Adimab Agreement") with Adimab LLC ("Adimab"), a company specializing in antibody discovery, humanization and optimization. Under the terms of the Adimab Agreement, Adimab granted the Company the rights to initiate certain research initiatives on a specified number of targets. Adimab also granted to the Company a license to certain Adimab core technologies, antibodies and products applicable to certain targets ("Adimab License").

In August 2020, the Company and Adimab entered into Amendment One to the Development and Option Agreement, which extended the period of time for the Company to evaluate candidate antibodies in advance of electing to exercise the option to acquire exclusive rights to licensed antibodies (the "Evaluation Term"), but did not otherwise change the terms of the Adimab License. The Evaluation Term was then further extended in December 2020 by entering into Amendment Two to the Development and Option Agreement, through delivery of a non-refundable payment of $100,000 by the Company to Adimab, which was creditable toward the option fee. The non-refundable payment was recorded immediately as research and development expense in the consolidated statements of operations.

Under the terms of the Adimab License, the Company must pay both an upfront fee and final fee of $200,000 for all research programs. The Company must also pay Adimab milestone fees with respect to each research program ranging from $150,000 to $200,000 based on the

achievement of technical milestones by Adimab for the applicable research program. In order to exercise any options in the Adimab Agreement, the Company must pay a $500,000 fee for each target option exercised.

For each target option exercised, the Company is also obligated to pay certain milestones ranging from $1.0 million to $4.0 million for certain clinical and commercialization achievements. Additionally, for licensed products sold during the applicable royalty term, the Company must pay Adimab royalties at percentages in the low-to-mid single digits.

The Adimab Agreement will expire upon the expiration of any options or if an option is exercised, on a country-by-country and licensed product-by-licensed product basis on the expiration of the last royalty term for a licensed product in the particular country. As of December 31, 2021, the Company exercised one target option, but has not recorded any milestone or royalty payments pursuant to the Adimab Agreement.

Clinical Trial Collaboration and Supply Agreement

In August 2021, the Company entered into a Clinical Trial Collaboration and Supply Agreement, or Clinical Supply Agreement, with Merck & Co., Inc., or Merck, to evaluate WTX-124 in combination with KEYTRUDA® (pembrolizumab), Merck's anti-PD-1 therapy. The planned clinical trial will be conducted by the Company and is designed to evaluate the safety and preliminary efficacy of WTX-124 as a monotherapy and in combination with pembrolizumab in patients with solid tumors. Under the terms of the Clinical Supply Agreement, the Company will sponsor the study and Merck will supply the Company with pembrolizumab in exchange for jointly owning any inventions or discoveries relative to the combined use of WTX-124 and pembrolizumab. Each party is responsible for its own internal costs and expenses to support the trial.

11. Income Taxes

During the years ended December 31, 2021 and 2020, the Company recorded no current or deferred income tax expenses or benefits as the Company has incurred losses since inception and has provided a full valuation allowance against its deferred tax assets.

A reconciliation of the expected income tax (benefit) computed using the federal statutory income tax rate to the Company's effective income tax rate is as follows:

	Year Ended December 31,	
	2021	2020
Income tax computed at federal statutory rate	21.0 %	21.0 %
State taxes, net of federal benefit	5.7	9.9
Change in valuation allowance	(27.2)	(42.0)
R&D credit carryovers	1.8	1.7
Interest expense	0.0	0.0
Stock-based compensation	(0.9)	(0.8)
Cancellation of tranche rights	0.0	10.2
Permanent differences	(0.4)	0.0
Effective income tax rate	0.0 %	0.0 %

The Company's deferred tax assets consist of the following (in thousands):

	As of December 31,	
	2021	2020
Deferred tax assets:		
Net operating losses	$ 22,831	$ 10,363
Tax credit carryforwards	1,918	1,021
Lease liability	4,393	731
Capitalized costs—net of amortization	111	124
Reserves and accruals	658	264
Stock-based compensation	500	—
Deferred tax assets	30,411	12,503
Valuation allowance	(26,110)	(11,776)
Deferred tax assets recognized	4,301	727
Deferred tax liabilities:		
Right of use asset	(3,762)	(711)
Fixed assets and depreciation	(6)	(12)
Construction in progress	(533)	—
Other	—	(4)
Deferred tax liabilities	(4,301)	(727)
Net deferred tax assets	$ —	$ —

The Company evaluated the positive and negative evidence bearing upon its ability to realize the deferred tax assets as of December 31, 2021 and 2020. Management considered the Company's cumulative net losses and concluded as of December 31, 2021 and 2020, that it was more likely than not that the Company would not realize the benefits of the deferred tax assets. Accordingly, a full valuation allowance was established against the net deferred tax assets as of December 31, 2021 and 2020. The valuation allowance increased by $14.3 million and $6.7 million for the years ended December 31, 2021 and 2020, respectively, primarily as a result of operating losses generated with no corresponding financial statement benefit.

The Company has incurred net operating losses ("NOL") since inception. As of December 31, 2021 and 2020, the Company had federal net operating loss carryforwards of $80.3 million and $35.9 million, respectively, available to reduce future federal taxable income. The carryforwards generated in 2017 expire in 2037. $80.2 million of carryforwards generated post 2017 do not expire. The TCJA enacted on December 22, 2017 limits a taxpayer's ability to utilize NOL deduction in a year to 80% taxable income for federal net operating losses arising in tax years beginning after 2017. The Coronavirus Aid, Relief, and Economic Security Act enacted on March 27, 2020 removes the 80% taxable income limitation for NOL deductions in taxable years beginning prior to January 1, 2021. As of December 31, 2021 and 2020, the Company had state net operating loss carryforwards of $74.5 million and $35.3 million, respectively, available to reduce future state taxable income, which expire at various dates beginning in 2037.

As of December 31, 2021 and 2020, the Company had federal research and development tax credit carryforwards of $1.3 million and $0.6 million, respectively, available to reduce future federal tax liabilities, which expire at various dates beginning in 2038. The Company also had state research and development tax credit carryforwards as of December 31, 2021 and 2020 of $0.6 million and $0.4 million, respectively, available to reduce future state tax liabilities, which expire at various dates beginning in 2033.

Utilization of the Company's net operating loss carryforwards and research and development tax credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986 due to ownership changes that have occurred previously or that could occur in the future. These ownership changes may limit the amount of carryforwards that can be utilized annually to offset future taxable income. In general, an ownership change, as defined by 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. The Company is in the process of performing a Section 382 study to assess whether a change of control has occurred or whether there have been multiple changes of control since inception. If the Company has experienced a change of control, as defined by Section 382, at any time since inception, utilization of the net operating loss carryforwards or research and development tax credit carryforwards would be subject to an annual limitation under Section 382, which is determined by first multiplying the value of the Company's stock at the time of the ownership change by the applicable long-term tax-exempt rate, and then could be subject to additional adjustments, as required. Any limitation may result in expiration of a portion of the net operating loss carryforwards or research and development tax credit carryforwards before utilization. Further, until the Section 382 study is completed, and any limitation is known, no amounts are being presented as an uncertain tax position.

The Company has not recorded any reserves for uncertain tax positions as of December 31, 2021 and 2020. The Company has conducted a study of research and development tax credit. The amounts of federal and state research and development tax credit carryforwards presented above have reflected the results from the study. A full valuation allowance has been provided against the Company's research and development credits.

The Company files tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In the normal course of business, the Company is subject to examination by federal and state jurisdictions, where applicable. There are currently no pending tax examinations. The Company's tax years are still open under statute from inception to the present.

12. Related Parties

During the year ended December 31, 2020, the Company recorded $31,000 of general and administrative expense in the accompanying consolidated statements of operations related to management services provided by MPM Capital. Additionally, as of December 31, 2020, the Company recorded $8,000 in accounts payable in the accompanying consolidated balance sheets related to the provision of management services by MPM Capital. The Company did not incur any expense with MPM Capital for the year ended December 31, 2021.

In December 2019, the Company entered into a consulting agreement with Briggs Morrison, M.D., a member of the Company's board of directors, for the provision of consulting, advisory and related services. Pursuant to the consulting agreement, in December 2019, the Company issued Dr. Morrison a stock option grant for 46,570 shares of common stock at an aggregate grant date fair value of $50,000, and agreed to reimburse certain of Dr. Morrison's expenses in connection with the performance of services under the agreement. The stock options have an exercise price of $1.56 per share and are scheduled to vest with respect to 2.0833% of the shares underlying the grant in equal monthly installments over four years following November 2019, subject to continuous service. The Company recognized $13,000 of expense related to this award in the research and development line in the consolidated statements of operations for each of the years ended December 31, 2021 and 2020.

13. 401(k) Savings Plan

The Company has a defined-contribution savings plan under Section 401(k) of the Internal Revenue Code (the "401(k) Plan"). The 401(k) Plan covers all employees who meet defined minimum age and service requirements, and allows participants to defer a portion of their annual compensation on a pretax basis. As currently established, the Company is not required to make and has not made any contributions to the 401(k) Plan to date.

14. Net Loss Attributable to Common Stockholders per Share

For purposes of the diluted net loss attributable to common stockholders per share calculation, redeemable convertible preferred stock, outstanding stock options, unvested restricted stock awards and warrants to purchase common stock are considered to be potentially dilutive

securities, however the following weighted-average amounts were excluded from the calculation of diluted net loss attributable to common stockholders per share because their effect would be anti-dilutive (in thousands):

	December 31,	
	2021	2020
Redeemable convertible preferred stock (as converted)	—	18,280
Outstanding stock options	3,266	2,059
Unvested restricted common stock	295	562
Warrants to purchase common stock	59	59
Total	3,620	20,960

EXHIBIT INDEX

Exhibit No.	Description of Exhibit
3.1	Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K, filed with the Securities and Exchange Commission on May 5, 2021, File No. 001-40366).
3.2	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K, filed with the Securities and Exchange Commission on May 5, 2021, File No. 001-40366).
4.1	Specimen Stock Certificate evidencing the shares of common stock of the Registrant (incorporated by reference to Exhibit 4.1 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1, filed with the Securities and Exchange Commission on April 26, 2021, File No. 333-255132).
4.2	Amended and Restated Investors' Rights Agreement, dated as of December 23, 2020, by and among the Registrant and the other parties thereto (incorporated by reference to Exhibit 4.2 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1, filed with the Securities and Exchange Commission on April 26, 2021, File No. 333-255132).
4.3*	Description of Securities Registered Pursuant to Section 12 of the Securities Exchange Act of 1934 of the Registrant.
10.1	2017 Stock Incentive Plan (incorporated by reference to Exhibit 10.1 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1, filed with the Securities and Exchange Commission on April 26, 2021, File No. 333-255132).
10.2	Form of Stock Option Agreement under 2017 Stock Incentive Plan (incorporated by reference to Exhibit 10.2 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1, filed with the Securities and Exchange Commission on April 26, 2021, File No. 333-255132).
10.3	Form of Restricted Stock Agreement under 2017 Stock Incentive Plan (incorporated by reference to Exhibit 10.3 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1, filed with the Securities and Exchange Commission on April 26, 2021, File No. 333-255132).
10.4	2021 Stock Incentive Plan (incorporated by reference to Exhibit 10.4 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1, filed with the Securities and Exchange Commission on April 26, 2021, File No. 333-255132).
10.5	Form of Stock Option Agreement under 2021 Stock Incentive Plan (incorporated by reference to Exhibit 10.5 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1, filed with the Securities and Exchange Commission on April 26, 2021, File No. 333-255132).
10.6	Form of Restricted Stock Agreement under 2021 Stock Incentive Plan (incorporated by reference to Exhibit 10.6 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1, filed with the Securities and Exchange Commission on April 26, 2021, File No. 333-255132).
10.7	Form of Restricted Stock Unit Agreement under 2021 Stock Incentive Plan (incorporated by reference to Exhibit 10.7 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1, filed with the Securities and Exchange Commission on April 26, 2021, File No. 333-255132).
10.8	2021 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.8 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1, filed with the Securities and Exchange Commission on April 26, 2021, File No. 333-255132).
10.9	Form of Indemnification Agreement between the Registrant and each of its Executive Officers and Directors (incorporated by reference to Exhibit 10.10 to the Registrant's Registration Statement on Form S-1, filed with the Securities and Exchange Commission on April 8, 2021, File No. 333-255132).
10.10#	Second Amended and Restated Assignment and License Agreement dated as of December 20, 2019, by and between the Registrant and Harpoon Therapeutics, Inc (incorporated by reference to Exhibit 10.11 to the Registrant's Registration Statement on Form S-1, filed with the Securities and Exchange Commission on April 8, 2021, File No. 333-255132).
10.11	Amended and Restated Royalty Transfer Agreement dated as of August 2, 2019, by and among MPM Oncology Impact Fund Charitable Foundation, Inc. and UBS Optimus Foundation (incorporated by reference to Exhibit 10.12 to the Registrant's Registration Statement on Form S-1, filed with the Securities and Exchange Commission on April 8, 2021, File No. 333-255132).
10.12	Lease Agreement dated as of March 28, 2019, by and between the Registrant and Cambridge 1030 Mass Ave, LLC (incorporated by reference to Exhibit 10.9 to the Registrant's Registration Statement on Form S-1, filed with the Securities and Exchange Commission on April 8, 2021, Registration No. 333-255132, File No. 333-255132).
10.13	Lease Agreement dated as of March 3, 2021, by and between the Registrant and ARE-480 Arsenal Street, LLC (incorporated by reference to Exhibit 10.14 to the Registrant's Registration Statement on Form S-1, filed with the Securities and Exchange Commission on April 8, 2021, File No. 333-255132).
10.14	Lease Agreement dated as of June 1, 2021, by and between the Registrant and ARE-MA Region No. 75, LLC. (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, filed with the Securities and Exchange Commission on June 2, 2021, File No. 001-40366).
10.15+	Employment Agreement dated as of April 23, 2021, by and between the Registrant and Daniel J. Hicklin, Ph.D. (incorporated by reference to Exhibit 10.15 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1, filed with the Securities and Exchange Commission on April 26, 2021, File No. 333-255132).
10.16+	Employment Agreement dated as of April 23, 2021, by and between the Registrant and Randi Isaacs M.D. (incorporated by reference to Exhibit 10.16 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1, filed with the Securities and Exchange Commission on April 26, 2021, File No. 333-255132).
10.17+	Employment Agreement dated as of April 23, 2021, by and between the Registrant and Cynthia Seidel-Dugan, Ph.D. (incorporated by reference to Exhibit 10.17 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1, filed with the Securities and Exchange Commission on April 26, 2021, File No. 333-255132).
10.18+	Employment Agreement dated as of April 23, 2021, by and between the Registrant and Reid Leonard, Ph.D. (incorporated by reference to Exhibit 10.18 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1, filed with the Securities and Exchange Commission on April 26, 2021, File No. 333-255132).

10.19+	Employment Agreement dated as of April 23, 2021, by and between the Registrant and Ellen Lubman, M.B.A. (incorporated by reference to Exhibit 10.19 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1, filed with the Securities and Exchange Commission on April 26, 2021, File No. 333-255132).
10.20+	Employment Agreement dated as of April 23, 2021, by and between the Registrant and Timothy W. Trost (incorporated by reference to Exhibit 10.20 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1, filed with the Securities and Exchange Commission on April 26, 2021, File No. 333-255132).
10.21+	Employment Agreement dated as of April 30, 2021 by and between the Registrant and Chulani Karunatilake (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q, filed with the Securities and Exchange Commission on November 10, 2021, File No. 001-40366).
21.1	Subsidiaries of the Registrant (incorporated by reference to Exhibit 21.1 to Amendment No. 1 to the Registrant's Registration Statement on Form S-1, filed with the Securities and Exchange Commission on April 26, 2021, Registration No. 333-255132).
23.1*	Consent of Deloitte & Touche LLP, Independent Registered Accounting Firm.
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1†	Certifications of Principal Executive Officer 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 (formatted as Inline XBRL with applicable taxonomy extension information contained in Exhibits 101)

*	Filed herewith.
†	The certifications attached as Exhibit 32.1 that accompany this Annual Report, are deemed furnished and not filed with the Securities and Exchange Commission and are not to be incorporated by reference into any filing of Werewolf Therapeutics, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Annual Report, irrespective of any general incorporation language contained in such filing.
+	Indicates management contract.
#	Portions of this exhibit have been omitted pursuant to Item 601(b)(10)(iv) of Regulation S-K because such information is not material and is the type of information that the registrant treats as private or confidential.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

WEREWOLF THERAPEUTICS, INC.

Date: March 24, 2022

By: /s/ Daniel J. Hicklin
Daniel J. Hicklin, Ph.D.
President and Chief Executive Officer

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

SIGNATURE	TITLE	DATE
/s/ Daniel J. Hicklin Daniel J. Hicklin, Ph.D.	President, Chief Executive Officer and Director (Principal Executive Officer)	March 24, 2022
/s/ Timothy W. Trost Timothy W. Trost	Chief Financial Officer and Treasurer (Principal Financial and Accounting Officer)	March 24, 2022
/s/ Luke Evnin Luke Evnin, Ph.D.	Chair of the Board of Directors	March 24, 2022
/s/ Sakae Asanuma Sakae Asanuma, C.F.A.	Director	March 24, 2022
/s/ Meeta Chatterjee Meeta Chatterjee, Ph.D.	Director	March 24, 2022
/s/ Derek DiRocco Derek DiRocco, Ph.D.	Director	March 24, 2022
/s/ Alon Lazarus Alon Lazarus, Ph.D.	Director	March 24, 2022
/s/ Briggs W. Morrison Briggs W. Morrison, M.D.	Director	March 24, 2022
/s/ Michael A. Sherman Michael A. Sherman, M.B.A.	Director	March 24, 2022

Exhibit 4.3

DESCRIPTION OF SECURITIES REGISTERED UNDER SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934, AS AMENDED

The following description of the securities of Werewolf Therapeutics, Inc. ("us," "our," "we" or the "Company") registered under Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), is intended as a summary only and therefore is not a complete description. This description is based upon, and is qualified by reference to, our certificate of incorporation, our bylaws and applicable provisions of the Delaware General Corporation Law (the "DGCL"). You should read our certificate of incorporation and bylaws, which are filed as Exhibit 3.1 and Exhibit 3.2, respectively, to the Annual Report on Form 10-K of which this Exhibit 4.3 is a part, for the provisions that are important to you.

Authorized Capital Stock

Our authorized capital stock consists of 200.000.000 shares of common stock, par value $0.0001 per share, and 5,000,000 shares of preferred stock, par value $0.0001 per share, all of which preferred stock is undesignated. Our common stock is registered under Section 12(b) of the Exchange Act.

Common Stock

Voting Rights. Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. Each election of directors by our stockholders will be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Any matters other than the election of directors to be voted upon by the stockholders at a meeting are decided by the vote of the holders of shares of stock having a majority in voting power of the votes cast by the holders of all of the shares of stock present or represented at the meeting and voting affirmatively or negatively on such matter, except when a different vote is required by law, our certificate of incorporation or our bylaws.

Dividends. Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend or other rights of any outstanding preferred stock.

Liquidation, Dissolution and Winding Up. In the event of our liquidation, dissolution or winding up, the holders of our common stock are entitled to receive proportionately all assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to any preferential or other rights of any outstanding preferred stock.

Other Rights. Holders of our common stock have no preference, preemptive, subscription, redemption or conversion rights. All outstanding shares of our common stock are fully paid and not liable to further calls or assessment by us. The rights, preferences and privileges of holders of our common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of our preferred stock that we may designate and issue in the future.

Preferred Stock

Under the terms of our certificate of incorporation, our board of directors is authorized to issue up to 5,000,000 shares of "blank check" preferred stock in one or more series without stockholder approval. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock. The issuance of preferred stock could impede the completion of a merger, tender offer or other takeover attempt.

Provisions of Our Certificate of Incorporation and Bylaws and the DGCL That May Have Anti-Takeover Effects

Board of Directors; Removal of Directors. Our certificate of incorporation and our bylaws divide our board of directors into three classes with staggered three-year terms. In addition, our certificate of incorporation and our bylaws provide that directors may be removed only for cause and only by the affirmative vote of the holders of at least two-thirds of our shares of capital stock present in person or by proxy and entitled to vote in an election of directors or class of directors. Under our certificate of incorporation and our bylaws, any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office. Furthermore, our certificate of incorporation provides that the authorized number of directors may be changed only by the resolution of our board of directors. The classification of our board of directors and the limitations on the ability of our stockholders to remove directors, change the authorized number of directors and fill vacancies could make it more difficult for a third party to acquire, or discourage a third party from seeking to acquire, control of our company.

Stockholder Action; Special Meeting of Stockholders; Advance Notice Requirements for Stockholder Proposals and Director Nominations. Our certificate of incorporation and our bylaws provide that any action required or permitted to be taken by our stockholders at an annual meeting or special meeting of stockholders may only be taken if it is properly brought before such meeting and may not be taken by written action in lieu of a meeting. Our certificate of incorporation and our bylaws also provide that, except as otherwise required by law, special meetings of the stockholders can only be called by our board of directors. In addition, our bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of stockholders, including proposed nominations of candidates for election to our board of directors. Stockholders at an annual meeting may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of our board of directors, or by a stockholder of record on the record date for the meeting who is entitled to vote at the meeting and who has delivered timely written notice in proper form to our secretary of the stockholder's intention to bring such business before the meeting. These provisions could have the effect of delaying until the next stockholder meeting stockholder actions that are favored by the holders of a majority of our outstanding voting securities. These provisions also could discourage a third party from making a tender offer for our common stock because even if the third party acquired a majority of our outstanding voting stock, it would be able to take action as a stockholder, such as electing new directors or approving a merger, only at a duly called stockholders meeting and not by written consent.

Super-Majority Voting. The DGCL provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or bylaws unless a corporation's certificate of incorporation or bylaws, as the case may be, requires a greater percentage. Our bylaws may be amended or repealed by a majority vote of our board of directors or the affirmative vote of the holders of at least two-thirds of the votes that all our stockholders would be entitled to cast in any annual election of directors. In addition, the affirmative vote of the holders of at least two-thirds of the votes that all our stockholders would be entitled to cast in any election of directors is required to amend or repeal or to adopt any provisions inconsistent with any of the provisions of our certificate of incorporation described above.

Delaware Business Combination Statute. We are subject to Section 203 of the DGCL. Subject to certain exceptions, Section 203 prevents a publicly held Delaware corporation from engaging in a "business combination" with any "interested stockholder" for three years following the date that the person became an interested stockholder, unless either the interested stockholder attained such status with the approval of our board of directors, the business combination is approved by our board of directors and stockholders in a prescribed manner or the interested stockholder acquired at least 85% of our outstanding voting stock in the transaction in which it became an interested stockholder. A "business combination" includes, among other things, a merger or consolidation involving us and the "interested stockholder" and the sale of more than 10% of our assets. In general, an "interested stockholder" is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person.

Exclusive Forum Selection. Our certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Court of Chancery of the State of Delaware does not have jurisdiction, the federal district court for the District of Delaware) shall, to the fullest extent permitted by law, be the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, other employees or stockholders to our company or our stockholders, (3) any action asserting a claim arising pursuant to any provision of the DGCL or as to which the DGCL confers jurisdiction on the Court of Chancery of the State of Delaware or (4) any action asserting a claim arising pursuant to any provision of our certificate of incorporation or bylaws (in each case, as they may be amended from time to time) or governed by the internal affairs doctrine. This choice of forum provision will not apply to actions arising under the Securities Act of 1933, as amended (the "Securities Act"), the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction. Unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States of America shall, to the fullest extent permitted by law, be the sole and exclusive forum for the resolution of any claims arising under the Securities Act. Although our certificate of incorporation contains the choice of forum provisions described above, it is possible that a court could rule that such a provision is inapplicable for a particular claim or action or that such provision is unenforceable.

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in Registration Statement No. 333-255636 on Form S-8 of our report dated March 24, 2022, relating to the financial statements of Werewolf Therapeutics, Inc. appearing in this Annual Report on Form 10-K for the year ended December 31, 2021.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
March 24, 2022

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, Daniel J. Hicklin, Ph.D., certify that:

1. I have reviewed this Annual Report on Form 10-K of Werewolf 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 and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) 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

   (c) 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 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 24, 2022

By: /s/ Daniel J. Hicklin
Daniel J. Hicklin, Ph.D.
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, Timothy W. Trost, certify that:

1. I have reviewed this Annual Report on Form 10-K of Werewolf 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 and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) 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

   (c) 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 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 24, 2022

By: /s/ Timothy W. Trost
Timothy W. Trost
Chief Financial Officer and Treasurer
(Principal Financial and 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 Annual Report on Form 10-K of Werewolf Therapeutics, Inc. (the "Company") for the period ending December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers of the Company hereby certifies, pursuant to 18 U.S.C. Section 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 Section 15(d), as applicable, of the Securities Exchange Act of 1934, as amended; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

: March 24, 2022 By: /s/ Daniel J. Hicklin
Daniel J. Hicklin, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

: March 24, 2022 By: /s/ Timothy W. Trost
Timothy W. Trost
Chief Financial Officer and Treasurer
(Principal Financial and Accounting Officer)