UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2022
OR

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

For the transition period from _____ to _____

Commission File Number: 001-39971

Landos Biopharma, Inc.
(Exact Name of Registrant as Specified in its Charter)

Delaware	**81-5085535**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
P.O. Box 11239 **Blacksburg, Virginia**	**24062**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (540) 218-2232

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common stock, par value $0.01 per share	LABP	The Nasdaq Stock Market LLC

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, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

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

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

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

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

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

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

The aggregate market value of the registrant's voting and non-voting common equity held by non-affiliates as of June 30, 2022 (the last business day of the registrant's most recently completed second fiscal quarter) based on the closing sale price of $0.73 as reported on the Nasdaq Stock Market on that date was $8.5 million.

As of March 16, 2023, the registrant had 31,168,449 shares of common stock, $0.01 par value per share, outstanding.

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SPECIAL CAUTIONARY NOTICE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, or this Annual Report, contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, that involve substantial risks and uncertainties. The forward-looking statements are contained principally in Part I, Item 1. "Business," Part I, Item 1A. "Risk Factors," and Part II, Item 7. "Management's Discussion and Analysis of Financial Condition and Results of Operations," but are also contained elsewhere in this Annual Report. In some cases, you can identify forward-looking statements by the words "may," "might," "will," "could," "would," "should," "expect," "intend," "plan," "objective," "anticipate," "believe," "estimate," "predict," "project," "potential," "continue" and "ongoing," or the negative of these terms, or other comparable terminology intended to identify statements about the future. These statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this Annual Report, we caution you that these statements are based on a combination of facts and factors currently known by us and our expectations of the future, about which we cannot be certain. Forward-looking statements include statements about:

- the timing, progress and results of our clinical trials of NX-13 and any other product candidates, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the trials will become available and our research and development programs;
- the timing of any submission of filings for regulatory approval of, and our ability to obtain and maintain regulatory approvals for NX-13 and any other product candidates for any indication;
- our expectations regarding the size of the patient populations, market acceptance and opportunity for and clinical utility of our product candidates, if approved for commercial use;
- our manufacturing capabilities and strategy, including the scalability and commercial viability of our manufacturing methods and processes;
- our expectations regarding the scope of any approved indication for NX-13 or any other product candidate;
- our ability to successfully commercialize our product candidates;
- our estimates of our expenses, ongoing losses, future revenue, capital requirements and our needs for or ability to obtain additional funding;
- our ability to establish or maintain collaborations, partnerships or strategic relationships;
- our ability to identify, recruit and retain key personnel;
- our ability to protect and enforce our intellectual property position for our product candidates, and the scope of such protection;
- our financial performance;
- our competitive position and the development of and projections relating to our competitors or our industry;
- the impact of laws and regulations;
- the impact of the COVID-19 pandemic and other global events; and
- our expectations regarding the time during which we will be an emerging growth company under the JOBS Act.

You should refer to “Item 1A. Risk Factors” in this Annual Report for a discussion of important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this Annual Report will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. The forward-looking statements in this Annual Report represent our views as of the date of this Annual Report. We anticipate that subsequent events and developments may cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this Annual Report.

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

All brand names or trademarks appearing in this Annual Report are the property of their respective owners. Solely for convenience, the trademarks and trade names in this Annual Report are referred to without the symbols ® and TM, but such references should not be construed as any indication that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

Unless the context requires otherwise, references in this report to “Landos,” the “Company,” “we,” “us,” and “our” refer to Landos Biopharma, Inc. and its subsidiaries.

PART I

Item 1. Business.

We are a clinical-stage biopharmaceutical company focused on the development of novel, oral, once-daily therapeutics for patients with certain immunology diseases. Our core expertise is the clinical development of compounds that target novel pathways at the interface of immunity and metabolism. Based on our understanding of the role that cellular metabolic pathways have on modulating inflammatory responses, we aim to inhibit these inflammatory responses by changing the metabolic processes in target cells. We believe the therapeutics we develop, if approved, could have a significant positive impact on the quality of life of patients suffering from immunology diseases.

Our current focus and lead candidate is NX-13, a novel, oral, gut-selective NLRX1 agonist. We are developing NX-13 as a once-daily oral treatment for ulcerative colitis, or UC, that targets NOD-like receptor X1, or NLRX1, a mitochondria-associated receptor that has been associated with the modulation of inflammatory cytokines for UC. NX-13 is designed to target NLRX1 and induce anti-inflammatory effects in CD4+ T cells and other cells in the gastrointestinal tract.

We announced top-line results from our NX-13 Phase 1b trial in UC patients in August 2022. The data showed favorable safety and tolerability profiles across a range of doses, as well as signals of clinical improvement as soon as two weeks in patients' symptoms and four weeks by endoscopy in exploratory endpoints. We believe that these early signals, as well as the data from long-term toxicology studies, support the potential of NX-13 as a new treatment for UC. We are continuing an in-depth analysis of the clinical, pharmacokinetic, or PK, and pharmacodynamic, or PD, data for NX-13. A preliminary analysis demonstrated promising signals of both target engagement and molecular dose response among the 250mg and 500mg immediate release, or IR, doses. We will be conducting a Phase 2 proof-of-concept clinical trial for NX-13, which will be dose ranging, blinded, placebo-controlled and statistically powered. We are on track for first site activation and patient enrollment for the NX-13 Phase 2 trial in the second quarter of 2023, and we expect to report top-line data from this trial by the fourth quarter of 2024.

In addition to NX-13, we have discovered several preclinical product candidates, comprising the following:

- LABP-73, an oral, small molecule NLRX1 pathway agonist in development for the treatment of asthma and Chronic Obstructive Pulmonary Disease, or COPD,
- LABP-66, an oral, small molecule NLRX1 pathway agonist in development for the treatment of multiple sclerosis, or MS, and Alzheimer's disease; and
- LABP-69, an oral, small molecule PLXDC2 pathway agonist in development for the treatment of diabetic nephropathy and rheumatoid arthritis, or RA.

Recent Events

In January 2023, we entered into a securities purchase agreement, or the Securities Purchase Agreement, with the institutional accredited investors named therein, or the Investors, pursuant to which we agreed to issue and sell to the Investors in a private placement, or the Private Placement, pre-funded warrants, or the Pre-Funded Warrants, to purchase an aggregate of 30,909,090 shares, or the Warrant Shares, of our common stock. Each Pre-Funded Warrant has an exercise price of $0.01 per Warrant Share. The purchase price per Pre-Funded Warrant was $0.54. The Pre-Funded Warrants issued in the Private Placement provide that the holder of the Pre-Funded Warrants will not have the right to exercise any portion of its Pre-Funded Warrants if such holder, together with its affiliates and any other persons whose beneficial ownership of common stock would be aggregated with the holder for purposes of Section 13(d) or Section 16 of the Securities Exchange Act of 1934, as amended, would beneficially own in excess of 35% of the number of shares of common stock outstanding immediately after giving effect to such exercise. The Warrant Shares will also be subject to certain registration rights under the Company's Amended and Restated Investors' Rights Agreement. The Private Placement closed on January 10, 2023. Gross proceeds of the Private Placement were approximately $16.7 million, before deducting offering expenses payable by us.

In February 2023, we entered into an asset purchase and redemption agreement, or the Purchase Agreement, with Dr. Bassaganya-Riera, Raquel Hontecillas and certain other stockholders, or together the Purchasers, whereby the Purchasers acquired (i) all of our right, title and interest in omilancor, LABP-104 and LABP-111 and any such derivatives and analogs that target LANCL proteins, or together the Acquired Compounds, (ii) a worldwide, perpetual, irrevocable, fully-paid up, royalty-free, exclusive, sublicensable and transferable license grant under the intellectual property rights retained by us and necessary or useful for the development, manufacture and commercialization of the Acquired Compounds, (iii) a royalty agreement providing, among other things, for the payment by us to the Purchasers of a royalty of 2% of all net sales by us of any products containing certain compounds that we will retain following the closing under the Purchase Agreement and (iv) $3,000,000 in cash in exchange for (x) 9,086,441 shares of our common stock held by the Purchasers and (y) a royalty agreement providing, among other things, for the payment by the Purchasers to us a royalty of 6% of all net sales by the Purchasers of any products containing any of the Acquired Compounds in consideration for the acquired intellectual property rights. The transactions contemplated by the Purchase Agreement closed simultaneously with signing.

In May 2021, we entered into an exclusive collaboration and license agreement, or the LianBio Agreement, with LianBio Respiratory Limited, or Lian, pursuant to which we granted Lian an exclusive license, or the License, to develop, manufacture and commercialize NX-13 and omilancor. In February 2023, we amended the LianBio Agreement to no longer cover the licensing of Licensed Technology relating to omilancor and developmental milestones events were amended to reflect the transfer of Licensed Technology relating to omilancor. Subsequent to the amendment, we are eligible to receive development milestone payments of up to $40.0 million as well as sales milestone payments of up to $105.0 million. We are also eligible to receive tiered low-double-digit royalties based on future net sales of NX-13 in the Territory, subject to reductions in specified circumstances.

Background in Autoimmune Diseases

Autoimmune diseases generally result from the loss of self-tolerance in the immune system, causing the immune system to attack healthy organs and tissues. This leads to inflammation of the organs and tissues, causing chronic pain and deterioration or destruction of organ function. Current therapies either broadly prevent the immune system from functioning, in the case of corticosteroids, aminosalicylates, or 5-ASA, and immunosuppressants, or systemically block specific molecules that promote inflammation in the case of biologics, S1P receptor modulators and JAK inhibitors. Existing approaches continue to leave unmet patient need.

Our Approach

Our mission is to create safe and effective oral medicines to engage novel targets in therapeutic areas of unmet medical need where current treatments have limited efficacy or safety and tolerability concerns. To achieve this mission, we are developing novel, oral therapeutic candidates that are designed to address the therapeutic gap in the current treatment paradigm for immunology diseases.

Our Strengths

Our distinctive strengths include:

- ***We have a strong team of experienced executive leaders and drug developers.*** We have created a team of experienced drug developers with deep experience in the clinical development of autoimmune drug compounds.
- ***We are pioneering a new paradigm in immunometabolism based on novel pathways.*** We have identified novel immunometabolic targets or pathways that may provide upstream control of established inflammatory and regulatory pathways and have created novel programs to target these pathways.
- ***We have discovered several preclinical and clinical-stage assets across the NLRX1 and PLXDC2 pathways.*** Currently in our portfolio, we have four product candidates, which target two novel immunometabolic targets. We have progressed NX-13, which targets NLRX1, into the clinic.

- ***We are developing a product candidate with a novel mechanism of action, or MOA, to address therapeutic gaps for patients with inflammatory bowel disease, or IBD, where current treatments have limited efficacy or safety and tolerability concerns.*** We believe we are the only company targeting the NLRX1 pathway for IBD. NLRX1 has been associated with the modulation of inflammatory cytokines for UC. NX-13 is designed to target NLRX1 and induce anti-inflammatory effects in CD4+ T cells and other immune cells in the gastrointestinal tract. We believe targeting this pathway may confer a unique advantage for faster onset and longer maintenance of clinical remission and reduction of the high flare rates in IBD patients. NX-13 is designed as a convenient, once-daily, oral therapeutic, which we believe may provide efficacy, safety and competitive advantages over currently available injectable, systemically distributed biologics and other oral therapeutics.
- ***We are targeting several indications characterized by unmet medical need and therapeutic gaps that represent a broad market opportunity.*** Based on clinical and preclinical data, we believe our product candidates, if approved, have the potential to address large therapeutic markets and specific therapeutic gaps in both UC and other immunology diseases.
- ***We have a strong intellectual property foundation.*** Our intellectual property portfolio includes composition of matter and method of use patents and patent applications covering NX-13 and each of our preclinical assets. The patent protection for these product candidates extends to 2039 for NX-13. Subsequent to the Purchase Agreement, our intellectual property portfolio includes more than 24 issued patents and 18 pending patent applications.

Our Strategy

We believe that we are uniquely positioned to identify and develop potentially safer and more effective novel, oral therapeutics for a range of immunology diseases. Our strategy consists of the following key components:

- ***Continue development of NX-13.*** We are focused on the successful advancement of our innovative pipeline of multiple pathways and programs with novel mechanisms of action. Our current and primary focus is the clinical development of NX-13.
- ***Maximize the value of our entire pipeline.*** Other than those rights licensed to Lian for NX-13, we have retained worldwide development and commercial rights to all of our therapeutic programs. We believe our broader, novel pipeline has significant optionality and is poised for partnering and continued development in the future. As such, we may continue to pursue development and commercialization collaborations for our clinical and preclinical programs.

Background on Immunometabolism

The field of immunometabolism describes the interplay and dual action of a number of enzymes, receptors, signaling molecules and substrates which have effects on both cellular metabolism and immune function. First, we have come to understand that alterations in the concentration of metabolic enzymes, substrates and products in the cell serve as messengers to trigger inflammatory responses in autoimmune diseases. The reverse is also true; immunology receptors transmit information about the environment through pathways that affect the metabolic profile of the cell to provide the cellular energy necessary for a specific behavior (e.g., an inflammatory response) to protect the organism. These metabolic processes are critical determinants of the function of immune cells. For example, pro-inflammatory effector Th1 and Th17 have a metabolic preference for glycolytic pathways whereas anti-inflammatory Treg cells prefer oxidative phosphorylation to produce energy. By targeting these immunometabolic hubs and shifting metabolism to oxidative from glycolytic metabolic pathways, there is a functional switch in immune cells that promotes regulatory functions.

Genes with inflammatory functions, such as TNF or IL-6, tend to be overexpressed during autoimmune responses and are easily identified due to the degree of their upregulation. The metabolic pathways of immune cells must also be configured to meet the demands of their function. However, even modest changes in genes with immunometabolic roles can be sufficient and critical in modulating inflammation. By altering the signals that drive differentiation and the metabolic pathways that support it, immune tolerance can be reestablished in patients where there is immune dysregulation, such as in autoimmune disease.

While critical to functions in immune cells, immunometabolic targets are also expressed in a wide range of mesenchymal- and epithelial-derived cells throughout the body. The effects within these cell types often mirror the described signaling events within Tregs, whereby the promotion of mitochondrial metabolism disfavors hyper-inflamed or hyper-proliferative states. In IBD, mitochondrial metabolism pathways account for the majority of downregulated genes relative to healthy controls, evidence of the hyper-inflammatory demands of the inflamed colon which is reliant on glycolytic pathways.

When mitochondrial metabolism restoration is achieved, chemokine production from intestinal epithelial cells is decreased, leading to suppression of neutrophil recruitment into the intestinal wall. In IBD, neutrophils are crucial histological markers of active disease as well as the primary source for calprotectin, a highly predictive fecal biomarker of response to treatment since the majority of drugs approved for treating IBD cause a drop in fecal calprotectin concentrations.

We are focused on developing novel oral therapeutics based on activating molecular targets within certain immunometabolic pathways to rebalance the effector and regulatory branches of the immune system. The imbalance of these two sides, resulting in aberrant inflammation against self-targets, is responsible for many autoimmune diseases. Our proprietary advanced artificial intelligence-based integrated computational and experimental precision medicine platform was used for efficient identification, segregation, and prioritization of these genes, described below, from high throughput datasets.

Our NLRX1 Pathway Product Candidates

The NLRX1 Pathway

We believe the mitochondrial associated receptor, NLRX1 (Nucleotide Oligomerization Domain, or NOD,-Like Receptor X 1), is favorably positioned to induce both metabolic and immunological effects. NLRX1 is unique among the family of NOD-Like Receptors, or NLRs, as one of three to primarily induce regulatory and anti-inflammatory effects. NLRs are pattern-recognition receptors, which are part of the environmental surveillance system detecting bacterial, viral and other foreign components. The most commonly studied NLRs are those associated with the inflammasome, a complex whose activation results in high levels of cytokine production and cell death that further increases inflammation. Polymorphisms in NLRP1, NLRP3, and other inflammasome associated NLRs, as well as inflammasome overactivity, are commonly identified in autoimmune and chronic inflammatory diseases. NLRX1 is the natural counterbalance to this process, serving to control and negatively regulate many of the processes induced by inflammasome activation.

NLRX1 has neither well-characterized nor prominent genetic mutations that would inhibit its activation by our compounds. NLRX1 regulates oxidative metabolism while also providing a mechanism to counteract the inflammatory potential of the resultant reactive oxygen species, or ROS. Through effects on c-Abl and Nrf2, NLRX1 activates expression of enzymes to increase intracellular antioxidant capacity, neutralizing ROS. The net downregulation of intracellular ROS and lactate production decreases NF-κB activity, a main signaling element upstream of many inflammatory cytokines. As a result, NLRX1 activation decreases a wide range of cytokines from both CD4+ T cell, myeloid, and non-immune cells.

NLRX1 Multimodal Mechanism of Action

- Increase mitochondrial metabolism
- Decrease cellular reactive oxygen species
- Downregulate cytokines like TNF and IFNγ (via antagonism of NF-kB)
- Decrease inflammasome formation (NLRP1 and NLRP3)
- Decrease differentiation of effector CD4+ T cells

At the cellular level, NLRX1 activation results a rebalance in CD4+ T cell subsets, decreased activation of macrophages and decreased stress-induced cell death for epithelial and other specialized cells. The decrease in lactate production and NF-κB activity results in proportionally lower Th17 cells relative to Treg cells with NLRX1 activation. Similarly, decreased NF-κB prevents polarization of macrophages into inflammatory subsets, favoring those associated with tissue repair and homeostasis. Additionally, NLRX1-associated ubiquitination of mitochondrial antiviral-signaling protein, or MAVS, is thought to contribute to decreased macrophage activation. In intestinal epithelial cells, airway epithelial cells and neurons, NLRX1 activation increases mitochondrial metabolism and prevents oxidative stress. These effects are beneficial to functions of these cell types, including cell survival, the maintenance of barrier integrity and expression of tight junction proteins. In addition, the added metabolic support favors apoptosis, a relatively silent form of cell death. NLRX1 can aid in the tissue homeostasis and repair processes to prevent chronic tissue damage and fibrosis.

Our lead product candidate targeting the NLRX1 pathway is NX-13 in development for UC.

Background on Ulcerative Colitis

Overview

UC is a chronic immunology disease with significant therapeutic gaps resulting from the safety issues, modest efficacy, loss of clinical response time, and dosing administration of current treatment options. We believe that an oral, once-daily, gut-selective small molecule that maintains safety and efficacy could address the therapeutic gaps in the UC treatment paradigm and have a significant positive impact on quality of life for UC patients.

Background on UC and Current Treatments

UC is a chronic, inflammatory bowel disease that causes inflammation, irritation, and ulcers in the lining of the large intestine (colon) and rectum. Symptoms include abdominal pain, rectal pain and bleeding, bloody stools, diarrhea, fever, weight loss, and malnutrition. Having UC puts a patient at increased risk of developing colon cancer. Diagnosis typically occurs in early adulthood and the disease requires maintenance treatment for the remainder of the patient's life. UC is estimated to affect over one million patients in the U.S. and over one million patients throughout the rest of the world.

Patients with UC are classified into mild-to-moderate, comprising 40% of patients, and moderate-to-severe, comprising 60% of patients, based on the level of symptoms experienced. Accordingly, the current therapeutic treatments for UC depend on the severity of the disease and are broadly divided into six classes:

Mild to Moderate UC

The following treatments are typically used in the treatment of mild to moderate UC:

- **5-ASA's** (mesalamine, sulfasalazine) are used as a first-line anti-inflammatory therapy in UC although the precise mechanism of action is not known. Many also require corticosteroids (see below) to address disease flares and eventually lose response to both drugs progressing to the use of immunosuppressants, biologics, or small molecule advanced therapies. Aminosalicylates are commonly preferred by physicians and patients for the treatment of IBD, due to high tolerability in most patients and their availability as generic oral drugs. Side effects include headache, nausea, dyspepsia, flatulence and diarrhea. Rare but more serious side effects include pleuritis, pericarditis, myocarditis, pancreatitis, cholestic hepatitis, nephritis and renal dysfunction.
- **Corticosteroids** (budesonide, prednisone) are used as induction agents and are prescribed for short periods to address disease flares in both mild to moderate and moderate to severe patients. Corticosteroids are generally administered through an oral or rectal route of administration and are available as generic drugs. Common side effects are mild to moderate in intensity and include headache, nausea, mood and sleep changes. Corticosteroids are not considered appropriate for long term use and are therefore not used for maintenance therapy due to the risk for bone loss, weight gain, lowered quality of life and cardiovascular complications.

- **Immunosuppressants** (methotrexate, thiopurines) are used to wean patients off steroid use and rarely as independent maintenance drugs in moderate to severe patients. Immunosuppressants are orally-administered, systemically-distributed agents and are available as generic drugs. Common side effects include a decrease in the number of white blood cells (leucopenia), headache, rash, nausea, and dyspepsia, alopecia, mild increase in levels of liver enzymes, peritoneal abscesses, and abnormally low levels of the protein albumin in the blood (hypoalbuminemia).

Moderate to Severe UC

The following treatments are typically used in the treatment of moderate to severe UC:

- **Biologics** (anti-TNF, anti-IL-12/IL-23, anti-integrin) are the primary maintenance therapy in moderate to severe UC. Biologics are injectable therapies and can be divided into two classes: those targeting cytokines and those targeting cell trafficking. Side effects include leucopenia, immunosuppression, cancer, infection, and death.
- **S1P Receptor modulators** (ozanimod) are an induction and maintenance therapy for moderate to severe patients that do not respond to other therapies. Similar to immunosuppressants, approved S1P modulators are oral agents that are systemically distributed. Common side effects of S1P modulators include upper respiratory infection, mild increase in levels of liver enzymes, orthostatic hypotension, headache, fever, nausea, arthralgia, hypertension, and increased risk for infections. Rare but serious side effects include serious infections or meningitis, progressive multifocal leukoencephalopathy, bradyarrythmia and atrioventricular conduction delays, liver damage, macular edema, and posterior reversible encephalopathy syndrome.
- **JAK inhibitors** (tofacitinib, upidacitinib) are an induction and maintenance therapy for severe patients that do not respond to other therapies, including biologics. Similar to immunosuppressants, approved JAK inhibitors are oral agents that are systemically distributed. Common side effects of JAK inhibitors include nasopharyngitis, elevated cholesterol levels, headache, upper respiratory tract infection, increased blood creatine phosphokinase, rash, diarrhea, and herpes zoster, mild neutropenia and anemia, and slight increase in the incidence of malignancies (lymphoma, breast cancer, and lung cancer). The FDA has a Black Box warning on the class for severe risks associates with serious infections, mortality, malignancy, major adverse cardiovascular events, or MACE, and thrombosis.

We believe that current therapeutics for the treatment of both mild to moderate and moderate to severe UC have the following limitations that we believe NX-13 if approved, may address:

- **Safety and tolerability concerns**. The majority of approved therapeutics for maintenance of moderate to severe UC (biologics and JAK inhibitors) work systemically, requiring high systemic exposures, resulting in effects on the immune system outside of the gastrointestinal tract. These effects result in increased risks for cancers, infections, blood clots and death. Given the chronic nature of UC, we believe there is a need for safer, long-term oral options. Despite a lower severity of disease, many of the mechanisms of action for current drugs in mild-to-moderate space are also tied to known toxicities and risks.
- **Inconvenient route of administration**. The main class of therapy in moderate to severe UC is biologics, which are injectable therapies administered through either intravenous or subcutaneous routes. Often, this requires a patient to visit a clinic or specialty care provider. 5-ASA's, the standard-of-care for mild-to-moderate UC, requires 2.4 to 4.8 grams per day (two to six tablets daily) when dosed orally. Depending on the response to oral dosing, rectal dosing of mesalamine is sometimes required.

- **Therapeutic gap**. We believe there is a treatment gap for the vast majority of moderate to severe patients between 5-ASA's failures and biologics use. Patients are faced with the option of staying on a sub-optimal therapy to which they are losing response or moving into classes of treatment with higher safety risks and more inconvenient dosing. The emergence of safety concerns for JAK inhibitors and S1P modulators have limited the use of oral, non-biologic immunomodulators that are currently in development for patients who have failed biologics. We believe there is an unmet need for safer and effective oral drugs that can bridge the treatment gap from 5-ASA's to biologics.

NX-13, Our Solution for the Treatment of UC

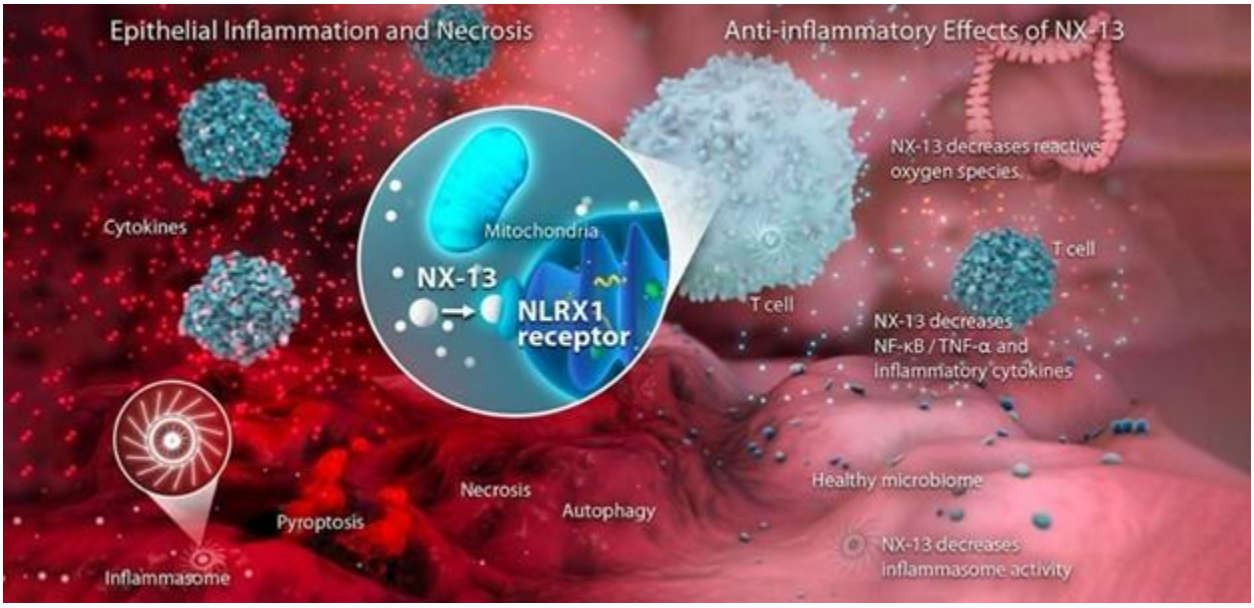
We believe that NX-13, if approved, has the potential to treat patients prior to their progression into biologics and address the main limitations of current therapeutics based on the clinical and preclinical data to date, potentially offering the following advantages:

- **Gut-selective PK with low systemic exposure**. In preclinical and clinical studies, we observed low systemic exposure with gut-selective exposure in humans.
- **Tolerability**. In initial clinical trials, NX-13 was well tolerated, with no differences in presentation of adverse events, or AEs, clinical chemistry, changes in white blood cell counts, electrocardiogram, or ECG, and other clinical measures at doses significantly higher the predicted efficacious dose compared to placebo patients. There have been no serious adverse events in any subjects receiving NX-13 to date.
- **Convenient, once-daily oral dosing.**
- **Innovative immunometabolic target not tied to toxicities**. We have designed NX-13 to activate a novel target, NLRX1, to induce immunometabolic effects that disfavor effector responses.

NX-13 Mechanism of Action Overview and Preclinical data

Mechanistically, the activation of NLRX1 could have multiple benefits in UC with the ability to modulate epithelial integrity, host-microbiome interactions, and mucosal immune responses. As such, we believe NX-13 could provide significant benefits compared to current therapeutics for UC.

The graphics below illustrate key elements of NLRX1 activation by NX-13.



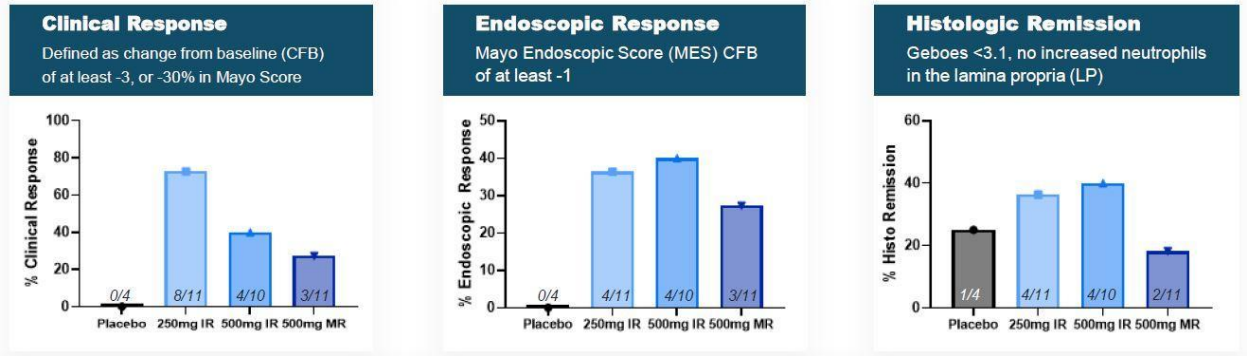
NX-13 is designed to target NLRX1 and provide therapeutic efficacy by reducing pro-inflammatory effects in CD4+ T cells and other immune cells of the gastrointestinal tract, to restore immune balance. NLRX1 was identified as an immunometabolic therapeutic target based on loss of function characterization in animal models of IBD in which the loss of NLRX1 increased disease severity and histological lesions, altered CD4+ T cell differentiation, disrupted epithelial barrier integrity, and negatively influenced gut microbial populations. Through the immunometabolic actions of NLRX1 leading to increased oxidative phosphorylation and decreased NF-κB activity in CD4+ T helper (Th) cells, NX-13 inhibits the differentiation of Th1 and Th17 subsets and overall immune activation. NX-13 is a gut-selective compound with minimal systemic absorption observed in preclinical and clinical studies.

As a once-daily, oral, gut-selective molecule, we believe NX-13 has a promising target product profile for the treatment of UC. Early nonclinical and clinical studies of NX-13 have not revealed any dose-limiting toxicities at doses well above the intended range. In preclinical comparative efficacy studies to 5-ASA, anti-TNF, and tofacitinib, we have observed significantly greater changes in disease activity, biomarkers and histological parameters with NX-13.

Clinical Development of NX-13

We presented the results of our Phase 1a clinical trial of NX-13 in 56 healthy volunteers in March 2021. The trial met all primary and secondary endpoints, and no serious adverse events were reported at any dose level. The data also demonstrated a signal of immunomodulatory activity in terms of lowering fecal calprotectin levels, increasing IL-10 concentrations, and decreasing IL-6 concentrations in plasma.

We announced top-line results from our NX-13 Phase 1b trial in 36 UC patients in August 2022. While the trial was not statistically powered (and therefore hypothesis generating only), the treated patients experienced reductions in multiple clinical activity measures after four weeks. The data showed favorable safety and tolerability profiles across a range of doses, as well as signals of rapid clinical improvement as soon as two weeks in patients' symptoms and four weeks by endoscopy in exploratory endpoints. This early signal, as well as the data from long-term toxicology studies, support the further evaluation of NX-13 as a potential new treatment for UC.



We are continuing an in-depth analysis of the clinical, PK and PD data for NX-13. A preliminary analysis showed promising signals of both target engagement and molecular dose response among the 250mg and 500mg immediate release, or IR, doses. We are planning to conduct a Phase 2 proof-of-concept clinical trial for NX-13, which will be dose ranging, blinded, placebo-controlled, and statistically powered. We are on track for first site activation and patient enrollment for the NX-13 Phase 2 trial in the second quarter of 2023 and expect to report top-line data from the trial by the fourth quarter of 2024.

We believe that through NLRX1 activation, NX-13, if approved, may change the treatment paradigm for patients with UC. Despite currently available treatments, there is still a significant unmet need in the treatment of UC. We believe this need can be met by therapies like NX-13, which are designed to provide (1) an oral, once-daily dosing with comparable efficacy to advanced therapies; (2) greater mucosal healing; and (3) improved efficacy and safety for long-term use. We believe that NX-13, with its unique MOA, good tolerability and lack of serious adverse events, once-daily dosing, and promising early clinical data, could, if approved, potentially transform the current treatment paradigm and be positioned for earlier and broader use in moderate-to-severe UC patients.

Preclinical Stage Product Candidates

LABP-69 for the Potential Treatment of Rheumatoid Arthritis and Diabetic Nephropathy

LABP-69 is a small molecule product candidate that targets PLXDC2 that we are developing for the potential treatment of rheumatoid arthritis and diabetic nephropathy. Rheumatoid arthritis is characterized by a swelling and loss of mobility in joints caused by excessive inflammation and immune cell infiltration into the joint synovium. Diabetic nephropathy is a main complication in both type 1 and type 2 diabetes and is the leading cause of end-stage renal disease.

LABP-69 aims to increase IL-10 secretion and down regulate pro-inflammatory signals and angiogenesis. Results in two rodent models of RA demonstrate the role of PLXDC2 and the effect of LABP-69 in abrogating disease severity. LABP-69 is designed to activate PLXDC2 in both a broad array of immune cells and non-immune cells, shifting them towards an anti-inflammatory state and compounding its therapeutic effects.

LABP-66 for the Potential Treatment of MS, Alzheimer's Disease, and other debilitating CNS diseases

LABP-66 is an oral, small molecule agonist of the NLRX1 pathway for the potential treatment of multiple sclerosis, or MS, Alzheimer's disease and other inflammatory central nervous system, or CNS, diseases. NLRX1 is a non-inflammasome-forming mitochondrial-associated NLR, expressed by immune cells systemically and in the CNS. NLRX1 activation down-regulates inflammation in animal models of injury and autoimmune diseases, including the experimental autoimmune encephalomyelitis, or EAE, model of MS and colitis models of IBD. Progressive MS presents with cortical lesions comprised of activated microglia and an overall increase in microglia in the brain. These microglia, as well as IL-12- and TNF-producing dendritic cells, contribute to direct neuronal damage as well as the ongoing demyelination that disrupts axonal architecture. In multiple EAE models, the loss of NLRX1 results in worsening of disease, greater microglial activation, and increased prevalence of spinal cord lesions.

NLRX1 activation can protect neurons from oxidative stress and ameliorate CNS inflammation. We believe LABP-66 may represent a novel approach to addressing an unmet clinical need in Alzheimer's disease and progressive MS, for which no current therapy slows the progression of cognitive decline and neurological damage.

LABP-73 for the Potential Treatment of Asthma and Chronic Obstructive Pulmonary Disease

LABP-73 is a small molecule product candidate that systemically targets NLRX1 for the potential treatment of Asthma and chronic obstructive pulmonary disease, or COPD. NLRX1 is a mitochondria-associated receptor involved in down-regulating inflammation during bacterial and viral exposure, colitis, MS and chronic pulmonary disease. Asthma encompasses a wide range of allergic and inflammatory diseases. Severe sub-types of asthma, including both neutrophilic and eosinophilic manifestations, lack effective treatment methods. COPD is an inflammatory disease of the lung characterized by chronic bronchitis and emphysema and caused primarily by environmental exposures and cigarette smoke. The current treatments for COPD primarily provide symptomatic relief. We believe that LABP-73, if successfully developed and approved, has the potential to improve on the current treatment options by addressing both epithelial and immune dysfunction to resolve neutrophil inflammation, improve pulmonary function and reverse underlying fibrosis.

Manufacturing

Our drug substance and drug product manufacturing are conducted at third-party contract manufacturing organizations, or CMOs, in India. All of our CMOs hold applicable licenses, certifications and/or approvals for cGMP manufacturing, analytical testing, packaging, and release operations from multiple drug regulation entities, including the U.S. Food and Drug Administration, or FDA. Each manufacturer has also been independently qualified through our own internal qualification processes.

Competition

The biotechnology and pharmaceutical industries, and particularly the market for the treatment of autoimmune diseases, are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary and novel products and product candidates. 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 many different sources, including major pharmaceutical and specialty pharmaceutical companies, compounding facilities, academic institutions and governmental agencies and public and private research institutions.

We are aware of several other products and product candidates as potential treatments for UC that would compete with NX-13, if approved. In particular, we expect to compete against companies that produce biologic drugs and certain generic products that currently serve the UC market, as well as companies that produce the aminosalicylates, steroids and immunosuppressants that are currently used to treat patients with mild to moderate disease. If approved, NX-13 is expected to compete against companies that produce, or are developing, injectable biologic therapeutics such as AbbVie Inc., Amgen Inc., Boehringer Ingelheim GmbH, Eli Lilly and Co., Janssen Pharmaceuticals, Inc., Pfizer, Inc., Roche Holding Ltd., Takeda Pharmaceutical Company Ltd. and UCB S.A., as well as companies that produce, or are developing, oral products such as Abivax SA, Bristol-Myers Squibb Co., Galapagos N.V., Gilead Sciences, Inc., Morphic Therapeutic, Prometheus Therapeutics, Inc., Protagonist Therapeutics, Inc., Reistone Biopharma, Roivant Sciences, Ltd., and Salix Pharmaceuticals.

NX-13 is a differentiated, orally active, therapeutic candidate that we believe is the first to target its pathway. We are not aware of any product candidate targeting the NLRX1 pathways in current clinical development.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer or more effective, have fewer or less severe side effects, are more convenient or are less expensive than NX-13 or any other product 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 our product, which could result in our competitors establishing a strong market position before we are able to enter the market.

Many of the companies against which we are competing, or against which we may compete in the future, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or that may be necessary for, our programs.

Intellectual property

Patents and Applications

Our success depends in part on our ability to obtain and maintain proprietary protection for our product candidates, technology, and know-how; to operate without infringing the proprietary rights of others; and to prevent others from infringing our proprietary rights. Our policy is to seek to protect our proprietary position by, among other methods, pursuing and obtaining patent protection in the U.S. and jurisdictions outside the U.S. Our patent portfolio is intended to cover our product candidates, their methods of use, and any other inventions that are commercially important to our business. We also rely on trade secret protection of our confidential information and know-how relating to our proprietary technology, platforms, and product candidates. The patent positions for our product candidates immediately following the Purchase Agreement are summarized below.

NX-13

We hold issued patents covering the NX-13 compound and various uses thereof in the U.S., Australia, Brazil, Canada, China, Europe, Israel, Japan, Mexico, New Zealand, and South Korea. Patent applications pursuing coverage of NX-13 are pending in Argentina, Chile, Eurasia, Hong Kong, and India. The issued patents and any patents issuing from the pending applications are projected to expire in 2039, absent any surrendered term, adjustments, or extensions.

LABP-69

We hold an issued U.S. patent covering the LABP-69 compound and its use in treating conditions such as diabetic nephropathy and rheumatoid arthritis. We have filed patent applications covering LABP-69 in Argentina, Canada, China, Europe, and Japan. The issued U.S. patent and any patents that may arise from the pending applications are projected to expire in 2041, absent any surrendered term, adjustments, or extensions.

LABP-66

We have filed patent applications covering the LABP-66 compound and uses thereof in the U.S., the PCT international patent system, and Argentina. The application in the U.S. has been accepted for issuance. Any patents that may arise from these applications are projected to expire in 2041, absent any surrendered term, adjustments, or extensions.

LABP-73

We have filed an application covering the LABP-73 compound and uses thereof in the PCT international patent system. Any patents that may arise from this application are projected to expire in 2042, absent any surrendered term, adjustments, or extensions.

Intellectual Property Protection

We cannot predict whether the patent applications we pursue will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide any proprietary protection from competitors. Further, any issued patents may expire before the expected expiration dates disclosed above due to actions taken during patent prosecution, such as submission of a disclaimer surrendering the term of a patent beyond a certain date. Even if our pending patent applications are granted as issued patents, those patents, as well as any patents we license from third parties, may be challenged, circumvented, or invalidated by third parties. While there are currently no contested proceedings or third-party claims relating to any of the patents or patent applications described above, we cannot provide any assurances that we will not have such proceedings or third-party claims at a later date or once any patent is granted.

The term of a patent depends upon the legal term of patents in the particular country in which it is obtained. In most countries in which we file, including the U.S., the patent term is 20 years from the earliest date of filing a non-provisional patent application.

In the U.S., the term of a patent that covers an FDA-approved drug may be eligible for patent term extension, which permits in some cases restoration of patent term as compensation for patent term lost during the FDA regulatory review process. In certain circumstances, the Hatch-Waxman Act permits a patent term extension of up to five years beyond the unextended expiration date of the U.S. patent. The length of the patent term extension is related to the length of time the approved drug is under regulatory review. Patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, and only one patent applicable to an approved drug may be extended. Provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug, or provide an additional period of protection for the approved pharmaceutical product following expiry of the patent. In the future, if our products receive FDA approval, we expect to apply for patent term extensions on patents covering those products. We plan to seek patent term extensions to any of our issued patents in any jurisdiction where these are available. There is no guarantee, however, that the applicable authorities, including the U.S. Patent and Trademark Office in the U.S. and the national patent offices in Europe or other jurisdictions, will agree with our assessment of whether such extensions should be granted, and, if granted, the length of such extensions.

In addition to our reliance on patent protection for our inventions, product candidates, and research programs, we also rely on trade secret protection for our confidential and proprietary information. 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 practices to protect our trade secrets.

Government Regulation

The FDA and comparable regulatory authorities in state and local jurisdictions and in other countries impose substantial and burdensome requirements upon companies involved in the clinical development, manufacture, marketing and distribution of drugs, such as those we are developing. These agencies and other federal, state and local entities regulate, among other things, the research and development, testing, manufacture, quality control, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion, distribution, post-approval monitoring and reporting, sampling and export and import of our product candidates.

U.S. Government Regulation

Preclinical Studies

Preclinical studies include laboratory evaluation (in-vitro) of product chemistry, toxicity and formulation, as well as animal studies (in-vivo) to assess potential safety and efficacy. An Investigational New Drug, or IND, sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data and any available clinical data or literature, among other things, to the FDA as part of an IND. Some preclinical testing may continue even after the IND is submitted. An IND becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Clinical Trials

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with Good Clinical Practice, or GCP, requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND (or equivalent submission ex-US). In addition, an Institutional Review Board, or IRB, or ethics committee, or EC, at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution. Information about certain clinical trials must be provided within specific timeframes to the National Institutes of Health, or the NIH, for public dissemination on their www.clinicaltrials.gov website.

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

- Phase 1: The drug is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dose determination and tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness.
- Phase 2: The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- Phase 3: The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB or EC can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

Marketing Approval

Assuming successful completion of the required clinical testing, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of a New Drug Application, or NDA, or Biologics Licensing Application, or BLA, requesting approval to market the product for one or more indications. In most cases, the submission of an NDA/BLA is subject to a substantial application user fee. Under the Prescription Drug User Fee Act, or PDUFA, the FDA has a goal of ten months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a "filing" decision.

In addition, under the Pediatric Research Equity Act of 2003, or PREA, certain NDAs or supplements to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, 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.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, 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 reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity.

The FDA may refer an application for a novel drug to an advisory committee. 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.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will inspect one or more clinical trial sites to assure compliance with GCP requirements.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a complete response letter. A complete response letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or preclinical testing in order for FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, it may limit the approved indications for use of 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 a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a risk of evaluation and mitigation strategy, or 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-marketing studies or surveillance programs. After approval, some 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.

Special FDA Expedited Review and Approval Programs

The FDA has various programs, including Fast Track designation, Breakthrough Therapy designation, Accelerated Approval, and Priority Review, which are intended to expedite or simplify the process for the development and FDA review of drugs that are intended for the treatment of serious or life-threatening diseases or conditions and demonstrate the potential to address unmet medical needs. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures.

Under the Fast Track program, the sponsor of a new drug candidate may request that FDA designate the drug candidate for a specific indication as a Fast Track drug concurrent with, or after, the filing of the IND for the drug candidate. Fast Track designation provides opportunities for frequent interactions with the FDA review team to expedite development and review of the product. FDA may initiate review of sections of a Fast Track drug's NDA before the application is complete. This rolling review is available if the applicant provides, and FDA approves, a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, FDA's time period goal for reviewing an application does not begin until the last section of the NDA is submitted.

In addition, a sponsor can request breakthrough therapy designation for a drug if it is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs designated as breakthrough therapies are eligible for intensive guidance from FDA on an efficient drug development program, organizational commitment to the development and review of the product including involvement of senior managers, and, like Fast Track products, are also eligible for rolling review of the NDA. Both Fast Track and breakthrough therapy products are also eligible for accelerated approval and/or priority review, if relevant criteria are met.

Under the FDA's accelerated approval regulations, the FDA may approve a drug for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments.

In clinical trials, a surrogate endpoint is a measurement of laboratory or clinical signs of a disease or condition that substitutes for a direct measurement of how a patient feels, functions, or survives. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. A drug 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, will allow FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated approval regulations are subject to prior review by FDA.

Once an NDA is submitted for a product intended to treat a serious condition, the FDA may assign a priority review designation if FDA determines that the product, if approved, would provide a significant improvement in safety or effectiveness. A priority review means that the goal for the FDA to review an application is six months, rather than the standard review of ten months under current PDUFA guidelines. Most products that are eligible for Fast Track breakthrough therapy designation are also likely to be considered appropriate to receive a priority review.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. In addition, the manufacturer of an investigational drug for a serious or life-threatening disease is required to make available, such as by posting on its website, its policy on responding to requests for expanded access. Furthermore, Fast Track designation, breakthrough therapy designation, and priority review do not change the standards for approval and may not ultimately expedite the development or approval process.

Orphan Designation

The FDA may grant orphan designation to drugs or biologics intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the U.S., or if it affects more than 200,000 individuals in the U.S., and there is no reasonable expectation that the cost of developing and marketing the product for this type of disease or condition will be recovered from sales in the U.S. Orphan designation must be requested before submitting an NDA or BLA. After the FDA grants orphan designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

In the U.S., orphan designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to orphan exclusivity, which means the FDA may not approve any other application to market the same product for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer with orphan exclusivity is unable to assure sufficient quantities of the approved orphan designated product. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan product exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same product as defined by the FDA or if our product candidate is determined to be contained within the competitor's product for the same indication or disease. If a drug or biological product designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan product exclusivity.

Post-approval Requirements

Drugs 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 program user fee requirements for any marketed products, as well as application fees for supplemental applications with clinical data.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs 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 requirements 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 mandatory 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.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs 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.

Coverage and Reimbursement

Sales of our product candidates, if approved, will depend, in part, on the extent to which the cost of such products will be covered and adequately reimbursed by third-party payors, such as government healthcare programs, commercial insurance and managed healthcare organizations. These third-party payors are increasingly limiting coverage and/or reducing reimbursements for medical products and services by challenging the prices and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. If these third-party payors do not consider our products to be cost-effective compared to other therapies, they may not cover our products after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

There is no uniform policy requirement for coverage and reimbursement for drug products among third-party payors in the U.S. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. The coverage determination process can be a time-consuming and costly process that may require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained or applied consistently. Even if reimbursement is provided, market acceptance of our products may be adversely affected if the amount of payment for our products proves to be unprofitable for healthcare providers or less profitable than alternative treatments, or if administrative burdens make our products less desirable to use.

In addition, the U.S. government, state legislatures and foreign governments have continued 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 our net revenue and results. Decreases in third-party reimbursement for our product candidates or a decision by a third-party payor to not cover our product candidates could reduce physician usage of our products candidates, once approved, and have a material adverse effect on our sales, results of operations and financial condition.

U.S. Healthcare Reform

There have been and continue to be proposals by the federal government, state governments, regulators and third-party payors to control or manage the increased costs of healthcare and, more generally, to reform the U.S. healthcare system. By way of example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, collectively referred to as the ACA, enacted in March 2010, has had and is expected to continue to have a significant impact on the healthcare industry. The ACA, among other things, imposed a significant annual fee on certain companies that manufacture or import branded prescription drug products, and established a new Medicare Part D coverage gap discount program, in which manufacturers must now agree to offer 70% point of-sale discounts off negotiated prices of applicable brand drugs and therapeutic biologics to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs and therapeutic biologics to be covered under Medicare Part D. The ACA also increased the Medicaid rebate rate and expanded the rebate program to include Medicaid managed care organizations. It also contained substantial new provisions intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against healthcare fraud and abuse, add new transparency requirements for the healthcare industry, impose new taxes and fees on pharmaceutical manufacturers, and impose additional health policy reforms, any or all of which may affect our business.

There have been executive, judicial and Congressional challenges to certain aspects of the ACA. For example, the Tax Cuts and Jobs Act of 2017, or the Tax Act, included a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". Additionally, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and, effective January 1, 2021, also eliminated the health insurance tax. On June 17, 2021, the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Thus, the ACA will remain in effect in its current form. Prior to the U.S. Supreme Court ruling on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how such challenges and the healthcare reform measures of the Biden administration will impact the ACA and our business.

Other legislative changes have also been proposed and adopted since the ACA was enacted. For example, the Budget Control Act of 2011 resulted in aggregate reductions in Medicare payments to providers of 2% per fiscal year, which went into effect in 2013 and, following passage of subsequent legislation, including the Infrastructure Investment and Jobs Act, will stay in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2021, unless additional Congressional action is taken. Under current legislation the actual reduction in Medicare payments will vary from 1% in 2022 to up to 3% in the final fiscal year of this sequester. Additionally, the American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. New laws may result in additional reductions in Medicare and other healthcare funding.

Further, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. Such scrutiny has resulted in several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level, the Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. For example, on July 24, 2020 and September 13, 2020, President Trump announced several executive orders related to prescription drug pricing that attempt to implement several of the Administration's proposals. The FDA currently recently released a final rule and guidance in September 2020, implementing a portion of President Trump's Executive Order announced on July 24, 2020 that directed the Department of Health and Human Services, or HHS to finalize the Canadian drug importation proposed rule previously issued by HHS and make other changes allowing for personal importation of drugs from Canada. The FDA final rule and additional FDA guidance provides pathways for states to build and submit importation plans for drugs from Canada. 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 until 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 safe harbor for fixed fees to pharmacy benefit managers for certain services rendered to manufacturers, the implementation of which have also been delayed pending review by the Biden administration until January 1, 2023. As a result of litigation challenging the Most Favored Nation model, on December 27, 2021, the Centers for Medicare & Medicaid Services, or CMS, published a final rule that rescinded the Most Favored Nation model interim final rule. In July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. No legislation or administrative actions have been finalized to implement these principles. It is unclear whether these or similar policy initiatives will be implemented in the future. At the state level, legislatures have become increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. It is also possible that additional governmental action is taken in response to the COVID-19 pandemic.

It is uncertain whether and how future legislation, whether domestic or foreign, could affect prospects for our product candidates or what actions foreign, federal, state, or private payors for healthcare treatment and services may take in response to any such healthcare reform proposals or legislation, particularly in light of the recent U.S. presidential election. Adoption of price controls and other cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures reforms may prevent or limit our ability to generate revenue, attain profitability or commercialize our product candidates.

Other Healthcare Laws and Compliance Requirements

We will also be subject to healthcare regulation and enforcement by the federal, state and foreign governments in which we will conduct our business once our products are approved. These fraud and abuse and transparency laws may impact, among other things, our financial arrangements and proposed sales, marketing and education programs.

The federal Anti-Kickback Statute, prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order, or recommendation of, an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

Moreover, the federal civil and criminal false claims laws, including the civil False Claims Act, which can be enforced through "qui tam" whistleblower actions, prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent, or making a false statement or record material to payment of a false claim or avoiding, decreasing, or concealing an obligation to pay money to the federal government. Additionally, the government may assert that a claim including items and services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act.

In addition, the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and their implementing regulations, also imposes obligations, including mandatory contractual terms, on "covered entities," including certain healthcare providers, health plans, healthcare clearinghouses, and their respective "business associates" that create, receive, maintain or transmit individually identifiable health information for or on behalf of a covered entity as well as their covered subcontractors, with respect to safeguarding the privacy, security and transmission of individually identifiable health information, as well as analogous state and foreign laws that 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.

The Physician Payments Sunshine Act requires applicable manufacturers of covered drugs to disclose payments and other transfers of value provided to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), and other healthcare professionals (such as physician assistants and nurse practitioners), teaching hospitals as well as information regarding physician ownership and investment interests.

The majority of states also have statutes or regulations similar to the aforementioned federal anti-kickback and false claims laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. In addition, we may be subject to reporting requirements under state transparency laws, as well as state laws that require pharmaceutical companies to comply with the industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government that otherwise restricts certain payments that may be made to health care providers and entities. In addition, certain states and local jurisdictions require the registration of pharmaceutical sales representatives.

Because of the breadth of these laws and the narrowness of available statutory and regulatory exceptions, it is possible that some of our business activities could be subject to challenge under one or more of such laws. If we or our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including significant administrative, civil and criminal penalties, damages, fines, imprisonment, disgorgement, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, exclusion of products from reimbursement under U.S. federal or state healthcare programs, and the curtailment or restructuring of our operations.

Government Regulation Outside of the U.S.

In addition to regulations in the U.S., we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical studies and any commercial sales and distribution of our products.

Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical studies or marketing of the product in those countries. Certain countries outside of the U.S. have a similar process that requires the submission of a clinical study application much like the IND prior to the commencement of human clinical studies.

The requirements and process governing the conduct of clinical studies, product licensing, pricing and reimbursement vary from country to country. If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Data Privacy and Security

Numerous state, federal and foreign laws, including consumer protection laws and regulations, govern the collection, dissemination, processing, use, access to, confidentiality and security of personal information, including health-related information. In the U.S., 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 and regulations (e.g., Section 5 of the FTC Act), govern the collection, use, disclosure, and protection of health-related and other personal information could apply to our operations or the operations of our partners. For example, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, and their respective implementing regulations, imposes privacy, security and breach notification obligations on certain health care providers, health plans, and health care clearinghouses, known as covered entities, as well as their business associates that perform certain services involving creating, receiving, maintaining or transmitting individually identifiable health information for or on behalf of such covered entities as well as their covered subcontractors. Entities that are found to be in violation of HIPAA as the result of a breach of unsecured protected health information, a complaint about privacy practices or an audit by HHS, may be subject to significant civil, criminal and administrative fines and penalties and/or additional reporting and oversight obligations if required to enter into a resolution agreement and corrective action plan with HHS to settle allegations of HIPAA non-compliance. Further, entities that knowingly obtain, use, or disclose individually identifiable health information maintained by a HIPAA covered entity in a manner that is not authorized or permitted by HIPAA may be subject to criminal penalties.

Even when HIPAA does not apply, according to the FTC, violating consumers' privacy rights or failing to take appropriate steps to keep consumers' personal information secure may constitute unfair acts or practices in or affecting commerce in violation of Section 5(a) of the FTC Act. The FTC expects a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. Individually identifiable health information is considered sensitive data that merits stronger safeguards.

In addition, certain state and non-U.S. laws, such as the GDPR govern the privacy and security of health information in certain circumstances, some of which are more stringent than HIPAA and many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. Failure to comply with these laws, where applicable, can result in the imposition of significant civil and/or criminal penalties and private litigation. For example, California recently enacted legislation, the California Consumer Privacy Act, or CCPA, which went into effect January 1, 2020. The CCPA, among other things, creates new data privacy obligations for covered companies and provides new privacy rights to California residents, including the right to opt out of certain disclosures of their information. The CCPA also creates a private right of action with statutory damages for certain data breaches, thereby potentially increasing risks associated with a data breach. In Europe, the GDPR went into effect in May 2018 and introduces strict requirements for processing the personal data of individuals within the EEA. In addition, the GDPR increases the scrutiny of transfers of personal data from clinical trial sites located in the EEA to the U.S. and other jurisdictions that the European Commission does not recognize as having "adequate" data protection laws. Recent legal developments in Europe have created complexity and compliance uncertainty regarding certain transfers of personal data from the EEA. For example, on July 16, 2020, the Court of Justice of the European Union, or CJEU, invalidated the EU-US Privacy Shield Framework, or Privacy Shield, under which personal data could be transferred from the EEA to U.S. entities who had self-certified under the Privacy Shield scheme. While the CJEU upheld the adequacy of the standard contractual clauses (a standard form of contract approved by the European Commission as an adequate personal data transfer mechanism, and potential alternative to the Privacy Shield), it made clear that reliance on them alone may not necessarily be sufficient in all circumstances. Use of the standard contractual clauses must now be assessed on a case-by-case basis taking into account the legal regime applicable in the destination country, in particular applicable surveillance laws and rights of individuals. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater. In addition, following Brexit and the end of the Transition Period, companies will have to comply with the GDPR and the GDPR as incorporated into United Kingdom national law, the latter regime having the ability to separately fine up to the greater of £17.5 million or 4% of global turnover. The relationship between the United Kingdom and the European Union in relation to certain aspects of data protection law remains unclear, for example around how data can lawfully be transferred between each jurisdiction, which exposes us to further compliance risk.

Employees and Human Capital Resources

As of December 31, 2022, we had 22 full-time employees in activities such as research and development, clinical development, finance, and administration. None of our employees are represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

Our human capital objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and additional employees. The principal purposes of our equity incentive plans are to attract, retain and motivate employees, consultants and directors through the granting of stock-based compensation awards.

Corporate Information

We were incorporated under the laws of the State of Delaware in January 2017. Our executive officers and employees work remotely in a "virtual office" setting, and our mailing address is P.O. Box 11239, Blacksburg, VA 24062, and our telephone number is (540) 218-2232.

Available Information

Our internet website address is *www.landosbiopharma.com.* In addition to the information about us and our subsidiaries contained in this Annual Report, information about us can be found on our website. Our website and information included in or linked to our website are not part of this Annual Report.

Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, are available free of charge through our website as soon as reasonably practicable after they are electronically filed with or furnished to the Securities and Exchange Commission, or SEC. Additionally the SEC maintains an internet site that contains reports, proxy and information statements and other information. The address of the SEC's website is *www.sec.gov*.

Item 1A. Risk Factors.

The following information sets forth risk factors that could cause our actual results to differ materially from those contained in forward-looking statements we have made in this Annual Report on Form 10-K and those we may make from time to time. You should carefully consider the risks described below, in addition to the other information contained in this Annual Report on Form 10-K and our other public filings. Our business, financial condition or results of operations could be harmed by any of these risks. The risks and uncertainties described below are not the only ones we face. Additional risks not presently known to us or other factors not perceived by us to present significant risks to our business at this time also may impair our business operations.

Selected Risks Affecting Our Business

Our business is subject to a number of risks of which you should be aware before making a decision to invest in our securities. These risks are more fully described in this "Risk Factors" section, including the following:

- We have incurred significant losses since our inception. We expect to incur losses over the next several years and may never achieve or maintain profitability.
- We have a limited operating history, have not yet started Phase 3 clinical trials and have no history of commercializing products, which may make it difficult for an investor to evaluate the success of our business to date and to assess our future viability.
- We will need substantial additional funding to meet our financial obligations and to pursue our business objectives. If we are unable to raise capital when needed, we could be forced to curtail our planned operations and the pursuit of our growth strategy.
- Our business and operations may be adversely affected by the COVID-19 pandemic.
- We currently have only one clinical-stage product candidate: NX-13. If we are unable to successfully develop, receive regulatory approval for and commercialize our product candidate for this or any other indication, or successfully discover and/or develop any other product candidates, or experience significant delays in doing so, our business will be harmed.
- The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming and inherently unpredictable. If we are not able to obtain required regulatory approval for our product candidates, our business will be substantially harmed.
- Success in preclinical studies or historical clinical trials may not be indicative of results in future clinical trials.
- We may not be successful in our efforts to increase our pipeline of product candidates, including by discovery of new pathways or targets, identifying molecules against those targets or pursuing additional indications for our current product candidates or in-licensing or acquiring additional product candidates for other diseases.
- We face substantial competition, which may result in a smaller than expected commercial opportunity and/or others discovering, developing or commercializing products before or more successfully than we do.
- We rely on third parties to conduct a significant portion of our existing clinical trials and potential future clinical trials for product candidates, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.
- We contract with third parties for the manufacture of NX-13 and any other product candidates for clinical drug supply and expect to continue to do so for commercialization if approved. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.
- If we are unable to obtain or protect intellectual property rights related to any of our product candidates, we may not be able to compete effectively in our market.

Risks Related to our Financial Position and Capital Needs

We have incurred significant losses since our inception. We expect to incur losses over the next several years and may never achieve or maintain profitability.

We are a clinical-stage biopharmaceutical company with a limited operating history. Since our inception, we have incurred significant net losses, and we expect to continue to incur significant expenses and operating losses for the foreseeable future. Our net losses were $39.3 million and $38.4 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of $133.4 million. On February 3, 2021, we completed our initial public offering, or IPO, in which we issued and sold 6,250,000 shares of our common stock at a public offering price of $16.00 per share for net proceeds of $91.2 million, after deducting underwriters' discounts and commissions. In May 2021, we received an upfront cash payment of $18.0 million in connection with the execution of the LianBio Agreement. Beginning in October 2022, we received grant revenue under our agreement with the NIH for eligible reimbursable expenses. In January 2023, we completed a private placement of pre-funded warrants to purchase our common stock, in which we received aggregate gross process of $16.7 million, before deducting offering expenses payable by us. We have no products approved for commercialization and have never generated any revenue from product sales.

We have devoted substantially all of our financial resources and efforts to the development of our clinical and preclinical product candidates, including conducting preclinical studies and clinical trials. We expect to continue to incur significant expenses and operating losses over the next several years. We expect that it could be several years, if ever, before we have a commercialized product. Our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially as we:

- conduct our ongoing and planned clinical trials of NX-13;
- pursue regulatory approval of our product candidates;
- seek to discover and develop additional clinical and preclinical product candidates;
- scale up our clinical and regulatory capabilities;
- establish a commercialization infrastructure and scale up external manufacturing and distribution capabilities to commercialize any product candidates for which we may obtain regulatory approval;
- adapt our regulatory compliance efforts to incorporate requirements applicable to marketed products;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, manufacturing and scientific personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts; and
- incur additional legal, accounting and other expenses in operating as a public company.

To become and remain profitable, we must succeed in developing and eventually commercializing product candidates that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, obtaining regulatory approval, and manufacturing, marketing and selling any product candidates for which we may obtain regulatory approval, as well as discovering and developing additional product candidates. We are only in the preliminary stages of most of these activities. We may never succeed in these activities and, even if we do, may never generate any revenue or revenue that is significant enough to achieve profitability.

Even if we achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, maintain our development efforts, obtain product approvals, diversify our offerings or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

We have a limited operating history, have not yet started Phase 3 clinical trials and have no history of commercializing products, which may make it difficult for an investor to evaluate the success of our business to date and to assess our future viability.

We commenced operations in 2017, and our operations to date have been largely focused on raising capital and advancing our clinical and preclinical product candidates, including undertaking preclinical studies and conducting clinical trials. To date, we have not yet demonstrated our ability to successfully complete pivotal clinical trials, obtain regulatory approvals, manufacture a product on a commercial scale, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing products.

We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. We may also need to transition from a company with a drug development focus to a company capable of supporting commercial activities. Our inability to adequately address these risks and difficulties or successfully make such a transition could adversely affect our business, financial condition, results of operations and growth prospects.

We will need substantial additional funding to meet our financial obligations and to pursue our business objectives. If we are unable to raise capital when needed, we could be forced to curtail our planned operations and the pursuit of our growth strategy.

Our operations have consumed substantial amounts of cash since inception. 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 continue to incur significant expenses and operating losses over the next several years as we complete our ongoing clinical trials of our product candidates, initiate future clinical trials of our product candidates, seek marketing approval for our current clinical product candidates and advance any of our other product candidates we may develop or otherwise acquire. In addition, our product candidates, if approved, may not achieve commercial success. 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 any product candidates that we develop or otherwise acquire, we expect to incur significant commercialization expenses related to product sales, marketing, distribution and manufacturing.

As of December 31, 2022, we had cash, cash equivalents and marketable securities of $44.4 million. We believe that our existing cash, cash equivalents and marketable securities as of December 31, 2022, in addition to the $16.7 million in gross proceeds from our private placement of pre-funded warrants in January 2023, will be sufficient to fund our operating expenses and capital requirements into the first half of 2025. This estimate is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we expect. Changes may occur beyond our control that would cause us to consume our available capital before that time, including changes in and progress of our development activities, acquisitions of additional product candidates, and changes in regulation. Our future capital requirements will depend on many factors, including:

- the scope, progress, costs and results of our ongoing and planned clinical trials, as well as the associated costs, including any unforeseen costs we may incur as a result or preclinical study or clinical trial delays due to the COVID-19 pandemic, Russia's invasion of Ukraine, or other delays, or additional trials that we have or may undertake as part of our clinical development plans;
- the scope, progress, costs and results of preclinical development, laboratory testing and clinical trials for any future product candidates we may decide to pursue;
- the extent to which we develop, in-license or acquire other product candidates and technologies;
- the costs and timing of process development and manufacturing scale-up activities associated with our product candidates and other programs we advance them through preclinical and clinical development;
- the number and development requirements of other product candidates that we may pursue;
- the costs, timing and outcome of regulatory review of our product candidates;

- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;
- our ability to establish collaborations to commercialize any of our product candidates; and
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims.

We will require additional capital to develop and commercialize our product candidates. If we receive regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution, depending on where we choose to commercialize. Additional funds may not be available on a timely basis, on favorable terms, or at all, and such funds, if available, may not be sufficient to enable us to continue to implement our long-term business strategy. Further, our ability to raise additional capital may be adversely impacted by worsening global economic conditions, rising inflation, disruptions to and volatility in the credit and financial markets in the U.S. and worldwide and other global events. For example, on March 10, 2023, Silicon Valley Bank was closed by the California Department of Financial Protection and Innovation. Uncertainty and liquidity concerns in the broader financial services industry remain, and the failure of Silicon Valley Bank and its potential near- and long-term effects on the biotechnology industry and is participants may also adversely affect our operations and stock price. The credit and financial markets in the U.S. and worldwide have recently been, and may continue to be, adversely impacted by the current military conflict between Russia and Ukraine and measures taken in response thereto, including the imposition of sanctions. If we are unable to raise sufficient additional capital, we could be forced to curtail our planned operations and the pursuit of our growth strategy.

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

Until such time, if ever, as we can generate substantial revenue, we may finance our cash needs through a combination of equity offerings, government or private party grants, debt financings and license and collaboration agreements. We do not currently have any other committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. For example, in January 2023 we completed a private placement of pre-funded warrants to purchase common stock, sold at a price of $0.54 per pre-funded warrant. If these pre-funded warrants, which have an exercise price of $0.01 per share, are exercised in the future, there will be significant dilution caused to our stockholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may be required to relinquish valuable rights to our technologies, future revenue streams or product candidates, grant licenses on terms that may not be favorable to us or commit to future payment streams. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. Market volatility resulting from the COVID-19 pandemic, the military conflict between Russia and Ukraine or other factors may further adversely impact our ability to access capital as and when needed.

Risks Related to the Discovery, Development and Commercialization of our Product Candidates

Our business and operations may be adversely affected by the COVID-19 pandemic.

Our business and operations may be adversely affected by the effects of COVID-19. Future remote work policies and other restrictions on the conduct of business operations related to the COVID-19 pandemic may negatively impact productivity and may disrupt our ongoing research and development activities and our clinical programs and timelines, the magnitude of which will depend, in part, on the length and severity of such measures.

Due to the COVID-19 pandemic we may experience related disruptions in the future that could severely impact our clinical trials, including:

- delays, difficulties or a suspension in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- risk that participants enrolled in our clinical trials will contract COVID-19 while the clinical trial is ongoing, which could impact the results of the clinical trial, including by increasing the number of observed adverse events; and
- interruptions in our ability to manufacture and deliver drug supply for trials.

Geopolitical risks, such as those associated with Russia's invasion of Ukraine, could result in increased market volatility and uncertainty, which could negatively impact our business, financial condition and results of operations.

The uncertain nature, magnitude and duration of hostilities stemming from Russia's military invasion of Ukraine, including the potential effects of sanctions limitations, retaliatory cyber-attacks on the world economy and markets, and potential shipping and supply chain delays, have contributed to increased market volatility and uncertainty, which could have an adverse impact on macroeconomic factors that affect our business. As a result of Russia's invasion of Ukraine, the U.S., the United Kingdom and the European Union governments, among others, have developed coordinated economic and financial sanctions packages. As the invasion of Ukraine continues, there can be no certainty regarding whether such governments or other governments will impose additional sanctions, or other economic or military measures against Russia.

The impact the invasion of Ukraine, including economic sanctions or additional war or military conflict, as well as potential responses to them by Russia, is currently unknown and they could adversely affect our business, including supply chain, activities of our collaborators, clinical development activities and manufacturing. In addition, the continuation of the invasion of Ukraine by Russia could lead to other disruptions, instability and volatility in global markets and industries that could negatively impact our operations, and further escalation of the conflict could have a broader impact that expands into other markets where we do business or conduct operations, including clinical trials. It is not possible to predict the broader consequences of this conflict, which could include further sanctions, embargoes, regional instability, geopolitical shifts and adverse effects on macroeconomic conditions, the availability of raw materials, supplies, freight and labor, currency exchange rates and financial markets, all of which could impact our business, financial condition and results of operations.

We currently have only one clinical-stage product candidate: NX-13. If we are unable to successfully develop, receive regulatory approval for and commercialize our product candidate for this or any other indication, or successfully discover and/or develop any other product candidates, or experience significant delays in doing so, our business will be harmed.

We currently have no products that are approved for commercial sale. We currently have only one clinical-stage product candidate, NX-13. To date, we have not yet conducted any pivotal clinical trials. We have not completed the development of any product candidates, and we may never be able to develop marketable products.

We have invested substantially all of our efforts and financial resources in the development of our clinical and preclinical product candidates. Our ability to generate revenue from our product candidates, which we do not expect will occur for several years, if ever, will depend heavily on the successful development, regulatory approval and eventual commercialization of our product candidates. The success of NX-13 or any other product candidates that we discover, develop or otherwise may acquire will depend on several factors, including:

- timely and successful completion of preclinical studies and clinical trials;
- sufficiency of our financial and other resources to complete the necessary preclinical studies and clinical trials;
- successful patient enrollment and completion of clinical trials;
- successful development of, or making arrangements with third-party manufacturers for, our commercial manufacturing processes for any of our product candidates that receive regulatory approval;
- timely receipt marketing approvals from applicable regulatory authorities;
- launching commercial sales of products, if approved;
- acceptance of our products, if approved, by patients, the medical community and third-party payors, for their approved indications;
- the prevalence and severity of adverse events experienced with our product candidates;
- the availability, perceived advantages, cost, safety and efficacy of alternative therapies for any product candidate, and any indications for such product candidate, that we develop, specifically alternative treatments for UC;
- our ability to produce our product candidates on a commercial scale;
- obtaining and maintaining patent, trademark and trade secret protection and regulatory exclusivity for our product candidates and otherwise protecting our rights in our intellectual property portfolio;
- maintaining compliance with regulatory requirements, including current good manufacturing practices, or cGMPs, and complying effectively with other procedures;
- maintaining a continued acceptable safety, tolerability and efficacy profile of the products following approval;
- obtaining and maintaining patent protection, trade secret protection and regulatory exclusivity, both in the U.S. and internationally;
- the protection of our rights in our intellectual property portfolio;
- the successful launch of commercial sales following any marketing approval;
- a continued acceptable safety profile following any marketing approval;
- commercial acceptance by patients, the medical community and third-party payors; and
- our ability to compete with other therapies.

We do not have complete control over any of these factors, including certain aspects of clinical development and the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing, distribution and sales efforts of any future collaborator. If we are not successful with respect to one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize the product candidates we develop, which would materially harm our business. If we do not receive marketing approvals for our product candidates, we may not be able to continue our operations.

The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming and inherently unpredictable. If we are not able to obtain required regulatory approval for our product candidates, our business will be substantially harmed.

The time required to obtain approval or other marketing authorizations by the FDA and comparable foreign authorities is unpredictable, and it typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations and the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate, and it is possible that we may never obtain regulatory approval for any product candidates we may seek to develop in the future. Neither we nor any current or future collaborator is permitted to market any drug product candidates in the U.S. until we receive regulatory approval of a NDA from the FDA. To date, we have only had limited discussions with the European Medicines Agency, or EMA, and other comparable foreign authorities regarding regulatory approval for our product candidates outside of the U.S.

Prior to obtaining approval to commercialize any drug product candidate in the U.S. or abroad, we must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA or foreign regulatory agencies, that such product candidates are safe, pure and effective for their intended uses. Results from preclinical studies and clinical trials can be interpreted in different ways. Even if we believe the preclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and other regulatory authorities. The FDA may also require us to conduct additional preclinical studies or clinical trials for our product candidates either prior to or after approval, or it may object to elements of our clinical development programs.

Of the large number of products in development, only a small percentage successfully complete the FDA or foreign regulatory approval processes and are commercialized. The lengthy approval and marketing authorization process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval and marketing authorization to market our product candidates, which would significantly harm our business, financial condition, results of operations and prospects.

We have invested a significant portion of our time and financial resources in the development of our clinical and preclinical product candidates. Our business is dependent on our ability to successfully complete preclinical and clinical development of, obtain regulatory approval for, and, if approved, successfully commercialize our product candidates in a timely manner.

Even if we eventually complete clinical testing and receive approval of a NDA or foreign marketing application for our product candidates, the FDA or the applicable foreign regulatory agency may grant approval or other marketing authorization contingent on the performance of costly additional clinical trials, including post-marketing clinical trials. The FDA or the applicable foreign regulatory agency also may approve or authorize for marketing a product candidate for a more limited indication or patient population than we originally request, and the FDA or applicable foreign regulatory agency may not approve or authorize the labeling that we believe is necessary or desirable for the successful commercialization of a product candidate. Any delay in obtaining, or inability to obtain, applicable regulatory approval or other marketing authorization would delay or prevent commercialization of that product candidate and would materially adversely impact our business and prospects.

In addition, the FDA and other regulatory authorities may change their policies, issue additional regulations or revise existing regulations, or take other actions, which may prevent or delay approval of our future products under development on a timely basis. Such policy or regulatory changes could impose additional requirements upon us that could delay our ability to obtain approvals, increase the costs of compliance or restrict our ability to maintain any marketing authorizations we may have obtained. For example, the European Union began transitioning to full implementation of the EU Clinical Trials Regulation, or CTR, applicable beginning in January 2022, and the United Kingdom's Medicines and Healthcare products Regulatory Agency has begun to transition the U.K. to a fully independent clinical trial regulatory framework following Brexit, both of which could result in significant uncertainties and delays. The new CTR seeks to simplify and streamline the approval of clinical trials in the EU. For example, the sponsor shall submit a single application for approval of a clinical trial via the EU Portal. As part of the application process, the sponsor shall propose a reporting Member State, who will coordinate the validation and evaluation of the application. The reporting Member State shall consult and coordinate with the other Member States in which the clinical trial is to take place (such Member States being referred to as the Member States Concerned). If an application is rejected, it can be amended and resubmitted through the EU Portal. If an approval is issued, the sponsor can start the clinical trial in all Member States Concerned. However, a Member State Concerned can in limited circumstances declare an "opt-out" from an approval. In such a case, the clinical trial cannot be conducted in that Member State. The CTR also aims to streamline and simplify the rules on safety reporting and introduces enhanced transparency requirements such as mandatory submission of a summary of the clinical trial results to the EU Database.

Clinical product development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs and experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

In order to obtain FDA approval to market a new drug product we must demonstrate proof of safety, purity and efficacy in humans. The risk of failure for product candidates is high. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety, purity, potency, and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing or at any time during the trial process, or the results of a clinical trial may not be sufficient, or may raise new questions, and may require us to conduct additional clinical trials for which we did not plan. 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. 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.

We have not completed all clinical trials required for the approval of any of our product candidates. We cannot assure you that any clinical trial that we are conducting, or may conduct in the future, will demonstrate consistent or adequate efficacy and safety to obtain regulatory approval to market our product candidates.

We may incur additional costs and experience delays in ongoing clinical trials for our product candidates, and we do not know whether future clinical trials, if any, will begin on time, need to be redesigned, enroll an adequate number of patients on time or be 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:

- regulators or institutional review boards 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 clinical trial contracts or clinical trial protocols with prospective trial sites or 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 trials of our product candidates may produce negative or inconclusive results, including failure to demonstrate statistical significance, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- we may fail to demonstrate statistical significance in early stage or Phase 2 clinical trials of our product candidates, which may impact the timing and design of late stage clinical trials for such product candidates;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or institutional review boards to suspend or terminate the trials;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- regulators or institutional review boards may require that we or our investigators suspend or terminate clinical development for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate; and
- 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.

In addition, we engaged CROs to conduct clinical trials outside the U.S., including in Ukraine. Although the route, length and impact of Russia's invasion is highly unpredictable, clinical trial activities have already been suspended, and may continue to be suspended or terminated, and patients could be forced to evacuate or voluntarily choose to relocate far from clinical trial sites, making them unavailable for initial or further participation in these clinical trials.

If we experience delays in the completion of, or termination of, any clinical trial of our product candidates, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenues from any of these product candidates will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenues.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not favorable or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval 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 requirements; or
- have the product removed from the market after obtaining marketing approval.

Success in preclinical studies or earlier clinical trials may not be indicative of results in future clinical trials.

Success in preclinical testing and early clinical trials does not ensure that later clinical trials will generate the same results or otherwise provide adequate data to demonstrate the efficacy and safety of a product candidate. Preclinical tests and Phase 1 and Phase 2 clinical trials are primarily designed to test safety, to study pharmacokinetics and pharmacodynamics and to understand the side effects of product candidates at various doses and schedules. Success in preclinical or animal studies and early clinical trials does not ensure that later large-scale efficacy trials will be successful nor does it predict final results. Our product candidates may fail to show the desired safety and efficacy in clinical development despite positive results in preclinical studies or having successfully advanced through initial clinical trials, particularly because we are targeting novel pathways that have not yet been tested in later-stage clinical trials.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in preclinical testing and earlier-stage clinical trials. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, we may experience regulatory delays or rejections as a result of many factors, including changes in regulatory policy during the period of our product candidate development. Any such delays could negatively impact our business, financial condition, results of operations and prospects.

We may seek orphan drug designation for some of our product candidates, and we may be unsuccessful, or may be unable to maintain the benefits associated with orphan drug designation, including the potential for market exclusivity, for product candidates for which we obtain orphan drug designation.

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

If a drug or biologic with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the drug or biologic is entitled to a period of marketing exclusivity, which precludes the FDA from approving another marketing application for the same drug and indication for that time period, except in limited circumstances. If our competitors are able to obtain orphan drug exclusivity prior to us, for products that constitute the "same drug" and treat the same indications as our product candidates, we may not be able to have competing products approved by the applicable regulatory authority for a significant period of time. The applicable period is seven years in the U.S.

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

Interim "top-line" and preliminary results 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 results from our preclinical studies and clinical trials, which are based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. Interim results from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or top-line results also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Differences between preliminary or interim data and final data could significantly harm our business prospects and may cause the trading price of our common stock to fluctuate significantly.

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

Our clinical trials may fail to demonstrate the safety and efficacy of our product candidates, or serious adverse or unacceptable side effects may be identified during the development of our product candidates, which could prevent or delay regulatory approval and commercialization, increase our costs or necessitate the abandonment or limitation of the development of some of our product candidates.

Before obtaining regulatory approvals for the commercial sale of our product candidates, we must demonstrate through lengthy, complex and expensive preclinical testing and clinical trials that our product candidates are safe, pure and effective for use in each target indication, and failures can occur at any stage of testing. Clinical trials often fail to demonstrate safety or efficacy of the product candidate studied for the target indication.

If our product candidates are associated with side effects in clinical trials or have characteristics that are unexpected, we may need to abandon their development or limit development to more narrow uses in which the side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. The FDA or an institutional review board may also require that we suspend, discontinue, or limit our clinical trials based on safety information, or that we conduct additional animal or human studies regarding the safety and efficacy of our product candidates which we have not planned or anticipated. Such findings could further result in regulatory authorities failing to provide marketing authorization for our product candidates or limiting the scope of the approved indication, if approved. Many product candidates that initially showed promise in early stage testing have later been found to cause side effects that prevented further development of the product candidate.

Additionally, if one or more of our product candidates receives marketing approval, and we or others identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such product;
- regulatory authorities may require additional warnings on the labels;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients;
- we may not be able to achieve or maintain third-party payor coverage and adequate reimbursement; and
- our reputation and physician or patient acceptance of our products may suffer.

There can be no assurance that we will resolve any issues related to any product-related adverse events to the satisfaction of the FDA or foreign regulatory agency in a timely manner or at all. Moreover, 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.

As an organization, we have never conducted pivotal clinical trials, and we may be unable to do so for any product candidates we may develop.

We will need to successfully complete pivotal clinical trials in order to obtain the approval of the FDA, EMA or other regulatory agencies to market our product candidates. Carrying out pivotal clinical trials is a complicated process. As an organization, we have limited experience in successfully executing earlier-stage clinical trials, and we have not previously conducted any later stage or pivotal clinical trials. In order to do so, we will need to expand our clinical development and regulatory capabilities, and we may be unable to recruit and train qualified personnel. We also expect to continue to rely on third parties to conduct our pivotal clinical trials. See "Risks related to our dependence on third parties." Consequently, we may be unable to successfully and efficiently execute and complete necessary clinical trials in a way that leads to NDA submission and approval of our product candidates. We may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approvals of product candidates that we develop. Failure to commence or complete, or delays in, our planned clinical trials, could prevent us from or delay us in commercializing our product candidates.

If we experience delays or difficulties in the enrollment and/or maintenance of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

Successful and timely completion of clinical trials will require that we enroll a sufficient number of patients. Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors, including the size and nature of the patient population and competition for patients with other trials. For example, we are aware of multiple clinical trials for the treatment of UC being conducted by competitors that may make it difficult for us to enroll sufficient patients. Trials may be subject to delays as a result of patient enrollment taking longer than anticipated or patient withdrawal. We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or foreign regulatory authorities. We cannot predict how successful we will be at enrolling subjects in future clinical trials. Subject enrollment is affected by other factors including:

- the eligibility criteria for the trial in question;
- the size of the patient population and process for identifying patients;
- the perceived risks and benefits of the product candidate in the trial;
- the availability of competing commercially available therapies and other competing drug candidates' clinical trials;
- the willingness of patients to be enrolled in our clinical trials;
- the efforts to facilitate timely enrollment in clinical trials;
- potential disruptions caused by the COVID-19 pandemic and the ongoing military conflict in Ukraine, including difficulties in initiating clinical sites, enrolling and retaining participants, diversion of healthcare resources away from clinical trials, travel or quarantine policies that may be implemented, and other factors;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- the proximity and availability of clinical trial sites for prospective patients.

Our inability to enroll a sufficient number of patients for clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in these clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing. Furthermore, we rely on and expect to continue to rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials and we will have limited influence over their performance.

Furthermore, even if we are able to enroll a sufficient number of patients for our clinical trials, we may have difficulty maintaining enrollment of such patients in our clinical trials.

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

As product candidates proceed through preclinical studies to late-stage clinical trials towards potential approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize processes and product characteristics. Such changes carry the risk that they will not achieve these intended objectives. Further, we rely on third-party contract manufacturers to manufacture our product candidates, which subjects us to additional risks, particularly with respect to control of the formulation of our candidates. See "We contract with third parties for the manufacture of NX-13 and any other product candidates for clinical drug supply and expect to continue to do so for commercialization if approved. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts." Any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the materials manufactured using altered processes. Such changes may also require additional testing, FDA notification or FDA approval. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and jeopardize our ability to commence sales and generate revenue.

We may not be successful in our efforts to increase our pipeline of product candidates, including by discovery of new pathways or targets, identifying molecules against those targets or pursuing additional indications for our current product candidates or in-licensing or acquiring additional product candidates for other diseases.

We may in-license or acquire additional product candidates for other diseases. We may not be able to identify or develop product candidates that are safe, tolerable and effective. Even if we are successful in continuing to build our pipeline, the potential product candidates that we identify, in-license or acquire may not be suitable for clinical development, including as a result of being shown to have harmful side effects or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance.

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

Because we have limited financial and management resources, we focus on development programs and product candidates that we identify for specific indications. As such, we are currently primarily focused on the development of NX-13 for the treatment of UC. We are reviewing our preclinical programs to optimize the priorities and sequence of our preclinical product candidates and their respective clinical applications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications for our product candidates that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. For example, there is no guarantee that we will receive royalties on the LANCL2 portfolio and we have no power over how the Purchasers develop them.

If we do not achieve our projected development goals in the time frames we announce and expect, the commercialization of our products may be delayed.

From time to time, we may estimate the timing of the accomplishment of various scientific, clinical, regulatory, manufacturing and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of preclinical studies and clinical trials and the submission of regulatory filings, including IND submissions. From time to time, we may publicly announce the expected timing of some of these milestones. For example, in January 2023, we announced that we are on track to initiate a Phase 2 proof-of-concept trial for NX-13 in the second quarter of 2023 and report top-line data by the fourth quarter of 2024. All of these milestones are, and will be, based on a variety of assumptions. The actual timing of these milestones can vary significantly compared to our estimates, and we may need to remove prior guidance as to the timing of these milestones, in some cases for reasons beyond our control. We may experience numerous unforeseen events during, or as a result of, any future clinical trials that we conduct that could delay or prevent our ability to receive marketing approval or commercialize our product candidates.

We may explore the use of NX-13 and potentially other product candidates, in combination with other therapies, which exposes us to additional risks.

We may explore the use of NX-13 and other future product candidates in combination with one or more other approved or unapproved therapies to treat UC.

Even if any product candidate we develop were to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to the risks that the FDA, EMA or comparable foreign regulatory authorities outside of the U.S. could revoke approval of the therapy used in combination with our product or that safety, efficacy, manufacturing or supply issues could arise with any of those existing therapies. If the therapies 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, EMA 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 also may choose to evaluate NX-13 or any other future product candidates in combination with one or more therapies that have not yet been approved for marketing by the FDA, EMA or comparable foreign regulatory authorities. We will not be able to market and sell NX-13 or any product candidate we develop in combination with an unapproved therapy for a combination indication if that unapproved therapy does not ultimately obtain marketing approval either alone or in combination with our product. In addition, unapproved therapies face the same risks described with respect to our product candidates currently in development and clinical trials, including the potential for serious adverse effects, delay in their clinical trials and lack of FDA approval.

If the FDA, EMA or comparable foreign regulatory authorities do not approve these other drugs or revoke their approval of, or if safety, efficacy, quality, manufacturing or supply issues arise with, the drugs we choose to evaluate in combination with our product candidate we develop, we may be unable to obtain approval of or market such combination therapy.

The withdrawal of the United Kingdom from the European Union, commonly referred to as "Brexit," may adversely impact our ability to obtain regulatory approvals of our product candidates, result in restrictions or imposition of taxes and duties on trade of our products between the United Kingdom and European Union, and may require us to incur additional expenses in order to develop, manufacture and commercialize our product candidates in the United Kingdom or European Union.

Following the result of a referendum in 2016, the United Kingdom left the European Union on January 31, 2020, commonly referred to as Brexit. Pursuant to the formal withdrawal arrangements agreed between the United Kingdom and the European Union, the United Kingdom was subject to a transition period until December 31, 2020, during which European Union rules continued to apply. A trade and cooperation agreement, or the Trade and Cooperation Agreement, that outlines the future trading relationship between the United Kingdom and the European Union applied provisionally from January 1, 2021, and formally entered into force on May 1, 2021.

There are ongoing effects of Brexit and significant uncertainty remains. By way of example, the Retained EU Law (Revocation and Reform) Bill 2022, which is currently progressing through the UK Parliament seeks to allow the UK Government to repeal or replace certain European Union Law that was incorporated into UK law effective as of the end of the Transition Period to provide for certainty. The outcome of such process is unclear at this stage, but such a move would be likely cause further uncertainty.

Since a significant proportion of the regulatory framework in the United Kingdom applicable to our business and our product candidates is derived from European Union directives and regulations, Brexit has materially impacted and could continue to further impact, the regulatory regime with respect to the development, manufacture, importation, approval and commercialization of our product candidates in the United Kingdom or the European Union. For example, Great Britain is no longer covered by the centralized procedures for obtaining European Union-wide marketing and manufacturing authorizations from the EMA and a separate process for authorization of drug products is required in Great Britain. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would limit our ability to generate revenue and achieve and sustain profitability. In addition, while the Trade and Cooperation Agreement provides for the tariff-free trade of medicinal products between the United Kingdom and the European Union there are additional non-tariff costs to such trade which did not exist prior to Brexit. Furthermore, Brexit has reduced trade between the European Union and the United Kingdom and there are frequent delays in the transit of goods between the European Union and the United Kingdom. The ongoing impact of Brexit may cause us to incur significant additional expenses to operate our business, which could significantly and materially harm or delay our ability to generate revenues or achieve profitability of our business. Any further changes in international trade, tariff and import/export regulations as a result of Brexit or otherwise may impose unexpected duty costs or other non-tariff barriers on us.

Risks Related to the Commercialization of our Product Candidates

Even if any of our product candidates receive marketing approval, they may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

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

- the efficacy, safety and potential advantages compared to alternative treatments;
- the timing of market introduction of the product candidate as well as competitive products;
- our ability to offer our products for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments;
- product labeling or product insert requirements of the FDA or foreign regulatory authorities, including any limitations or warnings contained in a product's approved labeling, including any black box warning;
- the availability of the approved product candidate for use as a combination therapy;
- the willingness of the target patient population to try new treatments and of physicians to prescribe these treatments;
- our ability to hire and retain a sales force in the U.S.;
- the strength of marketing and distribution support;
- the availability of third-party coverage and adequate reimbursement for our product candidates, once approved;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our products together with other medications.

If we are unable to establish sales, marketing and distribution capabilities for NX-13 or any other product candidate that may receive regulatory approval, we may not be successful in commercializing those product candidates if and when they are approved.

We do not have sales or marketing infrastructure. To achieve commercial success for any product candidate for which we may obtain marketing approval, we will need to establish a sales and marketing organization. In the future, we expect to build a focused sales and marketing infrastructure to market some of our product candidates in the U.S., if and when they are approved. There are risks involved with establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

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

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians in order to educate physicians about our product candidates, once approved;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

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

We face substantial competition, which may result in a smaller than expected commercial opportunity and/or others discovering, developing or commercializing products before or more successfully than we do.

The biotechnology and pharmaceutical industries, and particularly the market for the treatment of autoimmune diseases, are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary and novel products and product candidates. 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 many different sources, including major pharmaceutical and specialty pharmaceutical companies, compounding facilities, academic institutions and governmental agencies and public and private research institutions.

We are aware of several other products and product candidates as potential treatments for UC that would compete with NX-13, if approved. In particular, we expect to compete against companies that produce biologic drugs that currently dominate the UC market, as well as companies that produce the 5 ASA's, corticosteroids and immunosuppressants that are currently used to treat patients with mild to moderate UC.

In addition, our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer or more effective, have fewer or less severe side effects, are more convenient or are less expensive than NX-13 or any other product 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 our product, which could result in our competitors establishing a strong market position before we are able to enter the market.

Many of the companies against which we are competing, or against which we may compete in the future, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or that may be necessary for, our programs.

The success of NX-13 or any future product candidate, will depend significantly on coverage and adequate reimbursement or the willingness of patients to pay for these products.

We believe our success depends on obtaining and maintaining coverage and adequate reimbursement for NX-13 for the treatment of UC, and the extent to which patients will be willing to pay out-of-pocket for such products, in the absence of reimbursement for all or part of the cost. Additionally, in the U.S., there is no uniform policy of coverage and reimbursement among third-party payors. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own coverage and reimbursement policies. However, decisions regarding the extent of coverage and amount of reimbursement to be provided are made on a payor-by-payor basis. One payor’s determination to provide coverage for a drug product does not assure that other payors will also provide coverage, and adequate reimbursement.

Third-party payors determine which products they will cover and establish reimbursement levels. Even if a third-party payor covers a particular product, the resulting reimbursement payment rates may not be adequate. Reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor’s determination that a product is safe, effective and medically necessary; appropriate for the specific patient; cost-effective; supported by peer-reviewed medical journals; included in clinical practice guidelines; and neither cosmetic, experimental, nor investigational.

Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Further, such payors are increasingly challenging the price, examining the medical necessity and reviewing the cost effectiveness of medical product candidates. There may be especially significant delays in obtaining coverage and reimbursement for newly approved drugs. Third-party payors may limit coverage to specific product candidates on an approved list, known as a formulary, which might not include all FDA-approved drugs for a particular indication. We may need to conduct expensive pharmaco-economic studies to demonstrate the medical necessity and cost effectiveness of our products. Nonetheless, our product candidates may not be considered medically necessary or cost effective. We cannot be sure that coverage and reimbursement will be available for any product that we commercialize and, if reimbursement is available, what the level of reimbursement will be.

Foreign governments also have their own healthcare reimbursement systems, which vary significantly by country and region, and we cannot be sure that coverage and adequate reimbursement will be made available with respect to the treatments in which our products are used under any foreign reimbursement system.

There can be no assurance that NX-13 or any other product candidate, if approved for sale in the U.S. or in other countries, will be considered medically reasonable and necessary, that it will be considered cost-effective by third-party payors, that coverage or an adequate level of reimbursement will be available or that reimbursement policies and practices in the U.S. and in foreign countries where our products are sold will not adversely affect our ability to sell our product candidates profitably, if they are approved for sale.

The market for NX-13 or any other product candidates may be smaller than we expect.

Our estimates of the potential market opportunity for our product candidates include several key assumptions based on our industry knowledge, industry publications and third-party research reports. These assumptions include the number of patients who have the autoimmune diseases we intend to target, as well as the estimated reimbursement levels for each product candidate if approved. However, there can be no assurance that any of these assumptions are, or will remain, accurate. Further, new studies may change the estimated incidence or prevalence of these diseases, and the potentially addressable patient population for our product candidates may not ultimately be amenable to treatment with our product candidates. If the actual market for our product candidates is smaller than we expect, our revenues, if any, may be limited and it may be more difficult for us to achieve or maintain profitability.

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

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any products that we may develop. If we cannot successfully defend ourselves against claims that our product candidates or drugs caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or drugs that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards paid to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any products that we may develop.

Although we 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 as we expand our clinical trials or if we commence commercialization of our product candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

Risks Related to our Dependence on Third Parties

We rely on third parties to conduct a significant portion of our existing clinical trials and potential future clinical trials for product candidates, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.

To date, we have generally engaged CROs to conduct our ongoing and completed clinical trials. We expect to engage CROs for future clinical trials for our product candidates and expect to continue to rely on third parties, including clinical data management organizations, medical institutions and clinical investigators, to conduct those clinical trials. Any of these third parties may terminate their engagements with us, some in the event of an uncured material breach and some at any time for convenience. If any of our relationships with these third parties terminate, we may not be able to timely enter into arrangements with alternative third parties or to do so on commercially reasonable terms, if at all. Switching or adding CROs involves substantial cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we intend to carefully manage our relationships with our 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. Further, the performance of our CROs may also be impacted by the ongoing armed conflict in Ukraine.

In addition, any third parties conducting our clinical trials will not be our employees, and except for remedies 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 programs. 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, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. Consequently, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase substantially and our ability to generate revenue could be delayed significantly.

We rely on these parties for execution of our preclinical studies and clinical trials, and generally do not control their activities. 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 responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as good clinical practices, or GCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions. If we or any of our CROs or other third parties, including trial sites, fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, EMA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials complies with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP conditions. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

In addition, 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. The FDA 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 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 and may ultimately lead to the denial of marketing approval of our product candidates.

We also expect to rely on other third parties to store and distribute product supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential revenue.

We contract with third parties for the manufacture of NX-13 and any other product candidates for clinical drug supply and expect to continue to do so for commercialization if approved. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not have any cGMP manufacturing facilities. We currently rely, and expect to continue to rely, on third parties for the cGMP manufacture of NX-13 and any other product candidates that we may pursue, for clinical development. Any significant delay, including any delays as a result of the COVID-19 pandemic or the ongoing armed conflict in Ukraine, in the supply of a product candidate or raw material components for an ongoing clinical trial due to the need to replace a third-party CMO could considerably delay the completion of our clinical trials.

We also expect to rely on third-party manufacturers or third-party collaborators for the manufacture of commercial supply of NX-13 and any other product candidates for which we obtain marketing approval. The facilities used by our CMOs to manufacture our product candidates must be inspected by the FDA or other regulatory authorities after we submit our NDA or comparable marketing application to the FDA or other regulatory authority. We do not have control over a supplier's or manufacturer's compliance with laws, regulations and applicable cGMP standards or similar regulatory requirements and other laws and regulations, such as those related to environmental health and safety matters. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or other regulatory authorities, we may be unable to obtain regulatory approval of our marketing applications. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority finds deficiencies with or does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved.

We may be unable to enter into any agreements with future third-party manufacturers or to do so on acceptable terms. Even if we enter into such agreements, qualifying and validating such manufacturers may take a significant period of time and reliance on third-party manufacturers entails additional risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- the incurrence of upfront scale-up costs prior to commercial approval;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how;
- the possible increase in costs for the raw materials for our product candidates; and
- the possible termination or nonrenewal of any agreement by any third party at a time that is costly or inconvenient for us.

Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supply of our products.

Our product candidates, and any drugs that we may develop, may compete with other product candidates and drugs for access to manufacturing facilities. There are no assurances we would be able to enter into similar commercial arrangements with other manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us in a timely manner. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval.

We have entered into, and intend to continue to enter into, collaborations with third parties for the development and commercialization of product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

We have entered into, and intend to continue to enter into, agreements with third-party collaborators for the development and commercialization of our product candidates. Our likely collaborators for any collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and smaller biotechnology companies. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

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

- 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;
- collaborators may refuse to perform clinical trials or other obligations required for approval in a particular jurisdiction outside the U.S.;
- our collaborators' regulatory submissions may be denied by the applicable regulatory authorities;
- 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 on terms that are more economically attractive than ours;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator 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;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays 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; and
- collaborations may be terminated for the convenience of the collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our drug development or commercialization program could be delayed, diminished or terminated.

Risks Related to our Intellectual Property

If we are unable to obtain or protect intellectual property rights related to any of our product candidates, we may not be able to compete effectively in our market.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our product candidates. Our success depends in large part on our ability to obtain and maintain patent and other intellectual property protection in the U.S. and in other countries with respect to our proprietary technology and product candidates.

We cannot offer any assurances about which of our patent applications will issue, the breadth of any resulting patent or whether any of the issued patents will be found invalid and unenforceable or will be threatened by third parties. We cannot offer any assurances that the breadth of our granted patents will be sufficient to stop a competitor from developing and commercializing a product, including a generic product that would be competitive with one or more of our product candidates. Furthermore, any successful challenge to these patents or any other patents owned by or licensed to us after patent issuance could deprive us of rights necessary for the successful commercialization of any of our product candidates. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced.

The patent prosecution process is expensive and time-consuming. We may not be able to prepare, file and prosecute all necessary or desirable patent applications at a commercially reasonable cost or in a timely manner or in all jurisdictions. It is also possible that we 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. Moreover, depending on the terms of any future in-licenses to which we may become a party, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology in-licensed from third parties. Therefore, these patents and patent applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

In addition to the protection provided by our patent estate, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not amenable to patent protection. Although we generally require all of our employees to assign their inventions to us, and all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information, or technology to enter into confidentiality agreements, we are aware that certain employees have not signed such agreements and we cannot provide any assurances that all such agreements have been duly executed, or that our trade secrets and other confidential proprietary information will not be disclosed. Moreover, our competitors may independently develop knowledge, methods and know-how equivalent to our trade secrets. Competitors could purchase our products, if approved, and replicate some or all of the competitive advantages we derive from our development efforts for technologies on which we do not have patent protection. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

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. However, our agreements and security measures may be breached, and we may not have adequate remedies for any breach. Also, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret. In addition, others may independently discover our trade secrets and proprietary information. For example, the FDA is considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA's disclosure policies may change in the future. If we are unable to prevent material disclosure of the non-patented intellectual property related to our technologies to third parties, and there is no guarantee that we will have any such enforceable trade secret protection, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition.

Patent terms may be inadequate to protect our competitive position on our products for an adequate amount of time, and if we do not obtain protection under the Hatch-Waxman Amendments and similar non-U.S. legislation for extending the term of patents covering each of our product candidates, our business may be materially harmed.

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. Depending upon the timing, duration and conditions of FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments, and similar legislation in the European Union. The Hatch-Waxman Amendments permit a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval. 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 receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. If we are unable to obtain patent term extension or the term of any such extension is less than we request, the period during which we can enforce our patent rights for that product will be shortened and our competitors may obtain approval to market competing products sooner. As a result, our revenue from applicable products could be reduced and could have a material adverse effect on our business.

If we fail to comply with our obligations in any future intellectual property licenses with third parties, we could also lose rights that are material to our business.

Although we do not currently rely upon any in-licenses to certain patent rights and proprietary technology for the development our product candidates, we may choose to enter into license agreements in the future. These license agreements may impose diligence, development and commercialization timelines and milestone payment, royalty, insurance and other obligations on us. If we fail to comply with our obligations, our licensors may have the right to terminate such licenses, in which event we might not be able to develop, manufacture or market any product that is covered by the intellectual property we in-license from such licensor and may face other penalties. Such an occurrence would materially adversely affect our business prospects.

Licenses to additional third-party technology and materials that may be required for our development programs may not be available in the future or may not be available on commercially reasonable terms, or at all, which could have a material adverse effect on our business and financial condition. We may require the cooperation of our licensors and any upstream licensor for the prosecution, maintenance and enforcement of the licensed and sublicensed intellectual property relating to relevant product candidates, which may not be forthcoming. Therefore, we cannot be certain that the prosecution, maintenance and enforcement of these patent rights will be in a manner consistent with the best interests of our business. If we or our licensor fail to maintain such patents, or if we or our licensor lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated and our right to develop and commercialize any of our product candidates that are the subject of such licensed rights could be adversely affected. In addition to the foregoing, the risks associated with patent rights that we license from third parties will also apply to patent rights we may own in the future. Further, if we fail to comply with our development obligations under our license agreements, we may lose our patent rights with respect to such agreement on a territory-by-territory basis, which would affect our patent rights worldwide.

Termination of any future license agreements would reduce or eliminate our rights under these agreements and may result in our having to negotiate new or reinstated agreements with less favorable terms or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology. Any of the foregoing could prevent us from commercializing relevant product candidates, which could have a material adverse effect on our operating results and overall financial condition.

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

Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our future patents.

Our ability to obtain patents is highly uncertain because, to date, some legal principles remain unresolved, and there has not been a consistent policy regarding the breadth or interpretation of claims allowed in patents in the U.S. Furthermore, the specific content of patents and patent applications that are necessary to support and interpret patent claims is highly uncertain due to the complex nature of the relevant legal, scientific, and factual issues. Changes in either patent laws or interpretations of patent laws in the U.S. and other countries may diminish the value of our intellectual property or narrow the scope of our patent protection.

For example, on September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act included a number of significant changes to U.S. patent law. These included provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. The U.S. Patent and Trademark Office, or USPTO, has developed new and untested regulations and procedures to govern the full implementation of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, became effective in March 2013. The Leahy-Smith Act has also introduced procedures making it easier for third parties to challenge issued patents, as well as to intervene in the prosecution of patent applications. Finally, the Leahy-Smith Act contained new statutory provisions that require the USPTO to issue new regulations for their implementation, and it may take the courts years to interpret the provisions of the new statute. It is too early to tell what, if any, impact the Leahy-Smith Act will have on the operation of our business and the protection and enforcement of our intellectual property. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our future patents. Further, the U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening 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 actions 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 patents that we have owned or licensed or that we might obtain in the future. An inability to obtain, enforce, and defend patents covering our proprietary technologies would materially and adversely affect our business prospects and financial condition.

Similarly, changes in patent laws and regulations in other countries or jurisdictions, changes in the governmental bodies that enforce them or changes in how the relevant governmental authority enforces patent laws or regulations may weaken our ability to obtain new patents or to enforce patents that we may obtain in the future. Further, 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 U.S. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the U.S. and abroad. For example, if the issuance in a given country of a patent covering an invention is not followed by the issuance in other countries of patents covering the same invention, or if any judicial interpretation of the validity, enforceability or scope of the claims or the written description or enablement, in a patent issued in one country is not similar to the interpretation given to the corresponding patent issued in another country, our ability to protect our intellectual property in those countries may be limited. Changes in either patent laws or in interpretations of patent laws in the U.S. and other countries may materially diminish the value of our intellectual property or narrow the scope of our patent protection.

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

Competitors may infringe the patents we have applied for. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. If we initiate legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product or product candidate is invalid and/or unenforceable. In patent litigation in the U.S., counterclaims alleging invalidity and/or unenforceability are common, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent.

In an infringement proceeding, a court may decide that the patent claims we are asserting are invalid and/or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patent claims do not cover the technology in question. Third parties may also raise similar claims before administrative bodies in the U.S. or abroad, even outside the context of litigation. Such mechanisms include re-examination, post grant review, *inter partes* review and equivalent proceedings in foreign jurisdictions (for example, opposition proceedings). Such proceedings could result in revocation of or amendment to our patents in such a way that they no longer cover our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we, our patent counsel, and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing and could have a material adverse impact on our business.

Interference proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patent applications. An unfavorable outcome could require us to cease using the related technology or force us to take a license under the patent rights of the prevailing party, if available. Furthermore, our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the U.S.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

We may be unsuccessful in licensing or acquiring intellectual property from third parties that may be required to develop and commercialize our product candidates.

A third party may hold intellectual property, including patent rights that are important or necessary to the development and commercialization of our product candidates. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our product candidates, in which case we would be required to acquire or obtain a license to such intellectual property from these third parties, and we may be unable to do so on commercially reasonable terms or at all. The licensing or acquisition of third-party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could have a material adverse effect on our business.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain.

As our current and future product candidates progress toward commercialization, the possibility of a patent infringement claim against us increases. We cannot provide any assurance that our current and future product candidates do not infringe other parties' patents or other proprietary rights, and competitors or other parties may assert that we infringe their proprietary rights in any event. We may become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our current and future product candidates, including interference or derivation proceedings before the USPTO. Even if we believe such claims are without merit, a court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, which could have a negative impact on our ability to commercialize NX-13 or any future product candidates. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is high and requires us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would agree with us and invalidate the claims of any such U.S. patent. Moreover, given the vast number of patents in our field of technology, we cannot be certain that we do not infringe existing patents or that we will not infringe patents that may be granted in the future.

While we may decide to initiate proceedings to challenge the validity of these or other patents in the future, we may be unsuccessful, and courts or patent offices in the U.S. and abroad could uphold the validity of any such patent. Furthermore, because patent applications can take many years to issue and may be confidential for 18 months or more after filing, and because pending patent claims can be revised before issuance, there may be applications now pending which may later result in issued patents that may be infringed by the manufacture, use or sale of our product candidates. Regardless of when filed, we may fail to identify relevant third-party patents or patent applications, or we may incorrectly conclude that a third-party patent is invalid or not infringed by our product candidates or activities. If a patent holder believes that one of our product candidates infringes its patent, the patent holder may sue us even if we have received patent protection for our technology. Moreover, we may face patent infringement claims from non-practicing entities that have no relevant drug revenue and against whom our own patent portfolio may thus have no deterrent effect. If a patent infringement suit were threatened or brought against us, we could be forced to stop or delay research, development, manufacturing or sales of the drug or product candidate that is the subject of the actual or threatened suit.

If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue commercializing our product candidates. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if a license can be obtained on acceptable terms, the rights may be non-exclusive, which could give our competitors access to the same technology or intellectual property rights licensed to us. If we fail to obtain a required license, we may be unable to effectively market product candidates based on our technology, which could limit our ability to generate revenue or achieve profitability and possibly prevent us from generating revenue sufficient to sustain our operations. Alternatively, we may need to redesign our infringing products, which may be impossible or require substantial time and monetary expenditure. Under certain circumstances, we could be forced, including by court orders, to cease commercializing our product candidates. In addition, in any such proceeding or litigation, we could be found liable for substantial monetary damages, potentially including treble damages and attorneys' fees, if we are found to have willfully infringed the patent at issue. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could harm our business. Any claims by third parties that we have misappropriated their confidential information or trade secrets could have a similar negative impact on our business.

The cost to us in defending or initiating any litigation or other proceeding relating to patent or other proprietary rights, even if resolved in our favor, could be substantial, and litigation would divert our management's attention. 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. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could delay our research and development efforts and limit our ability to continue our operations.

We may be subject to claims that our employees, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties.

We employ individuals who were previously employed at other biotechnology or biopharmaceutical companies. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees, consultants, or independent contractors have inadvertently or otherwise used or disclosed confidential information of our employees' former employers or other third parties. We may also be subject to claims that former employers or other third parties have an ownership interest in our future patents. Litigation may be necessary to defend against these claims. There is no guarantee of success in defending these claims, and even if we are successful, litigation could result in substantial cost and be a distraction to our management and other employees.

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

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

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

If we rely on third parties to manufacture or commercialize our product candidates, or if we collaborate with additional third parties for the development of our product candidates, we must, at times, share trade secrets with them. We may also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development partnerships or similar agreements. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third-party contractors and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure could have an adverse effect on our business and results of operations.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our trade secrets. Despite our efforts to protect our trade secrets, we may not be able to prevent the unauthorized disclosure or use of our technical know-how or other trade secrets by the parties to these agreements. Moreover, we cannot guarantee that we have entered into such agreements with each party that may have or have had access to our confidential information or proprietary technology and processes. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. If any of the collaborators, scientific advisors, employees, contractors and consultants who are parties to these agreements breaches or violates the terms of any of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets as a result. Moreover, if confidential information that is licensed or disclosed to us by our partners, collaborators, or others is inadvertently disclosed or subject to a breach or violation, we may be exposed to liability to the owner of that confidential information. Enforcing a claim that a third party illegally obtained and is using our trade secrets, like patent litigation, is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the U.S. are sometimes less willing to protect trade secrets.

We may enjoy only limited geographical protection with respect to certain patents and we may not be able to protect our intellectual property rights throughout the world.

Filing and prosecuting patent applications and defending patents covering our product candidates in all countries throughout the world would be prohibitively expensive. 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 rights are not as strong as that in the U.S. or Europe. These products may compete with our product candidates, and our future patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

In addition, we may decide to abandon national and regional patent applications before they are granted. The examination of each national or regional patent application is an independent proceeding. As a result, patent applications in the same family may issue as patents in some jurisdictions, such as in the U.S., but may issue as patents with claims of different scope or may even be refused in other jurisdictions. It is also quite common that depending on the country, the scope of patent protection may vary for the same product candidate or technology.

While we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our product candidates. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate, which may have an adverse effect on our ability to successfully commercialize our product candidates in all of our expected significant foreign markets. If we encounter difficulties in protecting, or are otherwise precluded from effectively protecting, the intellectual property rights important for our business in such jurisdictions, the value of these rights may be diminished, and we may face additional competition from others in those jurisdictions.

The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws or rules and regulations in the U.S. and Europe, and many companies have encountered significant difficulties in protecting and defending such rights in such jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property rights, which could make it difficult for us to stop the infringement of our future patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in other jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our future patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing as patents, 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.

Some countries also have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, some countries limit the enforceability of patents against government agencies or government contractors. In those countries, the patent owner may have limited remedies, which could materially diminish the value of such patents. If we are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired.

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

Periodic maintenance fees, renewal fees, annuity fees and various other government fees on patents and/or applications will be due to be paid to the USPTO and various government patent agencies outside of the U.S. over the lifetime of our patents and/or applications and any patent rights we may obtain in the future. Furthermore, the USPTO and various non-U.S. government patent agencies require compliance with several procedural, documentary, fee payment and other similar provisions during the patent application process. In many cases, an inadvertent lapse of a patent or patent application can be cured by payment of a late fee or by other means in accordance with the applicable rules. There are situations, however, in which non-compliance can result in abandonment or lapse of the patents or patent applications, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, potential competitors might be able to enter the market, which could have a material adverse effect on our business.

Any trademarks we have obtained or may obtain may be infringed or otherwise violated, or successfully challenged, resulting in harm to our business.

We expect to rely on trademarks as one means to distinguish our product candidates, if approved for marketing, from the drugs of our competitors. Once we select new trademarks and apply to register them, our trademark applications may not be approved. Third parties may oppose or attempt to cancel our trademark applications or trademarks, or otherwise challenge our use of the trademarks. In the event that our trademarks are successfully challenged, we could be forced to rebrand our drugs, which could result in loss of brand recognition and could require us to devote resources to advertising and marketing new brands. Our competitors may infringe or otherwise violate our trademarks and we may not have adequate resources to enforce our trademarks. Any of the foregoing events may have a material adverse effect on our business.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

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

- others may be able to make products that are similar to or otherwise competitive with our product candidates but that are not covered by the claims of our current or future patents;
- an in-license necessary for the manufacture, use, sale, offer for sale or importation of one or more of our product candidates may be terminated by the licensor;
- we or future collaborators might not have been the first to make the inventions covered by our issued or future issued patents or our pending patent applications;
- we or future collaborators might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own or in-license may be held invalid or unenforceable as a result of legal challenges by our competitors;
- issued patents that we own or in-license may not provide coverage for all aspects of our product candidates in all countries;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop 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, results of operations and prospects.

Risks Related to Legal and Regulatory Compliance Matters

Our relationships with customers, healthcare providers and third-party payors are subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, and other healthcare laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

Healthcare providers and third-party payors in the U.S. and elsewhere will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare professionals, principal investigators, consultants, customers and third-party payors subject us to various federal and state fraud and abuse laws and other healthcare laws, including, without limitation, the federal Anti-Kickback Statute, the federal civil and criminal false claims laws and transparency laws, including the law commonly referred to as the Physician Payments Sunshine Act, and regulations promulgated under such laws. These laws will impact, among other things, our clinical research, proposed sales, marketing and educational programs, and other interactions with healthcare professionals. The laws that will affect our operations include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, individuals or entities from knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind in return for, or to induce, either the referral of an individual, or the purchase, lease, order or arrangement for or recommendation of the purchase, lease, order or arrangement for any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. The term "remuneration" has been broadly interpreted to include anything of value. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. A person does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation;
- the federal civil and criminal false claims laws, including, without limitation, the civil False Claims Act, which can be enforced by private citizens through civil whistleblower or qui tam actions, and civil monetary penalty laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from the federal government, including Medicare, Medicaid and other government payors, that are false or fraudulent or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim or to avoid, decrease or conceal an obligation to pay money to the federal government. A claim includes "any request or demand" for money or property presented to the U.S. federal government. Several pharmaceutical and other healthcare companies have been prosecuted under these laws for, among other things, allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of products for unapproved, and thus non-reimbursable, uses. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes which prohibit, among other things, a person from knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and their implementing regulations, also imposes obligations, including mandatory contractual terms, on "covered entities," including certain healthcare providers, health plans, healthcare clearinghouses, and their respective "business associates" that create, receive, maintain or transmit individually identifiable health information for or on behalf of a covered entity as well as their covered subcontractors, with respect to safeguarding the privacy, security and transmission of individually identifiable health information, as well as analogous state and foreign laws that 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;
- the federal transparency laws, including the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, medical devices, biologicals 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 the Centers for Medicare & Medicaid Services, or CMS, information related to: (1) payments or other "transfers of value'' made during the previous year to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other health care professionals (such as physician assistants and nurse practitioners), and teaching hospitals, as well as information regarding ownership and investment interests held by physicians and their immediate family members); and
- state and foreign law equivalents of each of the above federal laws and regulations; state laws that require manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, marketing expenditures or drug pricing; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or that otherwise restrict payments that may be made to healthcare providers; and state and local laws that require the registration of pharmaceutical sales representatives.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. 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 penalties, including, without limitation, civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participating in federal and state funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, contractual damages, diminished profits and future earnings, reputational harm and the curtailment or restructuring of our operations, any of which could harm our business.

The risk of our being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. The shifting compliance environment and the need to build and maintain robust and expandable systems to comply with multiple jurisdictions with different compliance and/or reporting requirements increases the possibility that a healthcare company may run afoul of one or more of the requirements.

Even if we obtain regulatory approval for NX-13 or any future product candidates, they will remain subject to ongoing regulatory oversight.

Even if we obtain any regulatory approval for NX-13 or any future product candidates, such product candidates, once approved, will be subject to ongoing regulatory requirements applicable to manufacturing, labeling, packaging, storage, advertising, promoting, sampling, record-keeping and submitting of safety and other post-market information, among other things. Any regulatory approvals that we receive for NX-13 or any future product candidates may also be subject to a risk evaluation and mitigation strategy, limitations on the approved indicated uses for which the drug may be marketed or to the conditions of approval, or requirements that we conduct potentially costly post-marketing testing, including Phase 4 trials and surveillance to monitor the quality, safety and efficacy of the drug. An unsuccessful post-marketing study or failure to complete such a study could result in the withdrawal of marketing approval. We will further be required to immediately report any serious and unexpected adverse events and certain quality or production problems with our products to regulatory authorities along with other periodic reports.

Any new legislation addressing drug safety issues could result in delays in product development or commercialization, or increased costs to assure compliance. We will also have to comply with requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drug products are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved label. As such, we will not be allowed to promote our products for indications or uses for which they do not have approval, commonly known as off-label promotion. Physicians, on the other hand, may prescribe products for off-label uses. Although the FDA and other regulatory agencies do not regulate a physician's choice of drug treatment made in the physician's independent medical judgment, they do restrict promotional communications from companies or their sales force with respect to off-label uses of products for which marketing approval has not been issued. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA approved labeling. The holder of an approved NDA must submit new or supplemental applications and obtain prior approval for certain changes to the approved product, product labeling, or manufacturing process. A company that is found to have improperly promoted off-label uses of their products may be subject to significant civil, criminal and administrative penalties.

In addition, drug manufacturers are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP requirements and adherence to commitments made in the NDA or foreign marketing application. If we, or a regulatory authority, discover previously unknown problems with a drug, such as adverse events of unanticipated severity or frequency, or problems with the facility where the drug is manufactured or if a regulatory authority disagrees with the promotion, marketing or labeling of that drug, a regulatory authority may impose restrictions relative to that drug, the manufacturing facility or us, including requesting a recall or requiring withdrawal of the drug from the market or suspension of manufacturing.

If we fail to comply with applicable regulatory requirements following approval of any of our product candidates, a regulatory authority may:

- issue an untitled letter or warning letter asserting that we are in violation of the law;
- seek an injunction or impose administrative, civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve a pending NDA or comparable foreign marketing application (or any supplements thereto) submitted by us or our strategic partners;
- restrict the marketing or manufacturing of the drug;
- seize or detain the drug or otherwise require the withdrawal of the drug from the market;
- refuse to permit the import or export of product candidates; or
- refuse to allow us to enter into supply contracts, including government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and harm our business, financial condition, results of operations and prospects.

Healthcare legislative or regulatory reform measures may have a negative impact on our business and results of operations.

In the U.S. and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of product candidates, restrict or regulate post-approval activities, and affect our ability to profitably sell any product candidates for which we obtain marketing approval.

Among policy makers and payors in the U.S. and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the U.S., the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the ACA, was passed, which substantially changed the way healthcare is financed by both the government and private insurers, and significantly impacts the U.S. pharmaceutical industry. The ACA, among other things: (1) established an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs; (2) expanded the entities eligible for discounts under the 340B drug pricing program; (3) increased the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively, and capped the total rebate amount for innovator drugs at 100% of the Average Manufacturer Price, or AMP; (4) expanded the eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability; (5) addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for certain drugs and biologics that are inhaled, infused, instilled, implanted or injected; (6) introduced a new Medicare Part D coverage gap discount program in which manufacturers must now agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; (7) created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and (8) established a Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

There have been judicial and Congressional challenges to certain aspects of the ACA, as well as efforts by the Trump administration to repeal or replace certain aspects of the ACA. While Congress has not passed comprehensive repeal legislation, several bills affecting the implementation of certain taxes under the ACA have been signed into law. Additionally, on June 17, 2021, the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period from February 15, 2021 through May 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. Further, on August 16, 2022, President Biden signed the Inflation Reduction Act of 2022, or IRA, into law which, among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and creating a new manufacturer discount program. It is unclear how such challenges, and the healthcare reform measures of the Biden administration will impact the ACA and our business.

Other legislative changes have been proposed and adopted since the ACA was enacted. These changes include aggregate reductions to Medicare payments to providers of 2% per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013, and due to subsequent legislative amendments to the statute, including the Infrastructure Investment and Jobs Act, will remain in effect until 2031, with the exception of a temporary suspension from May 1, 2020, through March 31, 2022, unless additional Congressional action is taken. Under current legislation the actual reduction in Medicare payments will vary from 1% in 2022 to up to 4% in the final fiscal year of this sequester. In addition, the American Taxpayer Relief Act of 2012, among other things, further 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, which could have an adverse effect on customers for our product candidates, if approved, and, accordingly, our financial operations. Further, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024.

Additionally, there has been heightened governmental scrutiny in the U.S. of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level, in July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, the U.S. Department of Health and Human Services, or HHS, released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. In addition, the IRA, among other things, (1) directs HHS to negotiate the price of certain single-source drugs and biologics covered under Medicare and (2) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. These provisions will take effect progressively starting in fiscal year 2023, although they may be subject to legal challenges. It is currently unclear how the IRA will be implemented but is likely to have a significant impact on the pharmaceutical industry. Further, the Biden administration released an additional executive order on October 14, 2022, directing HHS to submit a report on how the Center for Medicare and Medicaid Innovation can be further leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

We expect that these and 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 receive for any approved drug. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our drugs.

In addition, FDA regulations and guidance may be revised or reinterpreted by the FDA in ways that may significantly affect our business and our products. If executive actions impose restrictions on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted. Any new regulations or guidance, or revisions or reinterpretations of existing regulations or guidance, may impose additional costs or lengthen FDA review times for our product candidates. We cannot determine how changes in regulations, statutes, policies, or interpretations when and if issued, enacted or adopted, may affect our business in the future. Such changes could, among other things, require:

- additional clinical trials to be conducted prior to obtaining approval;
- changes to manufacturing methods;
- recalls, replacements, or discontinuance of one or more of our products; and
- additional recordkeeping.

Such changes would likely require substantial time and impose significant costs, or could reduce the potential commercial value of our product candidates, and could materially harm our business and our financial results. In addition, delays in receipt of or failure to receive regulatory clearances or approvals for any other products would harm our business, financial condition, and results of operations. Further, we cannot predict the likelihood, nature, or extent of healthcare reform initiatives that may arise from future legislation or administrative action.

Risks Related to Employee Matters and Managing our Growth

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

Each of our executive officers may currently terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or employees.

Recruiting and retaining qualified scientific and clinical personnel and, if we progress the development of our product pipeline toward scaling up for commercialization, manufacturing and sales and marketing personnel, will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

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

As of December 31, 2022, we had 22 full-time employees and have engaged various outside consultants, principally in the areas of corporate development and regulatory affairs. As we continue to build our organization and execute on our strategy, we expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of clinical product development, regulatory affairs and, if any of our product candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management, business, and development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

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

We are exposed to the risk that our employees, independent contractors, consultants, commercial collaborators, principal investigators, CROs, suppliers and vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates FDA regulations, including those laws requiring the reporting of true, complete and accurate information to the FDA, manufacturing standards, federal and state healthcare laws and regulations, and laws that require the true, complete and accurate reporting of financial information or data. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Misconduct by these parties could also involve the improper use of individually identifiable information, including, without limitation, information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a code of business conduct and ethics, but it is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. 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, including the imposition of significant civil, criminal and administrative penalties, including, without limitation, damages, fines, disgorgement, imprisonment, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations.

Risks Related to Ownership of our Common Stock

The trading price of the shares of our common stock has been and may continue to be volatile, and purchasers of our common stock could incur substantial losses.

Our stock price has been and may continue to be volatile. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may not be able to sell their common stock at or above the price paid for the shares. The market price for our common stock may be influenced by many factors, including:

- the commencement, enrollment or results of our clinical trials of any future clinical trials we may conduct, or changes in the development status of our product candidates;

- any delay in our regulatory filings for any product candidate we may develop, 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;
- the success of competitive products or announcements by potential competitors of their product development efforts;
- adverse results from, delays in or termination of clinical trials;
- adverse regulatory decisions, including failure to receive regulatory approval of our product candidates;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- unanticipated serious safety concerns related to the use of our product candidates;
- changes in financial estimates by us or by any equity research analysts who might cover our stock;
- conditions or trends in our industry;
- 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 biopharmaceutical 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 collaborations, joint ventures, capital commitments 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;
- sales of common stock by us, our insiders or our other stockholders;
- expiration of market stand-off or lock-up agreements;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- significant lawsuits, including patent or stockholder litigation;
- changes in the structure of healthcare payment systems;
- general political and economic conditions; and
- other events or factors, many of which are beyond our control.

The stock market in general, and the Nasdaq Capital Market and biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies, which has resulted in decreased stock prices for many companies notwithstanding the lack of a fundamental change in their underlying business models or prospects. Broad market and industry factors, including worsening economic conditions and other adverse effects or developments relating to the ongoing COVID-19 pandemic and the ongoing armed conflict in Ukraine, may negatively affect the market price of our common stock, regardless of our actual operating performance. The realization of any of the above risks or any of a broad range of other risks, including those described in this section, could have a significant and material adverse impact on the market price of our common stock.

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. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management's attention and resources from our business.

An active trading market for our common stock may not continue to be developed or sustained.

Prior to our initial public offering, there was no public market for our common stock. Although our common stock is listed on The Nasdaq Capital Market, an active trading market for our shares may never develop or be sustained. If an active market for our common stock does not develop or is not sustained, it may be difficult for you to sell shares of our common stock at an attractive price or at all.

If equity research analysts do not continue to publish research or reports, or publish unfavorable research or reports, about us, our business or our market, our stock price and trading volume could decline.

The trading market for our common stock may be influenced by the research and reports that equity research analysts publish about us and our business, and we have only limited research coverage by equity research analysts. Equity research analysts may elect not to initiate or continue research coverage of our common stock, and such lack of research coverage may adversely affect the market price of our common stock. We do not have any control over the analysts or the content and opinions included in their reports. The price of our stock could decline if one or more equity research analysts downgrade our stock or issue other unfavorable commentary or research. If one or more equity research analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which in turn could cause our stock price or trading volume to decline.

Future sales, or the possibility of future sales, of a substantial number of shares of our common stock could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. If our stockholders sell, or the market perceives that our stockholders intend to sell, substantial amounts of our common stock in the public market, the market price of our common stock could decline significantly.

We have filed a registration statement on Form S-3 registering the issuance and sale by us of up to a maximum aggregate offering price of $200.0 million of common stock, preferred stock, debt securities and warrants in one or more offerings and in any combination.

In addition, we have filed registration statements on Form S-8 registering the issuance of common stock subject to options or other equity awards issued or reserved for future issuance under our equity incentive plans. Shares registered under these registration statements on Form S-8 will be available for sale in the public market subject to vesting arrangements and exercise of options and the restrictions of Rule 144 in the case of our affiliates.

Additionally, the holders of an aggregate of approximately 45.8 million shares of our common stock, or their transferees, have rights, subject to some conditions, to require us to file one or more registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. If we were to register the resale of these shares, they could be freely sold in the public market. If these additional shares are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

Provisions in our corporate charter documents and under Delaware law may prevent or frustrate attempts by our stockholders to change our management and hinder efforts to acquire a controlling interest in us, and the market price of our common stock may be lower as a result.

There are provisions in our certificate of incorporation and bylaws that may make it difficult for a third party to acquire, or attempt to acquire, control of our company, even if a change of control was considered favorable by you and other stockholders. For example, our board of directors has the authority to issue up to 10,000,000 shares of preferred stock. The board of directors can fix the price, rights, preferences, privileges, and restrictions of the preferred stock without any further vote or action by our stockholders. The issuance of shares of preferred stock may delay or prevent a change of control transaction. As a result, the market price of our common stock and the voting and other rights of our stockholders may be adversely affected. An issuance of shares of preferred stock may result in the loss of voting control to other stockholders.

Our charter documents also contain other provisions that could have an anti-takeover effect, including:

- only one of our three classes of directors will be elected each year;
- stockholders will not be entitled to remove directors other than by a 66 2/3% vote and only for cause;
- stockholders will not be permitted to take actions by written consent;
- stockholders cannot call a special meeting of stockholders; and
- stockholders must give advance notice to nominate directors or submit proposals for consideration at stockholder meetings.

In addition, we are subject to the anti-takeover provisions of Section 203 of the Delaware General Corporation Law, which regulates corporate acquisitions by prohibiting Delaware corporations from engaging in specified business combinations with particular stockholders of those companies. These provisions could discourage potential acquisition proposals and could delay or prevent a change of control transaction. They could also have the effect of discouraging others from making tender offers for our common stock, including transactions that may be in your best interests. These provisions may also prevent changes in our management or limit the price that investors are willing to pay for our stock.

Concentration of ownership of our common stock among our existing executive officers, directors and principal stockholders may prevent new investors from influencing significant corporate decisions.

Our executive officers, directors and current beneficial owners of 5% or more of our common stock and their respective affiliates beneficially own a majority of our common stock. As a result, these persons, acting together, would be able to significantly influence all matters requiring stockholder approval, including the election and removal of officers or directors, any merger, consolidation, sale of all or substantially all of our assets, or other significant corporate transactions.

Some of these persons or entities may have interests different than yours. For example, because many of these stockholders purchased their shares at prices substantially below the current market price of our common stock and have held their shares for a longer period, they may be more interested in selling our company to an acquirer than other investors, or they may want us to pursue strategies that deviate from the interests of other stockholders.

We are an "emerging growth company" and a "smaller reporting company" and, as a result of the reduced disclosure and governance requirements applicable to emerging growth companies and smaller reporting companies, our common stock may be less attractive to investors.

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and we intend to take advantage of some of the exemptions from 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 in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation in our periodic reports, proxy statements and registration statements; and
- not being required to hold a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We cannot predict if investors will find our common stock less attractive because we will rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. We may take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until December 31, 2026 or, if earlier, (i) the last day of the fiscal year in which we have total annual gross revenue of at least $1.235 billion, (ii) the date on which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th, or (iii) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

Even after we no longer qualify as an emerging growth company, we may, under certain circumstances, still qualify as a "smaller reporting company," which would allow us to take advantage of many of the same exemptions from disclosure requirements, including reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements.

We have broad discretion in the use of our cash, cash equivalents and investments, including the proceeds from our initial public offering and our recent private placement of pre-funded warrants.

We have broad discretion over the use of our cash, cash equivalents and investments, including the proceeds from our initial public offering and our recent private placement of pre-funded warrants. You may not agree with our decisions, and our use of the proceeds may not yield any return on your investment. Our failure to apply our cash, cash equivalents, and investments effectively could compromise our ability to pursue our growth strategy and we might not be able to yield a significant return, if any, on our investment of these proceeds. You will not have the opportunity to influence our decisions on how to use our cash, cash equivalents, and investments.

Because we do not anticipate paying any cash dividends on our common stock in the foreseeable future, capital appreciation, if any, will be your sole source of gains and you may never receive a return on your investment.

You should not rely on an investment in our common stock to provide dividend income. We have not declared or paid cash dividends on our common stock to date. We currently intend to retain our future earnings, if any, to fund the development and growth of our business. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future. Investors seeking cash dividends should not purchase our common stock.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware and the federal district courts of the U.S. will be the exclusive forums for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the 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 breach of fiduciary duty;
- any action asserting a claim against us arising under the Delaware General Corporation Law, our amended and restated certificate of incorporation, or our amended and restated bylaws;
- any claim or cause of action seeking to interpret, apply, enforce or determine the validity of our restated certificate or our amended and restated bylaws;
- any claim or cause of action as to which the Delaware General Corporation Law confers jurisdiction on the Court of Chancery of the state of Delaware; and
- any action asserting a claim against us that is governed by the internal-affairs doctrine.

This provision would 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. 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 amended and restated certificate of incorporation further provides that the federal district courts of the U.S. will be the exclusive forum for resolving any complaint asserting a cause of action 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 amended and 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 a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, or other employees, which may discourage lawsuits against us and our directors, officers and other employees. If a court were to find either exclusive-forum provision in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with resolving the dispute in other jurisdictions, all of which could seriously harm our business.

If we fail to comply or regain compliance with the continued listing standards of the Nasdaq Capital Market, we may be delisted and the price of our common stock, our ability to access the capital markets and our financial condition could be negatively impacted.

Our common stock is currently listed on Nasdaq under the symbol "LABP." To maintain the listing of our common stock on the Nasdaq Capital Market, we are required to meet certain listing requirements, including, among others, maintaining a minimum closing bid price of $1.00 per share. In June 2022, the decline in the market price of our common stock resulted in a notice that we are not in compliance with the minimum bid price requirement for continued listing on the Nasdaq Global Market. In December 2022, Nasdaq approved our application to transfer to The Nasdaq Capital Market and notified us that we have been granted an additional 180-calendar day compliance period to regain compliance with the minimum bid price requirement. If we are not able to regain compliance within the compliance period offered by Nasdaq, we could be delisted, which would have a further material adverse effect on market prices of our common stock and stockholder liquidity. We intend to actively monitor the bid price of our common stock and will consider available options to regain compliance with the listing requirement; however, there can be no assurance that we will be able to regain compliance with the listing requirement or will otherwise be in compliance with other Nasdaq listing criteria. In addition, we are not currently in compliance with the Nasdaq requirement to have three directors that are independent under Rule 10A-3 under the Securities Exchange Act of 1934, as amended. If the Nasdaq Capital Market delists our securities from trading on its exchange for failure to meet the listing standards, we and our stockholders could face significant negative consequences including:

- limited availability of market quotations for our securities;
- a determination that the common stock is a "penny stock" which will require brokers trading in the common stock to adhere to more stringent rules, possibly resulting in a reduced level of trading activity in the secondary trading market for shares of common stock;
- a limited amount of analyst coverage; and
- a decreased ability to issue additional securities or obtain additional financing in the future.

General Risks

We maintain a large quantity of sensitive information, including confidential business and personal information in connection with the conduct of our clinical trials and related to our employees, and we are subject to laws and regulations governing the privacy and security of such information.

In the U.S., there are numerous federal and state privacy and data security laws and regulations governing the collection, use, disclosure and protection of personal information, including federal and state health information privacy laws, federal and state security breach notification laws, and federal and state consumer protection laws. Each of these constantly evolving laws can be subject to varying interpretations. In addition, we may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under HIPAA. Depending on the facts and circumstances, we could be subject to criminal penalties if we knowingly obtain, use, or disclose individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA.

Even when HIPAA does not apply, according to the Federal Trade Commission, or the FTC, violating consumers' privacy rights or failing to take appropriate steps to keep consumers' personal information secure may constitute unfair acts or practices in or affecting commerce in violation of Section 5(a) of the FTC Act. The FTC expects a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. Individually identifiable health information is considered sensitive data that merits stronger safeguards.

In addition, states are constantly adopting new laws or amending existing laws, requiring attention to frequently changing regulatory requirements. For example, California enacted the California Consumer Privacy Act, or the CCPA, which took effect on January 1, 2020, and has been dubbed the first "GDPR-like" law in the U.S. The CCPA gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing and receive detailed information about how their personal information is used by requiring covered companies to provide new disclosures to California consumers (as that term is broadly defined) and provide such consumers new ways to opt-out of certain sales of personal information. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. The CCPA may increase our compliance costs and potential liability. Some observers have noted that the CCPA could mark the beginning of a trend toward more stringent privacy legislation in the U.S.

Further, the California Privacy Rights Act of 2020, or the CPRA, expands the CCPA's requirements, including by adding a new right for individuals to correct their personal information and establishing a new regulatory agency to implement and enforce the law. Other states, such as Virginia, Colorado, Utah, and Connecticut, have also passed comprehensive privacy laws, and similar laws are being considered in several other states, as well as at the federal and local levels. While these states, like the CCPA, also exempt some data processed in the context of clinical trials, these developments further complicate compliance efforts, and increase legal risk and compliance costs for us, the third parties upon whom we rely, and our customers.

Outside the U.S., an increasing number of laws, regulations, and industry standards may govern data privacy and security. For example, our processing of personal data is or may become subject in certain circumstances to the European Union's General Data Protection Regulation, or EU GDPR, and/or the United Kingdom's so-called 'UK GDPR'. Each of these regulations requires stringent standards of data privacy and security concerning personal data and potentially significant sanctions. For example, companies may face temporary or definitive bans on processing of personal data and other corrective actions; fines of up to 20 million Euros under the EU GDPR / 17.5 million pounds sterling under the UK GDPR or, in each case, 4% of annual global revenue whichever is greater; or private litigation related to processing of personal data brought by classes of data subjects or consumer protection organizations authorized at law to represent their interests.

In addition, we may be unable to receive and/or further transfer onwards personal data that is processed subject to the EU GDPR and/or UK GDPR, or certain other data privacy and security regimes, due to limitations on cross-border data flows and/or actual or de facto data localization requirements. In particular, the EU GDPR and UK GDPR significantly restrict the transfer of personal data to the U.S. and other countries whose privacy laws are considered 'inadequate' for the purposes of either or both of those regulations. Although there are currently various mechanisms that may be used to effect such cross-border transfers of personal data in compliance with the EU GDPR and UK GDPR, such as the European Commission's 'Standard Contractual Clauses' and the United Kingdom's 'International Data Transfer Agreement / Addendum', all such mechanisms are subject to legal challenges, and there is no assurance that we can always satisfy or rely on these mechanisms to lawfully effect cross-border transfers of personal data where required. Other jurisdictions relevant to our operations may implement, or adopt stringent interpretations of, their own data localization and cross-border data transfer laws. If there is no lawful manner for us to effect or be the recipient of cross-border transfers of personal data in compliance with the EU GDPR and/or UK GDPR, and/or other applicable data privacy and security obligations, or if the requirements for a compliant transfer are too onerous, we could face significant adverse consequences, including the interruption or degradation of our operations, the need to relocate part of or all of our business or data processing activities to other jurisdictions at significant expense, increased exposure to regulatory actions, substantial fines and penalties, the inability to transfer data and work with partners, vendors and other third parties, and injunctions against our processing or transferring of personal data necessary to operate our business. Some European regulators have ordered certain companies to suspend or permanently cease certain transfers of personal data to recipients outside the EEA for allegedly violating the EU GDPR's cross-border data transfer limitations. Additionally, companies that transfer personal data to recipients outside of the EEA and/or UK to other jurisdictions, particularly to the U.S., are subject to increased scrutiny from regulators individual litigants and activist groups.

Compliance with these and any other applicable privacy and data security laws and regulations is a rigorous and time-intensive process, and we may be required to put in place additional mechanisms ensuring compliance with the new data protection rules. If we fail to comply with any such laws or regulations, we may face significant fines and penalties that could adversely affect our business, financial condition and results of operations. Furthermore, the laws are not consistent, and compliance in the event of a widespread data breach is costly.

Our business and operations would suffer in the event of computer system failures, cyberattacks or a deficiency in our cybersecurity.

In the ordinary course of our business, we and the third parties upon which we rely, process, collect, receive, store, use, transfer, protect, secure, dispose of, transmit, and share (collectively, processing) proprietary, confidential, and sensitive data, including personal data (such as health-related data), intellectual property, and trade secrets (collectively, sensitive information).

Despite the implementation of security measures, our internal computer systems, and those of third parties on which we rely, are vulnerable to intentional or accidental compromise, unauthorized access, or damage from computer viruses, malware, natural disasters, terrorism, war, telecommunication and electrical failures, cyberattacks or cyber-intrusions over the Internet, attachments to emails, persons inside our organization, or persons with access to systems inside our organization. The risk of a security breach or disruption, particularly through cyberattacks or cyber intrusion, including by computer hackers, "phishing" 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. These risks, as well as the number and frequency of cybersecurity events globally, may also be heightened during times of geopolitical tension or instability between countries. 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. For example, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. The techniques used by cyber criminals change frequently, may not be recognized until launched and can originate from a wide variety of sources, including outside groups such as external service providers, organized crime affiliates, terrorist organizations or hostile foreign governments or agencies.

We cannot assure you that our security measures will prevent significant breakdowns, data leakages or breaches in our systems or those of our CROs and other contractors and consultants. As a result of the COVID-19 pandemic, we may face increased cybersecurity risks due to our reliance on internet technology and the number of our employees that are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. For example, companies have experienced an increase in phishing and social engineering attacks from third parties in connection with the COVID-19 global pandemic. To the extent that any disruption or security breach was to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur material legal claims and liability and damage to our reputation, and the further development of our product candidates could be delayed.

Our business activities will be subject to the Foreign Corrupt Practices Act, or FCPA, and similar anti-bribery and anti-corruption laws.

As we expand our business activities outside of the U.S., including our clinical trial efforts, we will be subject to the FCPA and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate. The FCPA generally prohibits offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to a non-U.S. government official in order to influence official action, or otherwise obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. Our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, the healthcare providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, our dealings with these prescribers and purchasers will be subject to regulation under the FCPA. Recently the SEC and Department of Justice have increased their FCPA enforcement activities with respect to biotechnology and pharmaceutical companies. There is no certainty that all of our employees, agents, suppliers, manufacturers, contractors, or collaborators, or those of our affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity of these laws. Violations of these laws and regulations could result in fines, criminal sanctions against us, our officers, or our employees, the closing down of facilities, including those of our suppliers and manufacturers, requirements to obtain export licenses, cessation of business activities in sanctioned countries, implementation of compliance programs, and prohibitions on the conduct of our business. Any such violations could include prohibitions on our ability to offer our products in one or more countries as well as difficulties in manufacturing or continuing to develop our products, and could materially damage our reputation, our brand, our international expansion efforts, our ability to attract and retain employees, and our business, prospects, operating results, and financial condition.

If we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired.

We are subject to the reporting requirements of the Securities Exchange Act of 1934, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, and the rules and regulations of the stock market on which our common stock is listed. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting.

We may identify weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner, or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements. If that were to happen, the market price of our stock could decline and we could be subject to sanctions or investigations by the stock exchange on which our common stock is listed, the Securities and Exchange Commission or other regulatory authorities.

Our effective tax rate may fluctuate, and we may incur obligations in tax jurisdictions in excess of accrued amounts.

We are subject to taxation in more than one tax jurisdiction. As a result, our effective tax rate is derived from a combination of applicable tax rates in the various places that we operate. In preparing our financial statements, we estimate the amount of tax that will become payable in each of such places. Nevertheless, our effective tax rate may be different than experienced in the past due to numerous factors, including changes in the mix of our profitability from jurisdiction to jurisdiction, the results of examinations and audits of our tax filings, our inability to secure or sustain acceptable agreements with tax authorities, changes in accounting for income taxes and changes in tax laws, including recently enacted federal income tax laws. Any of these factors could cause us to experience an effective tax rate significantly different from previous periods or our current expectations and may result in tax obligations in excess of amounts accrued in our financial statements.

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

Our net operating loss carryforwards, or NOLs, and certain other tax attributes could expire unused and be unavailable to offset future income tax liabilities because of their limited duration or because of restrictions under U.S. tax law. As of December 31, 2022, we had U.S. federal and state NOLs of $89.0 million and $86.2 million, respectively. Our NOLs generated in the taxable year ended on or before December 31, 2017 are only permitted to be carried forward for 20 taxable years under applicable U.S. federal tax law. The federal NOLs as of December 31, 2022 include $2.1 million generated in the taxable year ended on or before December 31, 2017 that may be used to offset up to 100% of future taxable income and will begin to expire in 2037, unless previously utilized. Under the Tax Act, as modified by the CARES Act, federal net operating losses incurred in taxable years ended after December 31, 2017 and in future years may be carried forward indefinitely, but the deductibility of federal net operating losses generated in taxable years beginning after December 31, 2017, is limited. We have a full valuation allowance for deferred tax assets including NOLs.

In addition, under Section 382 of the Code, and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a cumulative change, by value, in our ownership by "5-percent stockholders" that exceeds 50 percentage points over a rolling three-year period, the corporation's ability to use its pre-change NOLs and other pre-change tax attributes to offset its post-change income or taxes may be limited. We have not determined whether we have undergone an ownership change in the past or as a result of our initial public offering. If an ownership change occurs and our ability to use our net operating loss carryforwards is materially limited, it would harm our future operating results by effectively increasing our future tax obligations.

We incur increased costs and demands upon management as a result of being a public company.

As a public company listed in the U.S., we incur significant additional legal, accounting and other costs. These additional costs could negatively affect our financial results. In addition, changing laws, regulations and standards relating to corporate governance and public disclosure, including regulations implemented by the SEC and The Nasdaq Stock Market, may increase legal and financial compliance costs and make some activities more time-consuming. These laws, regulations and standards are subject to varying interpretations and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. 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.

Failure to comply with these rules might also make it more difficult for us to obtain some types of insurance, including director and officer liability insurance, and we might be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these events could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, on committees of our board of directors or as members of senior management.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

We do not own or lease any physical premises. Our principal executive offices were located at 1800 Kraft Drive, Suite 216, Blacksburg, Virginia 24060, where we leased approximately 5,500 square feet of office and lab space under a lease that terminated on May 31, 2022. Our executive officers and employees work remotely in a "virtual office" setting, and our mailing address is P.O. Box 11239, Blacksburg, Virginia 24062.

Item 3. Legal Proceedings.

We are not subject to any material legal proceedings. From time to time, we may be involved in various claims and legal proceedings relating to claims arising out of our operations. We are not currently a party to any legal proceedings that, in the opinion of our management, are likely to have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Market Information for Common Stock

Our common stock is listed on The Nasdaq Capital Market under the symbol "LABP."

Holders of Record

As of March 16, 2023, we had 10 holders of record of our common stock, which excludes stockholders whose shares were held in nominee or street name by brokers. The actual number of common stockholders is greater than the number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividend Policy

We have never paid cash dividends on any of our capital stock and currently intend to retain our future earnings, if any, to fund the development and growth of our business.

Use of Proceeds from Initial Public Offering

On February 3, 2021, our Registration Statement on Form S-1, as amended (File No. 333-252083), was declared effective in connection with our initial public offering, pursuant to which we sold an aggregate of 6,250,000 shares of our common stock at a price to the public of $16.00 per share. The joint book-running managers of our initial public offering were J.P. Morgan Securities LLC, Jefferies LLC and SVB Leerink LLC, and Raymond James & Associates, Inc. acted as lead manager. There has been no material change in the planned use of proceeds from our initial public offering as described in our prospectus filed pursuant to Rule 424(b)(4) under the Securities Act with the SEC on February 4, 2021.

Recent Sales of Unregistered Securities

On January 4, 2023, we entered into a securities purchase agreement, or the Securities Purchase Agreement, with the institutional accredited investors named therein, or the Investors, pursuant to which we agreed to issue and sell to the Investors in a private placement, or the Private Placement, pre-funded warrants, or the Pre-Funded Warrants, to purchase an aggregate of 30,909,090 shares, or the Warrant Shares, of our common stock, $0.01 per share, or the Common Stock. Each Pre-Funded Warrant has an exercise price of $0.01 per Warrant Share. The purchase price per Pre-Funded Warrant was $0.54.

The Pre-Funded Warrants issued in the Private Placement are exercisable at any time but provide that the holder of the Pre-Funded Warrants will not have the right to exercise any portion of its Pre-Funded Warrants if such holder, together with its affiliates and any other persons whose beneficial ownership of Common Stock would be aggregated with the holder for purposes of Section 13(d) or Section 16 of the Securities Exchange Act of 1934, as amended, would beneficially own in excess of 35.00% of the number of shares of Common Stock outstanding immediately after giving effect to such exercise. The Warrant Shares will also be subject to certain registration rights under our Amended and Restated Investors' Rights Agreement.

We have relied on the exemption from the registration requirements of the Securities Act by virtue of Section 4(a)(2) thereof. In connection with the Investors' execution of the Securities Purchase Agreement, each Investor represented to us that it is an "accredited investor" as defined in Regulation D of the Securities Act and that the Pre-Funded Warrants purchased by it were acquired for its own account for investment only and with no present intention of distributing any of the Pre-Funded Warrants or Warrant Shares or any arrangement or understanding with any other persons regarding the distribution of the Pre-Funded Warrants or Warrant Shares.

The Private Placement closed on January 10, 2023. We received aggregate gross proceeds from the Private Placement of approximately $16.7 million, before deducting offering expenses payable by us.

Item 6. [Reserved]

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and related notes.

Company Overview

We are a clinical-stage biopharmaceutical company focused on the development of novel, oral, once-daily therapeutics for patients with certain immunology diseases. Our core expertise is the development of compounds that target novel pathways at the interface of immunity and metabolism. Based on our understanding of the role that cellular metabolic pathways have on modulating inflammatory responses, we aim to inhibit these inflammatory responses by changing the metabolic processes in target cells. We believe the therapeutics we develop, if approved, could have a significant positive impact on the quality of life of patients suffering from immunology diseases.

Our current focus and lead candidate is NX-13, a novel, oral gut-selective NLRX1 agonist. We are developing NX-13 as a once-daily oral treatment for ulcerative colitis, or UC, that targets NOD-like receptor X1, or NLRX1, a mitochondria-associated receptor that has been associated with the modulation of inflammatory cytokines for UC. NX-13 is designed to target NLRX1 and induce anti-inflammatory effects in CD4+ T cells and other cells in the gastrointestinal tract.

We announced top-line results from our NX-13 Phase 1b trial in UC patients in August 2022. The data showed favorable safety and tolerability profiles across a range of doses, as well as signals of clinical improvement as soon as two weeks in patients' symptoms and four weeks by endoscopy in exploratory endpoints. We believe that these early signals, as well as the data from long-term toxicology studies, support the potential of NX-13 as a new treatment for UC. We are continuing an in-depth analysis of the clinical, pharmacokinetic, or PK, and pharmacodynamic, or PD, data for NX-13. A preliminary analysis demonstrated promising signals of both target engagement and molecular dose response among the 250mg and 500mg immediate release, or IR, doses. We will be conducting a Phase 2 proof-of-concept clinical trial for NX-13, which will be dose ranging, blinded, placebo-controlled and statistically powered. We are on track for first site activation and patient enrollment for the NX-13 Phase 2 trial in the second quarter of 2023, and we expect to report top-line data from this trial by the fourth quarter of 2024.

In addition to NX-13, we have discovered several preclinical product candidates, comprising the following:

- LABP-73, an oral, small molecule NLRX1 pathway agonist in development for the treatment of asthma and Chronic Obstructive Pulmonary Disease, or COPD,
- LABP-66, an oral, small molecule NLRX1 pathway agonist in development for the treatment of multiple sclerosis, or MS, and Alzheimer's disease; and
- LABP-69, an oral, small molecule PLXDC2 pathway agonist in development for the treatment of diabetic nephropathy and rheumatoid arthritis, or RA.

In February 2023, we entered into an Asset Purchase and Redemption Agreement, or the Purchase Agreement, with Dr. Bassaganya-Riera, Raquel Hontecillas and certain other stockholders, or together the Purchasers, whereby the Purchasers acquired (i) all of our right, title and interest in omilancor, LABP-104 and LABP-111 and any such derivatives and analogs that target LANCL proteins, or together the Acquired Compounds, (ii) a worldwide, perpetual, irrevocable, fully-paid up, royalty-free, exclusive, sublicensable and transferable license grant under the intellectual property rights retained by us and necessary or useful for the development, manufacture and commercialization of the Acquired Compounds, (iii) a royalty agreement providing, among other things, for the payment by us to the Purchasers of a royalty of 2% of all net sales by us of any products containing certain compounds that we will retain following the closing under the Purchase Agreement and (iv) $3,000,000 in cash in exchange for (x) 9,086,441 shares of our common stock held by the Purchasers and (y) a royalty agreement providing, among other things, for the payment by the Purchasers to us a royalty of 6% of all net sales by the Purchasers of any products containing any of the Acquired Compounds in consideration for the acquired intellectual property rights. The transactions contemplated by the Purchase Agreement closed simultaneously with signing.

In May 2021, we entered into an exclusive collaboration and license agreement, or the LianBio Agreement, with LianBio Respiratory Limited, or Lian, pursuant to which we granted Lian an exclusive license, or the License, to develop, manufacture and commercialize NX-13 and omilancor. In February 2023, we amended the LianBio Agreement to no longer cover the licensing of Licensed Technology relating to omilancor and developmental milestones events were amended to reflect the transfer of Licensed Technology relating to omilancor. Subsequent to the amendment, we are eligible to receive development milestone payments of up to $40.0 million as well as sales milestone payments of up to $105.0 million. We are also eligible to receive tiered low-double-digit royalties based on future net sales of NX-13 in the Territory, subject to reductions in specified circumstances.

We have a limited operating history. Since inception, our operations have focused on developing our clinical and preclinical product candidates, organizing and staffing our company, business planning, raising capital, establishing our intellectual property portfolio and conducting clinical trials and preclinical studies. We do not have any product candidates approved for sale and have not generated any revenue from product sales. We have funded our operations primarily through the sale of equity securities.

Since our inception in 2017, we have funded operations through the issuance of convertible preferred stock and convertible promissory notes, through proceeds from our initial public offering, or IPO, through the upfront payment from a license and collaboration agreement with a related party and through the sale of pre-funded warrants in a private placement in January 2023. As of December 31, 2022, we had an accumulated deficit of $133.4 million and we expect to incur substantial operating losses for at least the next several years. As such, we will need to raise additional capital to initiate and complete our planned clinical trials, to continue and expand our research and development operations that support our planned development and clinical and regulatory activities, and to adequately prepare for commercialization of our product candidates that may achieve regulatory approval in the future. As of December 31, 2022, we had cash, cash equivalents and marketable securities of $44.4 million. We believe that our existing cash, cash equivalents and marketable securities as of December 31, 2022, in addition to the $16.7 million in gross proceeds from our private placement of pre-funded warrants in January 2023, will be sufficient to fund our operating expenses and capital requirements into the first half of 2025. We anticipate that our expenses may increase significantly in connection with our ongoing activities, as we:

- conduct our ongoing and planned clinical trials of NX-13;
- pursue regulatory approval of our product candidates;
- seek to discover and develop additional clinical and preclinical product candidates;
- scale up our clinical and regulatory capabilities;
- establish a commercialization infrastructure and scale up external manufacturing and distribution capabilities to commercialize any product candidates for which we may obtain regulatory approval;
- adapt our regulatory compliance efforts to incorporate requirements applicable to marketed products;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, manufacturing and scientific personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts; and
- incur additional legal, accounting and other expenses in operating as a public company.

Components of our Results of Operations

Revenue - License Fee

We recognize revenue under our collaboration agreement with Lian, which we entered into in May 2021.

Research and Development Expenses

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

- salaries, benefits, stock-based compensation and other related costs for personnel engaged in research and development functions;
- expenses incurred under agreements with third parties, including contract research organizations, or CROs, and other third parties that conduct research, preclinical activities and clinical trials on our behalf, as well as contract manufacturing organizations, or CMOs, that manufacture drug material for use in our clinical trials and preclinical studies;
- costs of outside consultants, including their fees and related travel expenses;
- the costs of laboratory supplies and acquiring, developing and manufacturing preclinical and clinical trial supplies; and
- allocated expenses for rent and maintenance of facilities and other operating costs.

We expense research and development costs as incurred. We track external development costs by product candidate or development program, but we do not allocate personnel costs or other internal costs to specific development programs or product candidates.

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have a higher development cost than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that our research and development expenses will decrease in 2023 relative to 2022 as a result of wind down of previous clinical trial activities. However, in the long term, we expect that they will increase and will comprise a larger percentage of our total expenses as we progress and complete our ongoing clinical trials, initiate new clinical trials, continue to discover and develop additional product candidates and prepare regulatory filings for any product candidates that successfully complete clinical trials.

The successful development of our product candidates is highly uncertain. At this time, we cannot determine with certainty the duration and costs of our existing and future clinical trials of our product candidates or any other product candidate we may develop or if, when, or to what extent we will generate revenue from the commercialization and sale of any product candidate for which we obtain marketing approval. We may never succeed in obtaining marketing approval for any product candidate. The duration, costs and timing of clinical trials and development of our product candidates and any other product candidate we may develop in the future will depend on a variety of factors, including:

- per patient trial costs;
- the number of patients who enroll in each trial;
- the number of trials required for approval;
- the number of sites included in the trials;
- the countries in which the trials are conducted;
- the length of time required to enroll eligible patients;
- the drop-out or discontinuation rates of patients;
- potential additional safety monitoring requested by regulatory agencies;
- the duration of patient participation in the trials and follow-up;

- the phase of development of the product candidate; and
- the efficacy and safety profile of the product candidate.

Our expenditures are subject to additional uncertainties, and we may never succeed in achieving regulatory approval for our product candidates. We may obtain unexpected results from our clinical trials. We may elect to discontinue, delay, or modify clinical trials of our product candidates. A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the U.S. Food and Drug Administration, or FDA, or another regulatory authority were to require us to conduct clinical trials beyond those that we anticipate will be required for the completion of clinical development of a product candidate, or if we experience significant delays in our clinical trials due to patient enrollment or other reasons, we would be required to expend significant additional financial resources and time on the completion of clinical development.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs 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 decrease slightly in 2023 relative to 2022 as we focus our resources toward the development of NX-13. However, in the long term, we expect that they will increase as we increase our personnel headcount to support our expanded infrastructure, including the development of a commercialization infrastructure for any product candidates for which we may obtain regulatory approval. Our expenditures are subject to uncertainties, including the terms and timing of regulatory approvals, and the expense of filing, prosecuting, defending and enforcing any patent claims or other intellectual property rights.

Interest and Other Income, net

Interest and other income, net, primarily consists of grant income received under the NIH grant agreement and interest income received from available-for-sale marketable securities. We were awarded a grant by the NIH for a phase 2 proof-of-concept efficacy study of omilancor in Crohn's disease patients. The grant award provided for reimbursement of actual, allowable costs incurred. Subsequent to the Purchase Agreement, any grant income to be earned under the NIH grant was transferred to the Purchasers.

Results of Operations

Comparison of the years ended December 31, 2022 and 2021

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

	Year Ended December 31,	
	2022	2021
Revenue - license fee:	$ —	$ 18,000
Operating expenses:		
Research and development	25,680	41,564
General and administrative	14,881	15,252
Total operating expenses	40,561	56,816
Loss from operations	(40,561)	(38,816)
Other income:		
Gain (loss) from foreign exchange	26	(18)
Interest and other income, net	1,259	412
Other income, net	1,285	394
Net loss	$ (39,276)	$ (38,422)

Revenue - License Fee

In May 2021, we entered into the LianBio Agreement to develop and commercialize NX-13 and omilancor in Greater China and select Asian markets. We recognized the $18.0 million upfront payment under the collaboration as revenue.

Research and Development Expenses

Research and development expenses were $25.7 million for the year ended December 31, 2022 compared to $41.6 million for the year ended December 31, 2021. The decrease of $15.9 million was primarily attributed to reduced clinical activities for our omilancor and LABP-104 programs due to the wind down of the related clinical trials, as well as decreases in employee-related expenses resulting from decreased headcount, partially offset by increases in costs associated with the clinical development of NX-13.

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

	Year Ended December 31,	
	2022	2021
External costs by clinical program:		
Omilancor	$ 8,314	$ 22,405
NX-13	7,381	6,247
LABP-104	1,543	3,319
Total external costs by clinical program:	17,238	31,971
Compensation	4,445	6,508
Other	3,997	3,085
Total research and development expenses	$ 25,680	$ 41,564

General and Administrative Expenses

General and administrative expenses were $14.9 million for the year ended December 31, 2022 compared to $15.3 million for the year ended December 31, 2021. The decrease of $0.4 million was primarily attributable to decreases in consulting costs and office related expenses.

Other Income, net

Other income, net, was $1.3 million for the year ended December 31, 2022 compared to other income, net of $0.4 million for the year ended December 31, 2021. The increase of $0.9 million was primarily due to the NIH grant revenue received in 2022.

Liquidity and Capital Resources

Since our inception, we have incurred significant operating losses and negative cash flows from our operations. We expect to incur significant expenses and operating losses for the foreseeable future as we advance the preclinical and clinical development of our research programs and product candidates. As a result, we will need additional capital to fund our operations, which we may obtain from additional equity or debt financings, collaborations, licensing arrangements or other sources.

We do not currently have any approved products and have never generated any revenue from product sales. To date, we have financed our operations primarily through the issuance of convertible preferred stock and convertible promissory notes, proceeds from our IPO, the upfront payment from the LianBio Agreement and the sale of pre-funded warrants in a private placement in January 2023 described below. On February 3, 2021, we completed our IPO in which we issued and sold 6,250,000 shares of our common stock and received net proceeds of $90.5 million, after deducting underwriters' discounts and commissions and expenses payable by us.

In March 2022, we filed a shelf registration statement on Form S-3, or the 2022 Shelf Registration Statement, with the SEC. The 2022 Shelf Registration Statement became effective in August 2022. The 2022 Shelf Registration Statement permits the offering, issuance and sale by us of up to a maximum aggregate offering price of $200.0 million of common stock, preferred stock, debt securities and warrants in one or more offerings and in any combination. As of December 31, 2022, we had $200.0 million of common stock remaining that can be sold under the 2022 Shelf Registration Statement, although this amount will be limited for as long as we are subject to General Instruction I.B.6 of Form S-3, which limits the amount of funds we can raise through primary public offerings of securities in any twelve-month period using a registration statement on Form S-3 to one-third of the aggregate market value of the shares of our common stock held by non-affiliates. Therefore, we will be limited in the amount of proceeds we are able to raise by selling shares of our common stock using Form S-3, including the 2022 Shelf Registration Statement, until such time as our public float held by non-affiliates exceeds $75.0 million.

On January 4, 2023, we entered into a securities purchase agreement, or the Securities Purchase Agreement, with the institutional accredited investors named therein, or the Investors, pursuant to which we agreed to issue and sell to the Investors in a private placement, or the Private Placement, pre-funded warrants, or the Pre-Funded Warrants, to purchase an aggregate of 30,909,090 shares, or the Warrant Shares, of our common stock. Each Pre-Funded Warrant has an exercise price of $0.01 per Warrant Share. The purchase price per Pre-Funded Warrant was $0.54. The Pre-Funded Warrants issued in the Private Placement are exercisable at any time but provide that the holder of the Pre-Funded Warrants will not have the right to exercise any portion of its Pre-Funded Warrants if such holder, together with its affiliates and any other persons whose beneficial ownership of common stock would be aggregated with the holder for purposes of Section 13(d) or Section 16 of the Securities Exchange Act of 1934, as amended, would beneficially own in excess of 35% of the number of shares of common stock outstanding immediately after giving effect to such exercise. The Warrant Shares will also be subject to certain registration rights under our Amended and Restated Investors' Rights Agreement. The Private Placement closed on January 10, 2023. Gross proceeds of the Private Placement were approximately $16.7 million, before deducting offering expenses payable by us.

As of December 31, 2022, we had approximately $44.4 million in cash, cash equivalents and marketable securities and an accumulated deficit of $133.4 million. We had no indebtedness as of December 31, 2022.

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

	Year Ended December 31,	
	2022	2021
Net cash used in operating activities	$ (45,771)	$ (27,061)
Net cash provided by (used in) investing activities	74,060	(58,706)
Net cash provided by financing activities	—	91,607
Net change in cash and cash equivalents	$ 28,289	$ 5,840

Operating Activities

Net cash used in operating activities for the year ended December 31, 2022 was $45.8 million, consisting primarily of our net loss of $39.3 million and a net change of $10.1 million in our operating assets and liabilities, partially offset by non-cash charges of $3.6 million. The net change in our operating assets and liabilities was primarily due to a decrease in accounts payable and other liabilities. The non-cash charges consist primarily of $2.0 million of stock-based compensation expense, $1.2 million related to the amortization of the premium on marketable securities and $0.6 million of depreciation expense. Net cash used in operating activities for the year ended December 31, 2021 was $27.1 million, consisting primarily of our net loss of $38.4 million, partially offset by non-cash charges of $5.5 million and a net change of $5.9 million in our operating assets and liabilities. The non-cash charges consist primarily of $4.1 million of stock-based compensation expense and $1.2 million related to the amortization of the premium on marketable securities. The net change in our operating assets and liabilities was primarily due to an increase in accounts payable and other liabilities.

Investing Activities

Net cash provided by investing activities for the year ended December 31, 2022 was $74.1 million, consisting of proceeds from sales and maturities of marketable securities, partially offset by purchases of available-for-sale marketable securities. Net cash used in investing activities for the year ended December 31, 2021 was $58.7 million, consisting of purchases of available-for-sale marketable securities and property and equipment, partially offset by proceeds from sales and maturities of marketable securities.

Financing Activities

Net cash provided by financing activities in the year ended December 31, 2021 of $91.6 million was primarily related to the net proceeds received from our IPO.

Funding Requirements

To date, we have not generated any revenues from the commercial sale of approved drug products, and we do not expect to generate substantial revenue for at least the next few years. If we fail to complete the development of our product candidates in a timely manner or fail to obtain their regulatory approval, our ability to generate future revenue will be compromised. We do not know when, or if, we will generate any revenue from our product candidates, and we do not expect to generate significant revenue unless and until we obtain regulatory approval of, and commercialize, our product candidates. Further, we do not know when, or if, we will generate any additional revenue under the LianBio Agreement as future payments are conditioned upon the achievement of development and commercialization milestones that are uncertain as of this date. We expect our expenses to proportionately increase in connection with our ongoing activities, particularly as we continue the research and development of, continue or initiate clinical trials of, and seek marketing approval for, our product candidates. In addition, if we obtain approval for any of our product candidates, we expect to incur significant commercialization expenses related to sales, marketing, manufacturing and distribution. We anticipate that we will need substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts.

Identifying potential product candidates and conducting preclinical studies and clinical trials is a time-consuming, expensive and uncertain process that takes many years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of product candidates that we do not expect to be commercially available in the near term, if at all.

We believe that our existing cash, cash equivalents and marketable securities as of December 31, 2022, in addition to the $16.7 million in gross proceeds from our private placement of pre-funded warrants in January 2023, will be sufficient to fund our operating expenses and capital requirements into the first half of 2025. We have based these estimates on assumptions that may prove to be imprecise, and we could utilize our available capital resources sooner than we expect.

Because of the numerous risks and uncertainties associated with research, development and commercialization of pharmaceutical drugs, it is difficult to estimate with certainty the amount of our working capital requirements. Our future funding requirements will depend on many factors, including:

- the scope, progress, costs and results of our ongoing and planned clinical trials of NX-13;
- the scope, progress, costs and results of preclinical development, laboratory testing and clinical trials for any future product candidates we may decide to pursue;
- the extent to which we in-license or acquire rights to other products, product candidates or technologies;
- the costs and timing of process development and manufacturing scale-up activities associated with our product candidates and other programs as we advance them through preclinical and clinical development;
- the number and development requirements of other product candidates that we may pursue;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution for any of our product candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;
- our ability to establish and maintain strategic collaborations, licensing or other agreements and the financial terms of such agreements; and
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights, and defending against any intellectual property-related claims.

Further, our operating results may change in the future, and we may need additional funds to meet operational needs and capital requirements associated with such operating plans.

Our future commercial revenue, if any, will be derived from sales of products that we do not expect to be commercially available for several years, if at all. Until such time, if ever, that we can generate product revenue sufficient to achieve profitability, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaboration agreements, other third-party funding, strategic alliances, licensing arrangements and marketing and distribution arrangements. Adequate additional financing may not be available to us on acceptable terms, or at all. We currently have no credit facility or committed sources of capital. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of existing stockholders. Pursuant to the Securities Purchase Agreement, the Investors are entitled to exercise the pre-funded warrants to purchase an aggregate of 30,909,090 shares of our common stock. If the Investors were to exercise their outstanding Pre-Funded Warrants, existing stockholders will recognize significant dilution. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through other third-party funding, collaboration agreements, strategic alliances, licensing arrangements or marketing and distribution arrangements, 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 unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market products or product candidates that we would otherwise prefer to develop and market ourselves.

Critical Accounting Estimates

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

While our significant accounting policies are described in more detail in the notes to our audited consolidated financial statements included in Item 8 of this Annual Report on Form 10-K, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

Revenue Recognition for Out-License Arrangements

To date, all of our revenue has been generated from the LianBio Agreement. We recognize revenue in accordance with Accounting Standards Codification, or ASC, Topic 606, *Revenue from Contracts with Customers*, or Topic 606. Under Topic 606, we recognize revenue when our customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements, we perform the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price, including variable consideration, if any; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy a performance obligation.

At contract inception and through December 31, 2022, we determined that the LianBio Agreement contains a single performance obligation to deliver the License, which represents functional intellectual property given the functionality of the License is not expected to change substantially as a result of our ongoing activities.

We determined that the upfront fixed payment of $18.0 million is the initial transaction price. The potential development milestone payments that we are eligible to receive upon the successful achievement of certain regulatory approvals or activities were excluded from the initial transaction price, as the milestone amounts were fully constrained based on the probability of achievement. The royalties and sales milestone payments are excluded from the transaction price under the sales- or usage-based royalty exception of Topic 606. We will reevaluate the transaction price, including all constrained amounts, at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur, and we will adjust our estimate of the transaction price as necessary. We will recognize the royalties and sales milestone payments as revenue when the associated sales occur, and relevant sales-based thresholds are met. As of June 30, 2021, we had completed the transfer of the License and know-how necessary and, as such, recognized the full $18.0 million upfront payment as revenue.

Research and Development Expenses

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

We base our expenses related to research and development activities on our estimates of the services received and efforts expended pursuant to quotes and contracts with vendors that conduct research and development on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the research and development expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid accordingly.

Stock-Based Compensation

Stock-based compensation expense represents the grant date fair value of employee stock option and award grants recognized as expense over the requisite service period of the awards (usually the vesting period) on a straight-line basis, net of actual forfeitures. We estimate the fair value of stock option grants using the Black-Scholes option pricing model. The Black-Scholes option pricing model requires the input of subjective assumptions, including the risk-free interest rate, the expected dividend yield of our common stock, the expected volatility of the price of our common stock and the expected term of the option. These estimates involve inherent uncertainties and the application of management's judgment. If factors change and different assumptions are used, our stock-based compensation expense could be materially different in the future. See Note 6 to our audited consolidated financial statements included in Item 8 in this Annual Report on Form 10-K for information concerning certain of the specific assumptions we used in applying the Black-Scholes option pricing model to determine the estimated fair value of our employee stock options granted for all periods presented.

Quantitative and Qualitative Disclosures about Market Risk

Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our cash is held in interest-bearing money market accounts. Our cash equivalents are held in U.S. government treasury securities and our marketable securities are held in fixed income and asset backed securities. Due to the short- term maturities of our cash equivalents and marketable securities and the low risk profile of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our cash equivalents and marketable securities.

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation had a material effect on our business, financial condition or results of operations during the years ended December 31, 2022 and 2021.

Recent Accounting Pronouncements

A description of recent accounting pronouncements that may potentially impact our financial position, results of operations or cash flows is disclosed in Note 1 to our audited consolidated financial statements included in Item 8 of this Annual Report on Form 10-K.

Emerging Growth Company and Smaller Reporting Company Status

We qualify as an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, as amended, or JOBS Act. As an "emerging growth company" we may take advantage of reduced reporting requirements that are otherwise applicable to public companies. These provisions include, but are not limited to:

- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended;
- not being required to comply with any requirements that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the consolidated financial statements (i.e., an auditor discussion and analysis);
- reduced disclosure obligations regarding executive compensation in our periodic reports, proxy statements and registration statements; and
- exemptions from the requirements of holding a non-binding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We may take advantage of these provisions until December 31, 2026. However, if any of the following events occur prior to that date, (i) our annual gross revenue exceeds $1.235 billion, (ii) we issue more than $1.0 billion of non-convertible debt in any three-year period or (iii) we become a "large accelerated filer," (as defined in Rule 12b-2 under the Exchange Act), we will cease to be an emerging growth company prior to the end of such five-year period. We will be deemed to be a "large accelerated filer" at such time that we (a) have an aggregate worldwide market value of common equity securities held by non-affiliates of $700.0 million or more as of the last business day of our most recently completed second fiscal quarter, (b) have been required to file annual and quarterly reports under the Exchange Act, for a period of at least 12 months and (c) have filed at least one annual report pursuant to the Exchange Act.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. We have elected to take advantage of this extended transition period.

We are also a "smaller reporting company," meaning that the market value of our shares held by non-affiliates is less than $700 million and our annual revenue was less than $100 million during the most recently completed fiscal year. We may continue to be a smaller reporting company if either (i) the market value of our shares held by non-affiliates is less than $250 million or (ii) our annual revenue was less than $100 million during the most recently completed fiscal year and the market value of our shares held by non-affiliates is less than $700 million. If we are a smaller reporting company at the time we cease to be an emerging growth company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, as a smaller reporting company, we may choose to present only the two most recent fiscal years of audited financial statements in our Annual Report on Form 10-K and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation.

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

We are a smaller reporting company as defined by Rule 12b-2 of the Exchange Act and are not required to provide the information required under this item.

Item 8. Financial Statements and Supplementary Data.

Landos Biopharma, Inc.
Index to Consolidated Financial Statements

Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of Landos Biopharma, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Landos Biopharma, Inc. (the Company) as of December 31, 2022 and 2021, the related consolidated statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity (deficit) and cash flows for each of the two years in the period ended December 31, 2022, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2022, in conformity with U.S. generally accepted accounting principles.

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/ Ernst & Young LLP

We have served as the Company's auditor since 2020.
Raleigh, North Carolina

March 23, 2023

Landos Biopharma, Inc.
Consolidated Balance Sheets
(In thousands, except share and per share amounts)

	December 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 36,640	$ 8,305
Marketable securities, available-for-sale	7,762	82,575
Prepaid expenses and other current assets	851	1,266
Total current assets	45,253	92,146
Property and equipment, net	—	707
Other assets	—	26
Total assets	$ 45,253	$ 92,879
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 3,435	$ 12,908
Accrued liabilities	2,687	3,703
Total current liabilities	6,122	16,611
Total liabilities	6,122	16,611
Commitments and contingencies (Note 4)		
Stockholders' equity:		
Preferred stock, $0.01 par value; 10,000,000 shares authorized, no shares issued and outstanding as of December 31, 2022 and 2021	—	—
Common stock, $0.01 par value; 200,000,000 shares authorized, 40,254,890 shares issued and outstanding as of December 31, 2022 and 2021	403	403
Additional paid-in capital	172,212	170,241
Accumulated other comprehensive loss	(57)	(225)
Accumulated deficit	(133,427)	(94,151)
Total stockholders' equity	39,131	76,268
Total liabilities and stockholders' equity	$ 45,253	$ 92,879

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

Landos Biopharma, Inc.
Consolidated Statements of Operations and Comprehensive Loss
(In thousands, except share and per share amounts)

	Years Ended December 31,	
	2022	2021
Revenue - license fee:	$ —	$ 18,000
Operating expenses:		
Research and development	25,680	41,564
General and administrative	14,881	15,252
Total operating expenses	40,561	56,816
Loss from operations	(40,561)	(38,816)
Other income:		
Gain (loss) from foreign exchange	26	(18)
Interest and other income, net	1,259	412
Other income, net	1,285	394
Net loss	$ (39,276)	$ (38,422)
Net loss per share, basic and diluted	$ (0.98)	$ (1.02)
Weighted-average shares used to compute net loss per share, basic and diluted	40,254,890	37,558,464
Comprehensive loss:		
Net loss	$ (39,276)	$ (38,422)
Unrealized gain (loss) on available-for-sale securities	168	(235)
Comprehensive loss	$ (39,108)	$ (38,657)

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

Landos Biopharma, Inc.
Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)
(In thousands, except share amounts)

	Convertible Preferred Stock		Common Stock					
	Shares	Amounts	Shares	Amounts	Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
Balance at December 31, 2020	11,260,608	$ 73,037	12,767,909	$ 71	$ 1,633	$ 10	$ (55,729)	$ (54,015)
Conversion of preferred stock to common stock upon closing of the initial public offering	(11,260,608)	(73,037)	20,549,478	262	72,775	—	—	73,037
Issuance of common stock, net of issuance costs	—	—	6,250,000	63	90,443	—	—	90,506
Stock compensation expense	—	—	—	—	4,118	—	—	4,118
Exercise of stock options	—	—	687,503	7	1,272	—	—	1,279
Unrealized loss on available-for-sale securities	—	—	—	—	—	(235)	—	(235)
Net loss	—	—	—	—	—		(38,422)	(38,422)
Balance at December 31, 2021	—	$ —	40,254,890	$ 403	$ 170,241	$ (225)	$ (94,151)	$ 76,268
Stock compensation expense	—	—	—	—	1,971	—	—	1,971
Unrealized gain on available-for-sale securities	—	—	—	—	—	168	—	168
Net loss	—	—	—	—	—	—	(39,276)	(39,276)
Balance at December 31, 2022	—	$ —	40,254,890	$ 403	$ 172,212	$ (57)	$ (133,427)	$ 39,131

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

Landos Biopharma, Inc.
Consolidated Statements of Cash Flows
(In thousands)

	Years Ended December 31,	
	2022	2021
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net loss	$ (39,276)	$ (38,422)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	577	196
Stock-based compensation expense	1,971	4,118
Amortization of premium on marketable securities	1,150	1,174
Non-cash loss on termination of lease	137	—
Gain on sale of equipment	(210)	—
Loss from foreign exchange	(46)	(18)
Changes in operating assets and liabilities:		
Prepaid expenses and other assets	415	(936)
Accounts payable	(9,473)	4,263
Other liabilities	(1,016)	2,564
Net cash used in operating activities	(45,771)	(27,061)
CASH FLOWS FROM INVESTING ACTIVITIES:		
Purchase of property and equipment	(7)	(440)
Proceeds from sale of property and equipment	236	—
Purchase of available-for-sale marketable securities	(3,671)	(174,853)
Proceeds from sales and maturities of marketable securities	77,502	116,587
Net cash provided by (used in) investing activities	74,060	(58,706)
CASH FLOWS FROM FINANCING ACTIVITIES:		
Proceeds from initial public offering, net of issuance costs	—	93,000
Financing costs paid	—	(1,907)
Proceeds from exercise of stock options	—	514
Net cash provided by financing activities	—	91,607
Net change in cash and cash equivalents	28,289	5,840
Cash and cash equivalents at beginning of period	8,305	2,416
Effect of exchange rates on cash	46	49
Cash and cash equivalents at end of period	$ 36,640	$ 8,305
Supplemental non-cash disclosure:		
NONCASH INVESTING AND FINANCING ACTIVITY:		
Non-cash gain on sale of fixed assets	$ 14	$ —
Purchase of fixed assts in accounts payable	$ —	$ 20
Conversion of Series A and B convertible preferred stock to common stock	$ —	$ 73,037
Operating right-of-use asset obtained in exchange for operating lease liability	$ 824	$ —
Derecognition of operating right-of-use asset and operating lease liability upon termination of lease	$ 714	$ —
Unrealized loss on available-for-sale marketable securities	$ (168)	$ (235)
Non-cash deferred financing costs	$ 25	$ —

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

1. Organization and Summary of Significant Accounting Policies

Organization and Business

Landos Biopharma, Inc. ("Landos" or "the Company") was incorporated in the state of Delaware in January 2017 and is a clinical-stage biopharmaceutical company focused on the discovery and development of oral therapeutics for patients with autoimmune diseases. The Company has several active development programs, each discovered internally, targeting novel pathways at the interface of immunity and metabolism.

Initial Public Offering

In February 2021, the Company completed its initial public offering ("IPO") in which it sold 6,250,000 shares of common stock at an initial public offering price of $16.00 per share. Proceeds from the initial public offering, net of underwriting discounts, commissions and offering costs paid by the Company, were approximately $90.5 million.

In addition, in connection with the completion of the Company's IPO, all outstanding shares of the Company's convertible preferred stock were converted into 20,549,478 shares of the Company's common stock.

Nasdaq Listing Rule Compliance

In June 2022, the Company received a notice from the Listing Qualifications Department of The Nasdaq Stock Market ("Nasdaq") notifying the Company that its listed securities did not maintain the minimum bid price requirement of $1.00 per ordinary share for continued listing on the Nasdaq Global Market. In December 2022, Nasdaq approved the Company's application to transfer to The Nasdaq Capital Market and notified the Company that it has been granted an additional 180-calendar day compliance period to regain compliance with the minimum bid price requirement. As part of the transfer, the Company provided notice to Nasdaq that it intended to cure the bid price deficiency by effecting a reverse stock split, if necessary, prior to the end of the compliance period. The Company intends to actively monitor the bid price of its common stock and will consider available options, including a reverse stock split, to regain compliance with the listing requirements.

Stock Split

On January 27, 2021, the Company's Board of Directors approved a 1.8249-for-1 stock split of the Company's outstanding common shares. On January 29, 2021, the Company amended its Amended and Restated Certificate of Incorporation to affect the stock split. The stock split resulted in an adjustment to the preferred share conversion price to reflect a proportional increase in the number of common shares to be issued upon conversion. The accompanying consolidated financial statements and notes to consolidated financial statements give retroactive effect to the stock split for all periods presented.

Basis of Presentation

The Company's consolidated financial statements are prepared in accordance with accounting principles generally accepted in the U.S. ("GAAP"). The consolidated financial statements include the accounts of the Company and its wholly owned subsidiary, Landos Biopharma Australia Pty Ltd. ("Landos Australia"). All intercompany balances and transactions have been eliminated in consolidation.

Liquidity

As of December 31, 2022, the Company had cash, cash equivalents and marketable securities of $44.4 million. The Company believes that its existing cash, cash equivalents and marketable securities as of December 31, 2022, in addition to the $16.7 million in gross proceeds from its private placement of pre-funded warrants in January 2023, will be sufficient to fund its planned operations for at least one year from the issuance of these consolidated financial statements. Since the Company's inception in 2017, it funded operations through the issuance of convertible preferred stock and convertible promissory notes, the proceeds from its IPO, and the upfront payment from the license and collaboration agreement (Note 7). As of December 31, 2022, the Company had an accumulated deficit of $133.4 million and expects to incur substantial operating losses for at least the next several years. As such, the Company will need to raise additional capital to initiate and complete its planned clinical trials, to continue and expand its research and development operations that support its planned discovery, development and clinical and regulatory activities, and to adequately prepare for commercialization of its product candidates that may achieve regulatory approval in the future.

Consolidated Financial Statements in U.S. Dollars

The Company's functional currency is the U.S. dollar as the U.S. dollar is the currency of the primary economic environment in which the Company has operated and expects to continue to operate in the foreseeable future. Transactions and balances denominated in dollars are presented at their original amounts. Transactions and balances denominated in foreign currencies have been re-measured to dollars. All transaction gains and losses from re-measurement of monetary balance sheet items denominated in non-dollar currencies are reflected in the consolidated statement of operations and comprehensive loss as other income, net. Net foreign currency transaction losses were not material for the years ended December 31, 2022 and 2021.

Use of Estimates

The preparation of consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of expenses during the reporting period. Significant estimates and assumptions made in the accompanying consolidated financial statements include but are not limited to estimates for clinical trial accruals and for periods prior to the Company's IPO, fair value of equity instruments. The Company evaluates its estimates and assumptions on an ongoing basis using historical experience and other factors and adjusts those estimates and assumptions when facts and circumstances dictate. Actual results could differ from those estimates.

Cash and Cash Equivalents

Cash and cash equivalents consist of cash and highly liquid investments with original maturities of three months or less at the date of purchase. The carrying amounts approximate fair value due to the short maturities of these investments. Cash equivalents consist primarily of amounts invested in money market funds and commercial paper and are stated at fair value.

Marketable Securities

The Company's investments in marketable securities are maintained by investment managers and consist of corporate debt securities with original maturities of over 90 days, all of which are considered available-for-sale debt securities. The Company classifies its available-for-sale securities as short-term marketable securities on the Consolidated Balance Sheets, even though the stated maturity date may be one year or more beyond the current Consolidated Balance Sheets date, as the Company views those securities as available for use in current operations, if needed.

Available-for-sale securities are carried at fair value with their unrealized gains and losses included in accumulated other comprehensive loss within stockholders' equity (deficit), until such gains and losses are realized in other income, net, within the Consolidated Statements of Operations and Comprehensive Loss or until an unrealized loss is considered other-than-temporary. Realized gains and losses are determined using the specific identification method.

The Company evaluates its investments with unrealized losses for other-than-temporary impairment. When assessing investments for other-than-temporary impairments in value, the Company considers such factors as, among other things, how significant the impairment in value is as a percentage of the original cost, how long the market value of the investment has been less than its original cost, the Company's ability and intent to retain the investment for a period of time sufficient to allow for any anticipated recovery in fair value and market conditions. If the Company determines from this analysis that it does not expect to receive cash flows sufficient to recover the entire amortized cost of the security, a credit loss exists, the impairment is considered other-than-temporary and is recognized in the Consolidated Statements of Operations and Comprehensive Loss.

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to a concentration of credit risk consist primarily of cash, cash equivalents, and marketable securities. Bank deposits are held by accredited financial institutions and these deposits may at times be in excess of insured limits. The Company limits its credit risk associated with cash and cash equivalents by placing them with financial institutions it believes are of high quality. The Company has not experienced any losses on its deposits of cash or cash equivalents as of December 31, 2022.

The Company's available-for-sale investments primarily consist of high-grade corporate debt, and potentially subject the Company to concentrations of credit risk. The Company has adopted investment guidelines that limit the amounts the Company may invest in any one type of investment and requires all investments held by the Company to be highly rated, thereby reducing credit risk exposure.

Deferred Offering Costs

At December 31, 2022, the Company had deferred offering costs totaling $25,000 consisting of legal fees directly attributable to a private placement completed after December 31, 2022. At December 31, 2020, the Company had deferred offering costs totaling $1.4 million consisting of legal, accounting, filing and other fees and costs directly attributable to the Company's IPO. Upon the closing of the IPO in February 2021, these deferred offering costs were offset against the proceeds received.

Property and Equipment, net

Property and equipment are stated at cost, less accumulated depreciation. Depreciation is calculated using the straight-line method over the estimated useful lives of the related assets. The estimated useful lives of laboratory equipment, furniture and fixtures ranges from five to seven years. Maintenance, repair and calibration costs are expensed as incurred.

Impairment of Long-Lived Assets

The Company evaluates its long-lived assets, including property and equipment, for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets or group of assets may not be fully recoverable. If indicators of impairment exist and the undiscounted future cash flows that the assets are expected to generate are less than the carrying value of the assets, the Company reduces the carrying amount of the assets through an impairment charge, to their estimated fair values based on a discounted cash flow approach or, when available and appropriate, to comparable market values. During the years ended December 31, 2022 and 2021, there were no such indicators.

Revenue Recognition for Out-License Arrangements

To date, all of the Company's revenue has been derived from its license agreement with LianBio Respiratory Limited ("Lian") (Note 7).

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. To determine revenue recognition for arrangements, the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price, including variable consideration, if any; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the Company satisfies a performance obligation.

License Revenue

The Company first assesses whether the goods or services promised within each contract are distinct to identify those that are performance obligations. This assessment involves subjective determinations and requires management to make judgments about the individual promised goods or services and whether such are separable from the other aspects of the contractual relationship. In assessing whether a promised good or service is distinct, and therefore a performance obligation, the Company considers factors such as the research, manufacturing and commercialization capabilities of the customer and the availability of the associated expertise in the general marketplace. The Company also considers the intended benefit of the contract in assessing whether a promised good or service is separately identifiable from other promises in the contract. If a promised good or service is not distinct, the Company is required to combine that good or service with other promised goods or services until it identifies a bundle of goods or services that is distinct. Arrangements that include rights to additional goods or services that are exercisable at a customer's discretion are generally considered options. The Company assesses if these options provide a material right to the customer and if so, they are considered performance obligations.

The transaction price is determined and allocated to the identified performance obligations in proportion to their stand-alone selling prices ("SSP") on a relative SSP basis. SSP is based on observable prices of the performance obligations or, when such prices are not observable, are estimated based on factors such as forecasted revenues or costs, development timelines, discount rates, and probabilities of technical and regulatory success.

If the consideration promised in a contract includes a variable amount, the Company estimates the amount of consideration to which it will be entitled in exchange for transferring the promised goods or services to a customer. The Company determines the amount of variable consideration by using the expected value method or the most likely amount method. The Company includes the amount of estimated variable consideration in the transaction price to the extent that it is probable that a significant reversal of cumulative revenue recognized will not occur. At the end of each subsequent reporting period, the Company re-evaluates the estimated variable consideration included in the transaction price and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis in the period of adjustment.

Milestone Payments

If an arrangement includes development, regulatory or commercial milestone payments, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the Company's control or the licensee's control, such as regulatory approvals, are generally not considered probable of being achieved until those approvals are received.

Royalties

For arrangements with licenses of intellectual property that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes royalty revenue and sales-based milestones at the later of (i) when the related sales occur, or (ii) when the performance obligation to which the royalty has been allocated has been satisfied. The Company recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) each performance obligation is satisfied at a point in time or over time, and if over time, recognition is based on the use of an output or input method.

The Company receives payments from its collaborators based on billing schedules established in each contract. Up-front and other payments may require deferral of revenue recognition to a future period until the Company performs its obligations under its collaboration arrangements. Amounts are recorded as accounts receivable when the Company's right to consideration is unconditional. The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the customer and the transfer of the promised goods or services to the customer will be one year or less.

Research and Development Expenses

Research and development costs consist primarily of external costs related to clinical development, contract manufacturing and discovery as well as personnel costs. The Company estimates preclinical and clinical study and research expenses based on the services performed, pursuant to contracts with research institutions that conduct and manage nonclinical and clinical studies and research services on its behalf. The Company records the costs of research and development activities based upon the estimated amount of services provided but not yet invoiced and includes these costs in accrued liabilities in the Consolidated Balance Sheets. These costs are a component of the Company's research and development expenses. The Company accrues for these costs based on factors such as estimates of the work completed and in accordance with agreements established with its third-party service providers under the service agreements. The Company makes significant judgments and estimates in determining the accrued liabilities balance in each reporting period. As actual costs become known, the Company adjusts its accrued liabilities.

Share-Based Compensation

The Company measures employee and non-employee stock-based awards, including stock options and purchase rights, at grant-date fair value and records compensation expense on a straight-line basis over the vesting period of the award. The Company uses the Black-Scholes option pricing model to value its stock option awards. The Company elects to account for forfeitures as they occur.

Income Taxes

The Company accounts for income taxes under the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements. Under this method, deferred tax assets and liabilities are determined on the basis of the differences between the financial statements and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. The effect of a change in tax rates on deferred tax assets and liabilities is recognized as income in the period that includes the enactment date.

The Company recognizes net deferred tax assets to the extent that the Company believes these assets are more likely than not to be realized. In making such a determination, management considers all available positive and negative evidence, including future reversals of existing taxable temporary differences, projected future taxable income, tax-planning strategies, and results of recent operations. If management determines that the Company would be able to realize its deferred tax assets in the future in excess of their net recorded amount, management would make an adjustment to the deferred tax asset valuation allowance, which would reduce the provision for income taxes.

The Company records uncertain tax positions on the basis of a two-step process whereby (1) management determines whether it is more likely than not that the tax positions will be sustained on the basis of the technical merits of the position and (2) for those tax positions that meet the more-likely-than-not recognition threshold, management recognizes the largest amount of tax benefit that is more than 50% likely to be realized upon ultimate settlement with the related tax authority. The Company recognizes interest and penalties related to unrecognized tax benefits within income tax expense. Any accrued interest and penalties are included within the related tax liability.

Research and Development Tax Incentives

Through programs administered by the Australian Tax Office, the Company is eligible, if specific criteria is met, to obtain research and development incentive tax credits (the "Australia R&D credit") based on a percentage of certain research and development activities undertaken by Australia by Landos Australia. During the year ended December 31, 2021, pursuant to the Australia R&D credit program, the Company received a refund of approximately $1.3 million, which has been recorded as a reduction of research and development expenses in the accompanying consolidated financial statements. Refunds received pursuant to the Australia R&D credit program are subject to audit for a period of four years by the taxing authorities.

In addition, Landos Australia incurs Goods and Services Tax ("GST") on services provided by Australian vendors. As an Australian entity, Landos Australia is entitled to a refund of the GST paid. The Company's estimate of the amount of cash refund it expects to receive related to GST incurred is included in prepaid and other current assets in the accompanying consolidated balance sheets.

NIH Grant Income

The Company was awarded a grant by the National Institute of Health ("NIH") for a phase 2 proof-of-concept efficacy study of omilancor in Crohn's disease patients. The grant award provided for reimbursement of actual, allowable costs incurred. The Company records the grant income as qualifying expenditures are incurred to Other income. During the year ended December 31, 2022, the Company recorded grant income of $1.0 million, which has been recorded to Other income in the Consolidated Statement of Operations and Comprehensive Loss.

Net Loss per Share

Basic loss per share is computed by dividing the net loss by the weighted-average number of shares of common stock outstanding during the period. Diluted loss per share is computed by dividing the net loss by the weighted-average number of shares of common stock together with the number of additional shares of common stock that would have been outstanding if all potentially dilutive shares of common stock had been issued. Since the Company was in a loss position for the periods presented, basic net loss per share is the same as diluted net loss per share since the effects of potentially dilutive securities are antidilutive.

The following outstanding shares of potentially dilutive securities have been excluded from diluted net loss per common share for the periods presented, because their inclusion would be anti-dilutive:

	Years Ended December 31,	
	2022	2021
Stock options to purchase common stock	3,308,652	1,688,789
Total	3,308,652	1,688,789

Comprehensive Loss

The Company's comprehensive loss is currently comprised of changes in unrealized losses on available-for-sale securities.

Segment Reporting

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision-maker in making decisions regarding resource allocation and assessing performance. The Company views its operations and manages its business in one operating segment.

Emerging Growth Company Status

The Company is an emerging growth company ("EGC"), as defined in the Jumpstart Our Business Startups Act of 2012 ("the JOBS Act"). Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. The Company has elected to use this extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date that it (i) is no longer an EGC or (ii) affirmatively and irrevocably opts out of the extended transition period provided in the JOBS Act. As a result, these combined and consolidated financial statements may not be comparable to companies that comply with the new or revised accounting pronouncements as of public company effective dates.

Recently Adopted Accounting Pronouncements

In February 2016, the FASB issued ASU 2016-02—Leases (Topic 842), requiring the recognition of lease assets and liabilities on the balance sheet. The standard: (a) clarifies the definition of a lease; (b) requires a dual approach to lease classification similar to current lease classifications; and (c) causes lessees to recognize leases on the balance sheet as a lease liability with a corresponding right-of-use asset for leases with a lease-term of more than twelve months. The standard was effective for public entities for fiscal years beginning after December 15, 2018 and is effective for nonpublic entities for fiscal years beginning after December 15, 2021. The Company adopted ASU 2016-02, as amended, by applying the modified retrospective approach for leases existing at, and entered into after January 1, 2022. As a result, prior periods are presented in accordance with the previous guidance in ASC 840, Leases (“ASC 840”). The Company has elected to apply the “practical expedient package,” which permits it to not reassess previous conclusions around lease identification, lease classification, and initial direct costs. Further, the Company made accounting policy elections to exclude leases with terms of 12 months or less from the recognition requirements and to not separate lease and non-lease components. On January 1, 2022, the Company recognized an initial right-of-use asset and lease liability of $0.8 million. The adoption of Topic 842 did not have an impact on the Company’s Consolidated Statements of Operations and Comprehensive Loss and did not require recognition of a cumulative-effect adjustment to the opening balance of retained earnings in the period of adoption. The Company elected to continue applying the guidance under ASC 840 for comparative periods, as allowed in Topic 842.

Recently Accounting Pronouncements Not Yet Adopted

In June 2016, the FASB issued ASU 2016-13—Financial Instruments (Topic 326) Measurement of Credit Losses on Financial Instrument (“CECL”), which requires an allowance for expected credit losses on financial assets be recognized as early as day one of the instrument. This ASU departs from the incurred loss model which means the probability threshold is removed. It considers more forward-looking information and requires the entity to estimate its credit losses as far as it can reasonably estimate. The ASU was effective for fiscal years beginning after December 15, 2019 for public business entities that are U.S. Securities and Exchange Commission ("SEC") filers, excluding entities eligible to be smaller reporting companies ("SRC"). For all other public business entities, including SRC, the ASU is effective for fiscal years beginning after December 15, 2022, including interim periods within those fiscal years. Early adoption is permitted for fiscal years beginning after December 15, 2018. The Company expects to adopt the new standard in the annual reporting period beginning after December 15, 2022 and does not expect the adoption of this ASU to have a material impact on the consolidated financial statements.

2. Fair Value Measurement

Financial assets and liabilities are recorded at fair value on a recurring basis in the Consolidated Balance Sheets. The carrying values of the Company's financial assets and liabilities, including cash and cash equivalents, prepaid and other current assets, accounts payable, and accrued expenses approximate their fair value due to the short-term maturity of these instruments. Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability (an exit price) in an orderly transaction between market participants at the reporting date. Assets and liabilities recorded at fair value in the consolidated financial statements are categorized based upon the level of judgment associated with the inputs used to measure their fair value. Hierarchical levels are directly related to the amount of subjectivity with the inputs to the valuation of these assets or liabilities as follows:

Level 1—Observable inputs such as unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date;

Level 2—Inputs (other than quoted prices included in Level 1) are either directly or indirectly observable inputs for similar assets or liabilities. These include quoted prices for identical or similar assets or liabilities in active markets and quoted prices for identical or similar assets of liabilities in markets that are not active;

Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities

Financial assets and liabilities subject to fair value measurements on a recurring basis and the level of inputs used in such measurements are as follows (in thousands):

	December 31, 2022			
	Level 1	Level 2	Level 3	Aggregate fair value
Assets:				
U.S. government treasury securities	$ 25,442	$ —	$ —	$ 25,442
Fixed income securities	—	6,639	—	6,639
Asset backed securities	—	1,123	—	1,123
Total assets	$ 25,442	$ 7,762	$ —	$ 33,204

	December 31, 2021			
	Level 1	Level 2	Level 3	Aggregate Fair Value
Assets:				
Money market funds	$ 3,180	$ —	$ —	$ 3,180
Fixed income securities	—	54,224	—	54,224
Asset backed securities	—	28,351	—	28,351
Total assets	$ 3,180	$ 82,575	$ —	$ 85,755

The contractual maturities of available for sale securities of December 31, 2022 and 2021, are as follows (in thousands):

	December 31,	
	2022	2021
Within one year	$ 6,669	$ 49,699
Within one to five years	1,093	32,876
Total contractual maturities	$ 7,762	$ 82,575

The Company's financial instruments consist of Level 1 and Level 2 assets. The Company values its Level 1 assets based on quoted prices in active markets for identical instruments. Level 1 assets consist primarily of highly liquid money market funds and U.S. government treasury securities that are included in cash equivalents. The Company values its Level 2 assets consisting of fixed income securities and asset backed securities with the help of a third-party pricing service using quoted market prices for similar instruments or nonbinding market prices that are corroborated by observable market data. The Company uses such pricing data as the primary input, to which no material adjustments have been made during the periods presented, to make its determination and assessments as to the ultimate valuation of these assets. The fair values of these instruments approximate amortized cost. There were no transfers into or out of Level 3 securities during the year ended December 31, 2022 and 2021.

3. Consolidated Balance Sheet Components

Property and Equipment, net

Property and equipment, net consists of the following:

	December 31,	
	2022	2021
Laboratory equipment	$ 166	$ 837
Furniture and fixtures	—	307
Construction in process	—	104
Total property and equipment	166	1,248
Less: accumulated depreciation	(166)	(541)
Total property and equipment, net	$ —	$ 707

Depreciation expense for property and equipment was $0.6 million and $0.2 million for the years ended December 31, 2022 and 2021, respectively. Costs for property and equipment not yet placed into service are capitalized as construction in process, and will be depreciated over the relevant estimated useful life once placed into service.

Accrued Liabilities

Accrued liabilities consist of the following:

	December 31,	
	2022	2021
Accrued research and development	$ 1,222	$ 1,575
Accrued general and administrative	271	996
Accrued payroll and employee benefits	1,194	1,132
Total accrued liabilities	$ 2,687	$ 3,703

4. Commitments and Contingencies

Liabilities for loss contingencies arising from claims, assessments, litigation, fines and penalties and other sources are recorded when it is probable that a liability has been incurred and the amount can be reasonably estimated. The Company believes there is no litigation pending or loss contingencies that could have, either individually or in the aggregate, a material impact on the Company's financial statements.

The Company enters into contracts in the normal course of business with third-party contract organizations for clinical trials, preclinical studies, manufacturing and other services and products for operating purposes. These contracts generally provide for termination following a certain period after notice and therefore the Company believes that its non-cancelable obligations under these agreements are not material.

Leases

The Company adopted ASC 842 on January 1, 2022 and accordingly, recognized operating lease right-of-use ("ROU") assets and operating lease liabilities based on the present value of the future minimum lease payments over the lease terms at the adoption date, using the Company's assumed incremental borrowing rate of 8%. The Company amortized the operating lease ROU assets and operating lease liabilities over the applicable lease term.

The Company leased office space for its corporate headquarters located in Blacksburg, Virginia, under a non-cancelable operating lease, which expired in May 2022. In August 2021, the Company entered into a three-year lease for an additional facility in Blacksburg, Virginia that was terminated in March 2022.

In connection with the termination of the lease in March 2022, the Company made a one-time cash payment of $0.2 million and included assets with a net book value of $0.1 million, resulting in a loss on the termination of the lease of $0.3 million, which is included in general and administrative costs in the accompanying Consolidated Statements of Operations and Comprehensive Loss. In addition, upon termination of the lease in March 2022, operating lease ROU assets and operating lease liabilities were reduced by approximately $0.7 million.

Rent expense was $0.1 million and $0.3 million for the years ended December 31, 2022 and 2021, respectively.

5. Convertible Preferred Stock and Stockholders' Equity (Deficit)

Convertible Preferred Stock

In connection with the completion of the Company's IPO in February 2021, all outstanding shares of the Company's convertible preferred stock automatically converted into 20,549,478 shares of common stock. Prior to its automatic conversion in the Company's initial public offering, the Company classified its convertible preferred stock outside of permanent equity since such stock was contractually redeemable outside of the Company's control.

Stock Split

On January 27, 2021, the Company's Board of Directors approved a 1.8249-for-1 stock split of the Company's outstanding common shares. On January 29, 2021, the Company amended its Amended and Restated Certificate of Incorporation to affect the stock split. The stock split resulted in an adjustment to the preferred share conversion price to reflect a proportional increase in the number of common shares to be issued upon conversion. The accompanying consolidated financial statements and notes to consolidated financial statements give retroactive effect to the stock split for all periods presented.

6. Stock-Based Compensation

2019 Equity Incentive Plan

In December 2019, the board of directors of the Company (the "Board") adopted the 2019 Equity Incentive Plan (the "2019 Plan"). The 2019 Plan provides for the grant of share-based awards, including stock options and restricted stock units, to employees, directors, and non-employee service providers of the Company. As of December 31, 2022, there are approximately 6,921,233 shares available for future grants. The number of shares of common stock reserved for issuance under the 2019 Plan automatically increases on January 1 of each calendar year, starting on January 1, 2020 and continuing through January 1, 2029, in an amount equal to the least of (i) 5% of the total number of shares of the Company's capital stock issued and outstanding on the last day of the calendar month before the date of each automatic increase; (ii) 1,000,000 shares; or (iii) a lesser number of shares determined by the Company's board of directors. Subject to this provision, the Company added 1,824,900 shares available for grant to the 2019 Plan effective January 1, 2023.

2021 Employee Stock Purchase Plan

In January 2021, the Board adopted the 2021 Employee Stock Purchase Plan (the "2021 ESPP"). The purpose of the 2021 ESPP is to secure the services of new employees, to retain the services of existing employees and to provide incentives for such individuals to exert maximum efforts toward the Company's success. The ESPP is intended to qualify as an "employee stock purchase plan" within the meaning of Section 423 of the Code for U.S. employees. As of December 31, 2022, there were approximately 791,251 shares available for future grants under the 2021 ESPP. The number of shares of common stock reserved for issuance under the 2021 ESPP automatically increases on January 1 of each calendar year, starting on January 1, 2022 and continuing through January 1, 2031, in an amount equal to the lesser of (i) 1% of the total number of shares of the Company's capital stock issued and outstanding on the last day of the calendar month before the date of each automatic increase; or (ii) a lesser number of shares determined by the Board. Subject to this provision, the Company added 402,548 shares available for grant to the 2021 ESPP effective January 1, 2023. As of December 31, 2022, no shares of common stock had been purchased under the 2021 ESPP.

2022 Inducement Plan

In March 2022, the Board adopted the 2022 Inducement Plan. The 2022 Inducement Plan is a non-stockholder approved stock plan under which the Company may grant equity awards to induce highly-qualified prospective officers and employees who are not currently employed by the Company to accept employment and provide them with a proprietary interest in the Company. The Company intends that the 2022 Inducement Plan be reserved for persons to whom the Company may issue securities without stockholder approval as an inducement pursuant to Nasdaq Marketplace Rule 5635(c)(4). The number of shares of common stock reserved for issuance under the 2022 Inducement Plan was initially determined to be 1,000,000 shares. As of December 31, 2022, there were 1,000,000 shares available for future grants under the 2022 Inducement Plan.

Former Executive Officer's Equity Awards

In November 2021, the Company modified certain shares of an equity award that had previously been granted to the Company's former Chief Executive Officer. The vesting of the unvested equity award was accelerated. During the year ended December 31, 2021, stock-based compensation expense of $0.3 million was recorded in connection with this modification and is included in general and administrative expenses in the accompanying consolidated statements of operations and comprehensive loss.

Summary of Company's Stock Option Activity

A summary of the Company's stock option activity is as follows:

	Number of Shares	Weighted Average Exercise Price	Weighted Remaining Contract Term (in years)	Aggregate Intrinsic Value (in thousands)
Balance as of December 31, 2021	1,688,789	$ 8.69	9.0	$ 1,651
Granted	3,112,681	0.90		
Exercised	—	—		
Forfeited/Expired	(1,492,818)	8.06		
Balance as of December 31, 2022	3,308,652	$ 1.65	9.4	$ —
Exercisable and vested at December 31, 2022	493,804	$ 4.52	8.8	$ —
Vested and expected to vest as of December 31, 2022	3,308,652	$ 1.65	9.4	$ —

The total intrinsic value of stock options exercised was $0 and $1.3 million for the years ended December 31, 2022 and 2021, respectively.

The weighted average fair value of options to purchase common stock granted in the years ended December 31, 2022 and 2021 was $0.90 and $7.19, respectively.

The fair value of each stock option award is estimated on the grant-date using the Black-Scholes option pricing model. The inputs used below are subjective and require significant judgment to determine.

	Years Ended December 31,	
	2022	2021
Expected term (in years)	6.0	5.7
Risk-free interest rate	3.2%	0.8%
Expected volatility	81.8%	70.2%
Dividend rate	—%	—%
Fair value of common stock	$ 0.6	$ 7.2

Risk-free interest rate. The Company bases the risk-free interest rate assumption on the U.S. Treasury's rates for U.S. Treasury zero-coupon bonds with maturities similar to those of the expected term of the award being valued.

Expected volatility. Due to our limited operating history and lack of Company-specific historical or implied volatility, the expected volatility assumption was determined by examining the historical volatilities of a group of industry peers whose share prices are publicly available, and is calculated based on a period consistent with the expected term of the option.

Expected term. The expected term represents the period of time that options are expected to be outstanding. Because the Company does not have historical exercise behavior, it determines the expected life assumption using the simplified method, which is an average of the contractual term of the option and its vesting period.

Expected dividend yield. The Company bases the expected dividend yield assumption on the fact that it has never paid cash dividends and has no present intention to pay cash dividends.

The allocation of stock-based compensation expense was as follows (in thousands):

	Years Ended December 31,	
	2022	2021
Research and development	$ 638	$ 2,545
General and administrative	1,333	1,573
Total stock-based compensation expense	$ 1,971	$ 4,118

At December 31, 2022, the unrecognized compensation cost related to outstanding time-based options was $2.0 million and is expected to be recognized as expense over approximately 3.2 years.

7. License and Collaboration Agreement

On May 14, 2021, the Company entered into an exclusive license and collaboration agreement (the "LianBio Agreement") with LianBio Respiratory Limited ("Lian"). Lian is a related party to the Company as a result of an affiliation of a member of the Company's board of directors at the time the LianBio Agreement was executed. Pursuant to the LianBio Agreement, the Company delivered to Lian an exclusive license and the know-how (the "License") to develop, manufacture and commercialize omilancor and NX-13 (the "Products") in the territory comprising the People's Republic of China ("PRC"), Hong Kong, Macau, Taiwan, Cambodia, Indonesia, Myanmar, Philippines, Singapore, South Korea, Thailand, and Vietnam (the "Territory"). Lian will bear (i) all costs and expenses for any development or commercialization of the Products in the Territory and (ii) all costs and fees associated with applying for regulatory approval of the Products in the Territory. The Company received a non-refundable payment of $18.0 million upon execution of the LianBio Agreement. In February 2023, we amended the LianBio Agreement to no longer cover the licensing of Licensed Technology relating to omilancor and developmental milestones events were amended to reflect the transfer of Licensed Technology relating to omilancor. Subsequent to the amendment, we are eligible to receive development milestone payments of up to $40.0 million as well as sales milestone payments of up to $105.0 million. We are also eligible to receive tiered low-double-digit royalties based on future net sales of NX-13 in the Territory, subject to reductions in specified circumstances.

In accordance with the LianBio Agreement, the Company agreed to supply to Lian all clinical and commercial requirements of Products. The terms of the agreement do not provide for either (i) an option to Lian to purchase Products from the Company at a discount from the standalone selling price or (ii) minimum purchase quantities. In addition, the Company and Lian formed a Joint Steering Committee ("JSC") to provide oversight to the activities performed under the LianBio Agreement; however, the substance of the Company's participation in the JSC does not represent an additional promised service, but rather, a right of the Company to protect its own interests in the arrangement.

The Company concluded that Lian meets the definition of a customer because the Company is delivering intellectual property and other services in which the parties are not jointly sharing the risks and rewards. Therefore, the Company concluded that the promises summarized above represent transactions with a customer within the scope of ASC 606. Given that Lian is not obligated to purchase any minimum amount or quantities of Products, the supply of Products for clinical and commercial purposes was determined to be an option for Lian, rather than a performance obligation of the Company at contract inception and will be accounted for if and when exercised. The Company also determined that Lian's option to purchase Products does not create a material right as the expected pricing is not at a discount. At contract inception and through December 31, 2022, the Company determined that the contract contains a single performance obligation to deliver the License, which represents functional intellectually property given the functionality of the License is not expected to change substantially as a result of the Company's ongoing activities.

The Company determined that the upfront fixed payment of $18.0 million is the initial transaction price. The potential development milestone payments that the Company is eligible to receive upon the successful achievement of certain regulatory approvals or activities were excluded from the transaction price, as the milestone amounts were fully constrained based on the probability of achievement. The royalties and sales milestone payments are excluded from the transaction price under the sales- or usage-based royalty exception of ASC 606. The Company will reevaluate the transaction price, including all constrained amounts, at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur, and the Company will adjust its estimate of the transaction price as necessary. The Company will recognize the royalties and sales milestone payments as revenue when the associated sales occur, and relevant sales-based thresholds are met. The Company assessed the arrangement with Lian and concluded that a significant financing component does not exist. As of June 30, 2021, the Company had completed the transfer of the License and know-how necessary and, as such, recognized the full $18.0 million upfront payment as revenue.

8. Income Taxes

The following table presents a reconciliation of the statutory federal rate and the Company's effective tax rate:

	Years Ended December 31,	
	2022	2021
Federal statutory income tax rate	21.00%	21.00%
State taxes, net of federal benefit	3.85%	4.72%
Permanent differences	(0.66)%	(0.31)%
Other credits	2.27%	1.58%
Foreign rate differential	0.06%	(0.05)%
Other	(0.01)%	(0.51)%
Change in valuation allowance	(26.51)%	(26.43)%
Provision for income taxes	—%	—%

The following table presents the significant components of the Company's deferred tax assets and liabilities for the periods presented:

	Years Ended December 31,	
	2022	2021
Deferred tax assets (liabilities):		
Accruals	$ 636	$ 384
Stock-based compensation	1,223	820
Fixed assets	33	(12)
Intangible assets	374	365
Unrealized gain	29	18
Prepaid assets	(64)	—
Capitalized research and development costs under Section 174	5,696	—
Net operating loss carryforwards	22,999	19,857
Research and development credits	3,181	2,385
Research and development credits unrecognized tax benefits	(318)	(319)
Valuation allowance	(33,789)	(23,498)
Net deferred tax assets (liabilities)	$ —	$ —

At December 31, 2022 and 2021, the Company evaluated all significant available positive and negative evidence, including the existence of losses in recent years and management's forecast of future taxable income, and, as a result, determined it was more likely than not that federal and state deferred tax assets, including benefits related to net operating loss carryforwards, would not be realized. The valuation allowance was increased from $23.5 million at December 31, 2021 to $33.8 million at December 31, 2022.

The Tax Cuts and Jobs Act ("TCJA") requires taxpayers to capitalize and amortize research and experimental ("R&D") expenditures under section 174 for tax years beginning after December 31, 2021. This rule became effective for the Company during the year and resulted in the capitalization of R&D costs $24.4 million. The Company will amortize these costs for tax purposes over 5 years if the R&D was performed in the U.S. and over 15 years if the R&D was performed outside the U.S. These rules also are in effect for its foreign subsidiaries and the calculation of global intangible low-taxes income ("GILTI") for the Company, of which $0.8 million of foreign R&D costs have been capitalized and will be amortized for tax purposes over 15 years. Given the Company's current period loss position, this adjustment does not currently have an impact on cash taxes.

As of December 31, 2022, the Company has $89.0 million and $86.2 million of federal and state net operating loss carryforwards, respectively. Federal net operating loss carryforward incurred prior to 2018 as well as the state net operating loss carryforward begin to expire in 2037. Federal net operating losses incurred in 2018 and after have an unlimited carryforward period. The Company also has $0.8 million of Australian net operating loss carryforwards which also have an unlimited carryforward period. Because the Company has incurred cumulative net operating losses since inception, all tax years remain open to examination by U.S. federal, state, and foreign income tax authorities.

The Company had an unrecorded tax benefit of $0.3 million due to uncertain tax positions as of December 31, 2022 and 2021. The Company's policy for recording interest and penalties is to record them as a component of interest expense and operating expenses, respectively. As of December 31, 2022, the Company had no accrued interest or penalties related to uncertain tax positions. The total unrecorded benefit would affect the effective tax rate but for the Company's valuation allowance. The Company does not expect a material change in unrecognized tax benefits within the next 12 months.

A reconciliation of the beginning and ending amounts of unrecognized tax benefits is as follows:

	Years Ended December 31,	
	2022	2021
Balance at the beginning of the year	$ 319	$ 139
Additions for tax positions taken in the current year	37	110
Addition (reduction) for prior tax positions	(38)	70
Balance at the end of the year	$ 318	$ 319

Potential 382 limitation

The Company's ability to utilize its net operating loss (NOL) and research and development (R&D) credit carryforwards may be substantially limited due to ownership changes that may have occurred or that could occur in the future, as required by Section 382 of the Internal Revenue Code of 1986, as amended (the Code), as well as similar state provisions. These ownership changes may limit the amount of NOL and R&D credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. In general, an "ownership change," as defined by Section 382 of the Code, results from a transaction or series of transactions over a three-year period resulting in an ownership change of more than 50 percent of the outstanding stock of a company by certain stockholders or public groups.

The Company has not completed a study to assess whether one or more ownership changes have occurred since the Company became a loss corporation under the definition of Section 382. If the Company has experienced an ownership change, utilization of the NOL or R&D credit carryforwards would be subject to an annual limitation, 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 such limitation may result in the expiration of a portion of the NOL or R&D credit carryforwards before utilization. Until a study is completed and any limitation known, no amounts are being considered as an uncertain tax position or disclosed as an unrecognized tax benefit under ASC-740. Any carryforwards that expire prior to utilization as a result of such limitations will be removed from deferred tax assets with a corresponding reduction of the valuation allowance. Due to the existence of the valuation allowance, it is not expected that any possible limitation will have an impact on the results of operations of the Company.

9. Subsequent Events

Securities Purchase Agreement

On January 4, 2023, the Company entered into a securities purchase agreement (the "Securities Purchase Agreement") with the institutional accredited investors named therein (the "Investors"), pursuant to which the Company agreed to issue and sell to the Investors in a private placement (the "Private Placement") pre-funded warrants (the "Pre-Funded Warrants") to purchase an aggregate of 30,909,090 shares (the "Warrant Shares") of the Company's common stock. Each Pre-Funded Warrant has an exercise price of $0.01 per Warrant Share. The purchase price per Pre-Funded Warrant was $0.54.

The Pre-Funded Warrants issued in the Private Placement provide that the holder of the Pre-Funded Warrants will not have the right to exercise any portion of its Pre-Funded Warrants if such holder, together with its affiliates and any other persons whose beneficial ownership of common stock would be aggregated with the holder for purposes of Section 13(d) or Section 16 of the Securities Exchange Act of 1934, as amended, would beneficially own in excess of 35% of the number of shares of common stock outstanding immediately after giving effect to such exercise. The Warrant Shares will also be subject to certain registration rights under the Company's Amended and Restated Investors' Rights Agreement.

The Private Placement closed on January 10, 2023. Gross proceeds of the Private Placement were approximately $16.7 million, before deducting offering expenses payable by the Company.

LianBio Agreement Amendment and Asset Purchase and Redemption Agreement

On February 28, 2023, the Company entered into an amendment (the "Amendment") to the LianBio Agreement with Lian. Pursuant to the terms of the Amendment, the Company acknowledged acquisition of the ownership of certain Licensed Technology (as defined in the agreement) relating to its proprietary compound known as omilancor by NImmune Biopharma, Inc. (a corporation that was newly formed by Dr. Josep Bassaganya-Riera, Ph.D., former Chief Executive Officer of the Company, in connection with the transactions described below) and together with Lian provided that the LianBio Agreement no longer covers the licensing of Licensed Technology relating to omilancor. Furthermore, developmental milestone events were amended to reflect the transfer of Licensed Technology relating to omilancor.

On February 28, 2023, the Company entered into an Asset Purchase and Redemption Agreement (the "Purchase Agreement") with Dr. Bassaganya-Riera, a related party who is the former Chief Executive Officer of the Company and a principal owner of the Company's common stock at the time of the transaction, Raquel Hontecillas and certain other stockholders (together the "Purchasers") whereby Purchasers acquired (i) all of the Company's right, title and interest in omilancor, LABP-104 and LABP-111 and any such derivatives and analogs that target LANCL proteins (together the "Acquired Compounds"), (ii) a worldwide, perpetual, irrevocable, fully-paid up, royalty-free, exclusive, sublicensable and transferable license grant under the intellectual property rights retained by the Company and necessary or useful for the development, manufacture and commercialization of the Acquired Compounds, (iii) a royalty agreement providing, among other things, for the payment by the Company to the Purchasers of a royalty of 2% of all net sales by the Company of any products containing certain compounds that the Company retained following the closing of the Purchase Agreement and (iv) $3,000,000 in cash in exchange for (x) 9,086,441 shares of the common stock of the Company held by the Purchasers and (y) a royalty agreement providing, among other things, for the payment by the Purchasers to the Company a royalty of 6% of all net sales by the Purchasers of any products containing any of the Acquired Compounds in consideration for the acquired intellectual property rights. The transactions contemplated by the Purchase Agreement closed simultaneously with signing.

Silicon Valley Bank

On March 10, 2023, Silicon Valley Bank ("SVB") was closed by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation as receiver. At the time of the closure, the Company held a cash balance of low single digit millions of dollars in a deposit account with SVB. On March 15, 2023, the Company successfully transferred all funds from this SVB account to one of its other banks not affiliated with SVB without incurring any loss.

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," as defined in Rule 13a-15(e) and Rule 15d-15(e) under the Exchange Act that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to our management, including our principal executive and financial officer, as appropriate to allow timely decisions regarding required disclosure.

Our management, with the participation of our Chief Executive Officer, has evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act), as of the end of the period covered by this Form 10-K. Based on such evaluation, our Chief Executive Officer has concluded that as of December 31, 2022, our disclosure controls and procedures were effective to provide reasonable assurance that the information required to be disclosed by us in this Form 10-K was (a) reported within the time periods specified by SEC rules and regulations, and (b) communicated to our management, including our Chief Executive Officer, to allow timely decisions regarding any required disclosure.

Management's Annual Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as such term as defined in Exchange Act Rule 13a-15(f). Internal control over financial reporting is a process designed under the supervision and with the participation of our management, including our principal executive and financial officer, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with accounting principles generally accepted in the United States of America.

As of December 31, 2022, our management assessed the effectiveness of our internal control over financial reporting using the criteria set forth by the Committee of Sponsoring Organizations (COSO) of the Treadway Commission in Internal Control-Integrated Framework (2013 Framework). Based on this assessment, our management concluded that, as of December 31, 2022, our internal control over financial reporting was effective based on those criteria.

Changes in Internal Control Over Financial Reporting

There were no changes in our internal control over financial reporting identified in management's evaluation pursuant to Rules 13a-15(d) or 15d-15(d) of the Exchange Act during the quarter ended December 31, 2022 that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Inherent Limitations on Effectiveness of Internal Controls

In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable, not absolute, assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs. Our management, including our Chief Executive Officer, believes that our disclosure controls and procedures and internal control over financial reporting are designed to provide reasonable assurance of achieving their objectives and are effective at the reasonable assurance level. However, our management does not expect that our disclosure controls and procedures or our internal control over financial reporting will prevent all errors and all fraud.

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.

Information required by this item is incorporated by reference to our Proxy Statement for the 2023 Annual Meeting of Stockholders.

Item 11. Executive Compensation.

Information required by this item is incorporated by reference to our Proxy Statement for the 2023 Annual Meeting of Stockholders.

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

Information required by this item is incorporated by reference to our Proxy Statement for the 2023 Annual Meeting of Stockholders.

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

Information required by this item is incorporated by reference to our Proxy Statement for the 2023 Annual Meeting of Stockholders.

Item 14. Principal Accountant Fees and Services.

Information required by this item is incorporated by reference to our Proxy Statement for the 2023 Annual Meeting of Stockholders.

PART IV

Item 15. Exhibits and Financial Statement Schedules.

Financial Statements

The following report and financial statements of the Company are included in this Annual Report on Form 10-K:

- Report of Independent Registered Public Accounting Firm
- Consolidated Balance Sheets
- Consolidated Statements of Operations and Comprehensive Loss
- Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)
- Consolidated Statement of Cash Flows
- Notes to Consolidated Financial Statements

Financial Statements Schedules

All financial statement schedules have been omitted as they are not required, they are not applicable, or the required information is included in the financial statements or notes to the financial statements.

Exhibit Number	Description
3.1	Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K (File No. 001-39971), filed with the Securities and Exchange Commission on February 8, 2021).
3.2	Amended and Restated Bylaws (incorporated by reference to Exhibit 3.2 to the Company's Current Report on Form 8-K (File No. 001-39971), filed with the Securities and Exchange Commission on February 8, 2021).
4.1	Form of Pre-Funded Warrant (incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K (File No. 001-39971), filed with the Securities and Exchange Commission on January 5, 2023).
4.2	Description of the Company's Common Stock (incorporated by reference to Exhibit 4.2 to the Company's Annual Report on Form 10-K (File No. 001-39971), filed with the Securities and Exchange Commission on March 31, 2021).
10.1	Amended and Restated Investors' Rights Agreement, by and among the Company and certain of its stockholders, dated August 9, 2019 (incorporated by reference to Exhibit 10.1 to the Company's Registration Statement on Form S-1 (File No. 333-252083), filed with the Securities and Exchange Commission on January 13, 2021).
10.2+	2019 Equity Incentive Plan, as amended (incorporated by reference to Exhibit 10.2 to the Company's Registration Statement on Form S-1 (File No. 333-252083), filed with the Securities and Exchange Commission on January 28, 2021).
10.3+	Form of Indemnification Agreement with Executive Officers and Directors (incorporated by reference to Exhibit 10.3 to the Company's Registration Statement on Form S-1 (File No. 333-252083), filed with the Securities and Exchange Commission on January 28, 2021).
10.4+	Employment Agreement by and between the Registrant and Dr. Josep Bassaganya-Riera, effective as of January 1, 2020 (incorporated by reference to Exhibit 10.4 to the Company's Registration Statement on Form S-1 (File No. 333-252083), filed with the Securities and Exchange Commission on January 13, 2021).
10.5+	2021 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.5 to the Company's Registration Statement on Form S-1 (File No. 333-252083), filed with the Securities and Exchange Commission on January 28, 2021).
10.6+	Non-Employee Director Compensation Policy (incorporated by reference to Exhibit 10.6 to the Company's Annual Report on Form 10-K (File No. 001-39971), filed with the Securities and Exchange Commission on March 31, 2021).
10.7+	Separation and Release of Claims Agreement by and between the Company and Josep Bassaganya-Riera, dated November 6, 2021 (incorporated by reference to Exhibit 10.7 to the Company's Annual

	Report on Form 10-K (File No. 001-39971), filed with the Securities and Exchange Commission on March 24, 2022).
10.8+	Employment Agreement by and between the Company and Tim M. Mayleben, effective as of December 17, 2021 (incorporated by reference to Exhibit 10.8 to the Company's Annual Report on Form 10-K (File No. 001-39971), filed with the Securities and Exchange Commission on March 24, 2022).
10.9+	Employment Agreement by and between the Company and Patricia L. Bitar, effective as of December 17, 2021 (incorporated by reference to Exhibit 10.9 to the Company's Annual Report on Form 10-K (File No. 001-39971), filed with the Securities and Exchange Commission on March 24, 2022).
10.10†	Exclusive Collaboration and License Agreement by and between the Company and Lian Respiratory Limited, dated May 14, 2021 (incorporated by reference to Exhibit 1.1 to the Company's Quarterly Report on Form 10-Q (File No. 001-39971), filed with the Securities and Exchange Commission on July 29, 2021).
10.11+	Separation and Release of Claims Agreement by and between the Company and Jyoti Chauhan, dated May 4, 2022. (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q (File No. 001-39971), filed with the Securities and Exchange Commission on August 11, 2022).
10.12+	Employment Agreement by and between the Company and Gregory Oakes, effective as of June 20, 2022. (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q (File No. 001-39971), filed with the Securities and Exchange Commission on August 11, 2022).
10.13^	Securities Purchase Agreement by and between the Company and the investors that are a party thereto, dated January 4, 2023 (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K (File No. 001-39971), filed with the Securities and Exchange Commission on January 5, 2023).
10.14	Amendment No. 1 to the Amended and Restated Investor's Rights Agreement, dated January 10, 2023, by and between the Company and the investors that are a party thereto (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K (File No. 001-39971), filed with the Securities and Exchange Commission on January 13, 2023).
10.15+*	Offer Letter by and between the Company and Fabio Cataldi, effective as of September 5, 2022.
10.16+*	Offer Letter by and between the Company and Patrick Truesdell, effective as of May 3, 2022.
10.17+*	Severance Agreement (pursuant to employment agreement) by and between the Company and Patrick Truesdell, effective as of December 8, 2022.
10.18†^	Asset Purchase and Redemption Agreement, by and between the Company and the counter parties identified therein, dated February 28, 2023. (incorporated by reference to Exhibit 99.1 to the Company's Current Report on Form 8-K (File No. 001-39971), filed with the Securities and Exchange Commission on February 28, 2023).
10.19†*	First Amendment to License and Collaboration Agreement, by and between the Company and LianBio Respiratory Limited, dated February 28, 2023.
23.1*	Consent of Ernst & Young LLP, independent registered public accounting firm
31.1*	Certification of Principal Executive and Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1*	Certification of Principal Executive and Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS*	Inline XBRL Instance Document. – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.
101.SCH*	Inline XBRL Taxonomy Extension Schema Document.
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document.
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document.
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document.
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document.
104*	Cover Page Interactive Data File (embedded within the Inline XBRL document).

* Filed herewith.

+ Indicates management contract or compensatory plan.

These certifications are being furnished solely to accompany this annual report pursuant to 18 U.S.C. Section 1350, and are not being filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and are not to be incorporated by reference into any filing of the registrant, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

† Certain portions of this exhibit (indicated by asterisks) have been omitted because they are not material and would likely cause competitive harm to the registrant if publicly disclosed.

^ Schedules and exhibits have been omitted pursuant to Item 601(a)(5) of Regulation S-K. A copy of any omitted schedule and/or exhibit will be furnished to the SEC upon request.

Item 16. Form 10-K Summary

Not applicable.

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.

LANDOS BIOPHARMA, INC.

Date: March 23, 2023

By: /s/ Gregory Oakes
Gregory Oakes
Chief Executive Officer

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Gregory Oakes as his true and lawful attorney-in-fact and agent, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign this Annual Report on Form 10-K of Landos Biopharma, Inc., and any or all amendments thereto, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent full power and authority to do and perform each and every act and thing requisite or necessary to be done in and about the premises hereby ratifying and confirming all that said attorney-in-fact and agent, or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

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/ Gregory Oakes Gregory Oakes	Chief Executive Officer and Director *(Principal Executive and Financial Officer)*	March 23, 2023
/s/ Patrick Truesdell Patrick Truesdell	Vice President and Controller *(Principal Accounting Officer)*	March 23, 2023
/s/ Christopher Garabedian Christopher Garabedian	Chairman of the Board of Directors	March 23, 2023
/s/ Roger Adsett Roger Adsett	Director	March 23, 2023
/s/ Fred Callori Fred Callori	Director	March 23, 2023
/s/ Tiago Girao Tiago Girao	Director	March 23, 2023
/s/ Tim M. Mayleben Tim M. Mayleben	Director	March 23, 2023