neoleukin™
THERAPEUTICS

2021 ANNUAL REPORT

neoleukin.com

LETTER TO STOCKHOLDERS

March 2022

To our stockholders,

Emblazoned across one of the walls at Neoleukin's new headquarters is our mission statement: *We use our science to reinvent how therapies are created with a goal to meaningfully improve patients' lives.*

In 2021, we took a big step toward making that vision a reality by initiating a phase 1 trial with NL-201, a drug designed using computational methods to solve problems related to the native immune regulator, interleukin-2 (i.e., IL-2). To our knowledge, this is the first time that a fully de novo protein has been tested in humans and marks a new phase in the development of therapeutic proteins that are unlike anything that exists in nature. I am proud that our team was able to accomplish this transition to a clinical stage company less than three years from incorporation and in the midst of a pandemic.

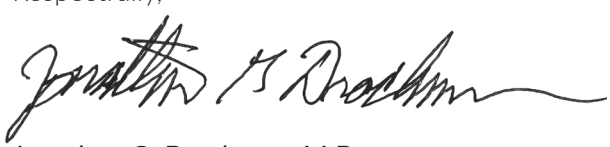
Our clinical team, led by Chief Medical Officer Priti Patel, M.D., has made excellent progress in execution of the trial, and we look forward to presenting the first interim dose-escalation data in the second half of 2022. While this will be an important event in the history of Neoleukin, it is an equally momentous time for the field of protein design, and we expect to learn a tremendous amount about de novo protein technology that will help guide future efforts by our scientists.

In September 2021, we hired Bill Arthur as our Head of Research. Bill is an expert in cancer biology, target validation, and the preclinical development of targeted cancer therapeutics. Our scientists and collaborators continue to generate compelling preclinical data supporting the development of NL-201 and other molecules in our early research pipeline. Our plans to begin studying additional pathways for NL-201 in clinic are supported by these findings, including the combination with PD-1 inhibitors and the treatment of patients with hematologic malignancies, such as B cell lymphomas and multiple myeloma.

During 2021, we grew our team to more than 90 employees and added significant drug development experience to our Research and Development organization. Already in 2022, we have hired talented leaders in Translational Sciences and Cancer Biology, and we announced the appointment of Donna Cochener, General Counsel, to our executive team. Throughout our growth, we've focused on building a culture that emphasizes diversity, equity, and inclusion, working to ensure that all voices are welcome and are heard.

We greatly appreciate the support and interest from our stockholders and look forward to keeping you updated on developments at Neoleukin during 2022.

Respectfully,



Jonathan G. Drachman, M.D.
CEO and President, Neoleukin Therapeutics, Inc.

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2021

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: 001-36327

Neoleukin Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**98-0542593**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

188 East Blaine Street, Suite 450
Seattle, Washington, 98102
(Address of principal executive offices, including zip code)

Registrant's telephone number, including area code: (866) 245-0312

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 $0.000001	**NLTX**	**The Nasdaq Global Market**

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

None

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

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 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 during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

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

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

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

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

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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant was approximately $322.8 million as of the last business day of the registrant's most recently completed second fiscal quarter, based upon the closing sale price on The Nasdaq Global Market reported for such date. This excludes an aggregate of 7,444,418 shares of the registrant's common stock held as of such date by officers, directors, and stockholders that the registrant has concluded are or were affiliates of the registrant. Exclusion of such shares should not be construed to indicate that the holder of any such shares possesses the power, direct or indirect, to direct or cause the direction of the management or policies of the registrant or that such person is controlled by or under common control with the registrant.

There were 42,493,971 shares of the registrant's Common Stock issued and outstanding as of February 28, 2022.

DOCUMENTS INCORPORATED BY REFERENCE

Part III incorporates information by reference from the registrant's definitive proxy statement to be filed with the Securities and Exchange Commission pursuant to Regulation 14A, not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, in connection with the registrant's 2022 Annual Meeting of Stockholders (the "***2022 Proxy Statement***").

NEOLEUKIN THERAPEUTICS, INC.

Annual Report on Form 10-K
For the Year Ended December 31, 2021

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Except as otherwise indicated herein or as the context otherwise requires, references in this report to, "the Company," "we," "us," "our" and similar references refer to Neoleukin Therapeutics, Inc. (formerly Aquinox Pharmaceuticals, Inc.), a Delaware corporation. The name "Neoleukin" is a trademark of the Company in the United States. This report also contains references to registered marks, trademarks and trade names of other companies that are property of their respective holders. All other trademarks, registered marks and trade names appearing in this report are the property of their respective holders.

PART I

This Annual Report on Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements are based on our management's beliefs and assumptions and on information currently available to our management. All statements other than statements of historical facts are "forward-looking statements" for purposes of these provisions, including those relating to future events or our future financial performance. In some cases, you can identify forward-looking statements by terminology such as "may," "might," "will," "should," "expect," "plan," "anticipate," "project," "believe," "estimate," "predict," "potential," "intend" or "continue," the negative of terms like these or other comparable terminology, and other words or terms of similar meaning in connection with any discussion of future operating or financial performance. These statements are only predictions. All forward-looking statements included in this Annual Report on Form 10-K are based on information available to us on the date hereof, and we assume no obligation to update any such forward-looking statements. Any or all of our forward-looking statements in this document may turn out to be wrong. Actual events or results may differ materially. Our forward-looking statements can be affected by inaccurate assumptions we might make or by known or unknown risks, uncertainties and other factors. We discuss many of these risks, uncertainties and other factors in this Annual Report on Form 10-K in greater detail under the heading "Item 1A—Risk Factors." We caution investors that our business and financial performance are subject to substantial risks and uncertainties.

Item 1. Business.

Overview

We are a biopharmaceutical company creating next generation immunotherapies for cancer, inflammation, and autoimmunity using *de novo* protein design technology. We use sophisticated computational methods to design proteins that demonstrate specific pharmaceutical properties that provide potentially superior therapeutic benefit over native proteins. Existing protein engineering treatments generally involve the modification of native proteins. With our proprietary platform, which we refer to as our Neoleukin platform, we design new protein scaffolds from the ground up, capable of demonstrating specific biological properties. Through this method we are able to produce proteins that, while resembling native proteins, may have novel molecular interfaces, differential activation of specific cell types, increased stability, or improved biodistribution compared to native proteins in order to deliver greater therapeutic benefit. *De novo* proteins have the capacity to be cytokine receptor agonists, antagonists, or result in conditional activation of specific cytokine receptors such that they may regulate inflammation or the immune response to cancer and inflammatory conditions. We are initially focused on key cytokine mimetics, which we refer to as Neoleukin *de novo* cytokine mimetics. Neoleukin *de novo* cytokine mimetics can be modified to adjust affinity, thermodynamic stability, resistance to biochemical modification, pharmacokinetic characteristics, and targeting to tumor or inflamed tissues.

Our lead product candidate, NL-201, is a *de novo* protein designed to mimic the therapeutic activity of the cytokines interleukin-2, or IL-2, and interleukin-15, or IL-15, for the potential treatment of various types of cancer, including renal cell carcinoma, or RCC, melanoma, and hematological malignancies, while limiting the toxicity caused by the preferential binding of native IL-2 and IL-15 to non-target cells. In preclinical studies, a closely-related precursor to NL-201 demonstrated higher levels of activity and lower toxicity in multiple murine solid tumor syngeneic models as compared to recombinant, native IL-2.

De Novo Protein Design Technology

Our Neoleukin platform uses a set of advanced computational algorithms and methods to design functional *de novo* proteins. A protein is generally defined as one or more chains of covalently-linked amino acids – totaling at least 50 amino acids – that assemble into a 3-dimensional structure. Human cells contain tens of thousands of different proteins; however this is still only a small subset of all possible amino acid sequences that can be assembled to form a protein. While protein engineering to date has largely been conducted through the modification of native proteins, with our Neoleukin platform we are able to explore the full sequence space, guided by the physical principles that underlie protein folding, and design functional proteins from the ground up. Our *de novo* proteins fit the above definition of a protein, but, unlike native proteins, are designed using our proprietary computational algorithms and methods. Successful *de novo* protein design is a cutting-edge process that requires both the advanced computational tools and deep insight into how a sequence of amino acids will fold into a stable 3-dimensional protein. To design a Neoleukin *de novo* cytokine mimetic using our Neoleukin platform, we begin with an accurate model of the biological target. This is typically a high-resolution crystal structure but may instead be a computationally-modeled structure. Then, critical points of contact between molecular interfaces are identified so that essential interactions can be maintained or strengthened, and undesirable interactions can be avoided. Next, we use a computational algorithm to build idealized 3-dimensional topologies of the biological target and the Neoleukin *de novo* cytokine mimetic. Finally, we use a separate computational algorithm to select amino acids for each position within the idealized 3-dimensional topologies that maximizes interactions at the desired interface and the thermodynamic stability of the resulting protein. These amino acid sequences are then expressed in bacteria, tested in our laboratory, and further modified to optimize the final sequence. The resulting protein is unlike anything that exists in nature and can be fine-tuned to improve on the desired biological activity.

While we are currently focused on the design of Neoleukin *de novo* cytokine mimetics, we believe this approach could be used broadly to widen the therapeutic window and improve drug-like characteristics of therapeutic proteins, including chemical stability, pharmacokinetic properties, or novel routes of administration. Furthermore, we believe that the Neoleukin platform can also be used to generate *de novo* proteins that inhibit activation of specific receptors, a property that could be valuable for treatment of inflammatory or autoimmune conditions. Computational design of therapeutic proteins is in a very early stage of development. The potential is vast, and we are focused on continuing to improve the technology and realizing the tremendous potential of *de novo* protein design to improve human health.

Our Strategy

Our business model is focused on three primary goals:

- Develop proprietary *de novo* protein immunotherapies for the treatment of cancer and inflammatory conditions;
- Become the leader in *de novo* protein design for therapeutic applications by strengthening our intellectual property, including know-how; and
- Collaborate with leading biotechnology, pharmaceutical, and academic partners to expand the scope and application of our platform.

The key elements of our strategy are:

- ***Rapidly advance NL-201 to clinical proof-of-concept.*** NL-201 is our lead product candidate and we believe it is the first entirely *de novo* therapeutic protein to be evaluated in a clinical setting. In 2021, we initiated a Phase 1 clinical trial in patients with advanced, relapsed, or refractory solid tumors. The Phase 1 trial is currently ongoing with interim data expected in the second half of 2022. We also plan to expand our ongoing trial of NL-201 by adding a combination arm with Merck's KEYTRUDA® (pembrolizumab) in mid-2022. In addition, we plan to initiate a Phase 1 clinical trial in hematological malignancies with NL-201 in 2022.
- ***Generate preclinical data for additional product candidates.*** Our research activities are currently focused on the development of novel *de novo* cytokine receptor agonists and antagonists to expand our pipeline. We are currently optimizing and evaluating several early research projects as potential clinical candidates. We initially intend to develop *de novo* protein therapeutics to address significant unmet medical needs in oncology, inflammation, and autoimmune indications.
- ***Expand the capabilities of the Neoleukin platform.*** *De novo* protein design is in the early stages of development and has the potential to generate therapeutics to treat a wide range of human diseases. We believe that there will be a rapid evolution in the enabling technology, such that it will be feasible to design more complex and dynamic proteins in the future. We intend to devote a significant amount of resources to building our talent, methods, and infrastructure in order to position Neoleukin as a leader in the design and development of *de novo* protein therapeutics.
- ***Build partnerships to leverage the Neoleukin platform.*** There is substantial interest in the field of *de novo* protein design for therapeutic applications. We intend to seek partners that can provide additional resources and expertise to further advance our pipeline and broaden our potential targets. We may also strategically pursue one or more collaborations to design, out-license, or co-develop *de novo* proteins.

NL-201

Our lead product candidate, NL-201, is an IL-2/IL-15 immunotherapy designed to eliminate binding to the alpha subunit of the IL-2 receptor (also known as CD25) while enhancing binding to the beta and gamma subunits. In multiple preclinical animal models, a precursor to NL-201, demonstrated substantial antitumor activity without detectable binding to CD25, as compared to native IL-2. Following these preclinical studies, we further refined our precursor to extend its half-life, resulting in the NL-201 product candidate. We have since completed multi-dose, non-GLP and GLP toxicology studies of NL-201 in rats and non-human primates, as well as initiated a first in-human clinical trial. This included completion of GLP in-life dosing with no unexpected toxicities observed. NL-201 is intended to be used as either a single-agent or in combination with complementary therapeutic modalities, including checkpoint inhibitors. In addition, we believe NL-201 holds promise in combination with cell therapy to expand and maintain populations of transplanted CAR-T and natural killer, or NK, cells.

IL-2 is one of the few immuno-oncology drugs with demonstrated activity as a single agent. IL-2 has a confirmed mechanism of action for treating tumors; however, it has encountered issues as a therapeutic due to the biased activation of cells that contain CD25. CD25 induces conformational changes in IL-2 that enable high-affinity binding to the beta and gamma subunits of the IL-2 receptor. Preferential binding to endothelial cells expressing CD25 is believed to exacerbate vascular leak syndrome, while preferential activation of CD25-expressing regulatory T cells can inhibit anti-cancer immune responses. Due to IL-2's potential for high toxicity, with vascular leak syndrome and cytokine storm being frequent side effects, and reduced efficacy over time, its use as a therapeutic has been limited. Further, low-dose treatments have generally been insufficient to demonstrate therapeutic activity.

While the problem posed by IL-2 is well understood, it has been difficult to modify native IL-2 to retain potent activation of IL-2 receptor signaling while eliminating binding to CD25. Instead of modifying native IL-2, computational methods were used to design a new sequence with the proper intermolecular interactions to efficiently bind the beta and gamma subunits while eliminating CD25 binding. As opposed to traditional recombinant protein therapeutics, *de novo* proteins are entirely novel sequences with limited homology to native proteins. While there is a potential that patients may mount an anti-drug immune response against NL-201, we believe that this risk may be mitigated by several factors, including the stability of the protein and its resistance to proteolytic degradation.

Immunotherapy Market Overview

Over the past several decades, the potential of the immune system to control and/or eliminate cancer has been better understood and appreciated. Immunotherapies, including allogeneic stem cell transplantation, checkpoint inhibitors, and cellular therapies have led to impressive improvements in patient outcomes. Immunotherapy is one of the fastest growing segments of the oncology market and immune checkpoint inhibitors are one of the most widely used classes of cancer immunotherapy. Checkpoint inhibitors promote an anti-cancer immune response by blocking inhibitory signals between cancer cells and the immune microenvironment. Patients with metastatic cancers, who previously had generally poor prognoses, now have the opportunity to achieve durable responses with checkpoint inhibitors. The initial drug in this class, ipilimumab, was approved by the United States Food and Drug Administration, or FDA, in 2011. Since that time, many additional checkpoint inhibitors have been approved by the FDA. In addition to checkpoint inhibitors, other notable cancer immunotherapies expected to improve cancer outcomes over the next decade include bi-specific T-cell engagers, immune agonists, and cellular therapies.

Limitations of Current Treatments

Despite achieving success in a subset of patients, checkpoint inhibitors often fail to control tumor growth. In addition, some patients do not tolerate checkpoint inhibitor therapy regimens. While checkpoint inhibitors work to block the mechanisms by which malignant cells evade immunological surveillance by anti-cancer T cells, they are less effective in patients who lack a favorable tumor microenvironment, expression of the inhibitory ligand, or sufficient tumor-specific antigens. For these patients, novel approaches to immunotherapy are needed that complement and/or enhance checkpoint inhibition. What is needed is a new class of agents that activate immune cells in the tumor microenvironment.

We believe that stimulation of the IL-2 and IL-15 pathways is an attractive approach to generate an anti-cancer immune response because it promotes the proliferation and activation of both CD8+ effector T cells and NK cells. Recombinant human IL-2, or aldesleukin, is a proven therapy and is approved for the treatment of adults with metastatic RCC or metastatic melanoma. However, significant toxicity has resulted in multiple boxed warnings in the labeling, including a requirement that administration occur in the hospital under supervision of an experienced physician. As a result of these toxicities, aldesleukin is not frequently used clinically. In addition, aldesleukin has a relatively modest rate of durable remissions, potentially because it preferentially stimulates the proliferation of regulatory T cells, which can inhibit the antitumor response. We believe there is a clear clinical need for an agent that stimulates an immunological response to cancer with greater selectivity and less toxicity than aldesleukin.

Ongoing Clinical Development

NL-201 is currently being evaluated in a Phase 1 clinical trial in advanced solid tumors. The Phase 1 clinical trial is planned to enroll up to 120 patients with advanced, relapsed, or refractory solid tumors. Patients will receive monotherapy, intravenous NL-201 and may continue treatment until disease progression. The trial is assessing safety, pharmacokinetics, pharmacodynamics, immunogenicity, and antitumor activity. When the recommended dose and schedule are determined, we expect to enroll indication-specific expansion cohorts of patients with renal cell carcinoma and melanoma. The trial is being conducted at multiple sites in North America and Australia.

In addition to our ongoing Phase 1 clinical trial of NL-201 for advanced solid tumors, we plan to initiate a Phase 1 clinical trial of NL-201 in hematological malignancies in 2022. NL-201 has also shown potential for enhanced antitumor activity in preclinical studies when combined with other therapies such as checkpoint inhibitors, CAR-T cell therapy, and tumor-targeting antibodies. On January 10, 2022, we announced a clinical collaboration with Merck to evaluate NL-201 in combination with KEYTRUDA® (pembrolizumab). We plan to amend the ongoing solid tumor trial in order to add a pembrolizumab combination arm with up to an additional 132 patients.

UW License Agreement

On July 8, 2019, Neoleukin Therapeutics, Inc., or Former Neoleukin, entered into an Exclusive License Agreement with the University of Washington, or UW, under which UW (on behalf of itself and Stanford University) granted us an exclusive worldwide license under certain patent rights, to make, have made, use, offer to sell, sell, offer to lease or lease, import, export or otherwise offer to dispose of licensed products in all fields of use, and a nonexclusive worldwide license to use certain know-how. The foregoing licenses may be sublicensed by us without UW's consent, subject to certain limited conditions. We assumed the benefits and obligations of the Exclusive License Agreement in connection with the completion of the merger of Former Neoleukin into the Company. The Exclusive License Agreement was amended effective as of July 24, 2020 to, among other things, (i) add a jointly owned patent application family directed to *de novo* cytokine antagonists to the agreement, (ii) specify royalties, milestone payments and sublicense consideration payments payable by Neoleukin for licensed products under certain patent rights related to the jointly owned patent application, (iii) specify the term for achievement of performance milestones for licensed products under certain patents rights related to the jointly owned patent application, and (iv) terminate UW's right to participate in equity financings. The Exclusive License Agreement was amended a second time, effective as of December 15, 2021 to, among other things, add a second jointly owned patent application family directed to *de novo* cytokine antagonists to the agreement subject to the same terms of the first jointly owned patent application family.

As consideration for the licensed rights, Former Neoleukin issued shares of common stock to UW, representing five percent of its fully-diluted capitalization on the date on which the Exclusive License Agreement was executed. Additionally, we are required to pay UW: (i) an annual maintenance fee starting in January 2022 (but excluding any year in which minimum annual royalties are paid); (ii) up to $875,000 in combined development and regulatory milestone payments with respect to each distinct class of licensed product; (iii) up to $10.0 million in combined commercial milestone payments based on cumulative net sales of licensed products within each distinct class of licensed product; (iv) a low single digit royalty on net sales of licensed products sold by us and our sublicensees, which may be subject to reductions, and subject to minimum annual royalty payments following the first commercial sale of a licensed product; (v) a certain percentage of any sublicense consideration (other than royalties) we receive from sublicensees, ranging from 50% to low single digit percentages based on the stage of development at the time the sublicense is executed; and (vi) a certain percentage of consideration we receive from an acquisition of us or our assets, ranging from 50% to zero based on the stage of development at the relevant time. We are obligated to pay royalties on a country-by-country basis until the expiration of the last valid claim within the licensed patent rights in such country.

The Exclusive License Agreement will expire upon the expiration of the last valid claim within the licensed patent rights. We may terminate the Exclusive License Agreement upon prior written notice to UW. UW may terminate the Exclusive License Agreement by giving a specified number of days' notice if we permanently cease operations, become insolvent or similar, or if we challenge the validity of the licensed patent rights. In addition, UW may terminate the Exclusive License Agreement for material breach that is not cured within a specified number of days, which cure period is to be at least doubled if we are proceeding diligently to cure the default.

Other Research Programs

Beyond our initial focus on NL-201, our research team is working on further applying *de novo* protein design principles to develop therapeutics to address significant unmet medical needs in immuno-oncology, inflammation, and autoimmunity. Our research is powered by our Neoleukin platform, which is our computational framework for developing highly selective, hyper-stable *de novo* immunomodulatory proteins. Beyond NL-201, we are developing targeted and conditionally active IL-2/IL-15 mimetics, as well as cytokine mimetic programs for other oncology targets. Our research team is also actively applying our Neoleukin platform to generate *de novo* receptor agonist and antagonist candidates against multiple targets of interest for inflammatory and autoimmune indications. As we validate additional candidates, they will enter our preclinical pipeline.

Due to the COVID-19 pandemic, we investigated the application of our *de novo* protein technology to prevent or treat SARS-CoV-2 virus infection, and, in November 2020, we announced the publication of our scientific work in the journal *Science* detailing the creation of NL-CVX1, a *de novo* protein decoy that is specifically designed to block infection of SARS-CoV-2, the virus which causes the COVID-19 disease. Our findings demonstrated that NL-CVX1 blocks infection of human cells in vitro, even when a high viral burden is used. Furthermore, intranasal administration of NL-CVX1 protected Syrian hamsters from a lethal dose of SARS-CoV-2. In June 2021, in response to the evolving COVID-19 therapeutic landscape, including the widespread availability of effective vaccines, we suspended plans to advance this research program into clinical trials.

Intellectual Property

Our intellectual property strategy is centered around robust protection of our pipeline molecules and enabling technologies. We have licensed rights to patents and patent applications stemming from provisional patent applications that our scientific co-founders authored while they were employees at UW. We have also licensed rights to two provisional patent applications that we jointly own with UW. These patents and patent applications, as applicable, include disclosure and claims encompassing our NL-201 product candidate, the composition of matter of key molecule families, as well as methods of using the computational algorithms that form the basis of our Neoleukin platform. We have secured an exclusive license from UW to develop and commercialize products covered by these patents and patent applications. For NL-201 and related technology, two U.S. patents have issued and will expire in 2039, absent any patent term adjustments or extensions. A third U.S. patent has issued directed to certain targeted Il-2/IL-15 mimetics which will expire in 2039, absent any patent term adjustments or extensions. Additional patent applications are pending in the United States and world-wide. Any patents that may issue from these patent applications in-licensed from UW are expected to expire in 2039, absent any patent term adjustments or extensions. As our product candidate and other programs advance through research and development, we expect to seek to identify and protect new inventions, and we have filed applications on new inventions such as methods of administration and combination therapies.

Also, through our research efforts, we anticipate generating intellectual property covering novel compounds and improvements on existing molecules. We expect that patents that result from this new research will remain Neoleukin's exclusive property, except to the extent jointly developed with third parties. In addition, our research team is extending and enhancing our computational technology and capabilities. We intend to protect improvements to the Neoleukin platform through a combination of new patent filings and/or the maintenance of trade secrets, as appropriate. We file U.S. non-provisional applications and PCT applications that claim the benefit of the priority date of earlier filed provisional applications, when appropriate. The PCT system allows a single application to be filed within 12 months of the original priority date of the patent application, and to designate all of the 153 PCT member states in which national patent applications can later be pursued based on the international patent application filed under the PCT. The PCT searching authority performs a patentability search and issues a non-binding patentability opinion which can be used to evaluate the chances of success for the national applications in foreign countries prior to having to incur the filing fees. Although a PCT application does not issue as a patent, it allows the applicant to seek protection in any of the member states through national-phase applications. At the end of the period of 2 1/2 years from the first priority date of the patent application, separate patent applications can be pursued in any of the PCT member states either by direct national filing or, in some cases by filing through a regional patent organization, such as the European Patent Organization. The PCT system delays expenses, allows a limited evaluation of the chances of success for national/regional patent applications and enables substantial savings where applications are abandoned within the first 2 1/2 years of filing.

We intend to pursue patent issuance and protection in key commercial markets where we expect significant product sales may occur.

Competition

The biotechnology and pharmaceutical industries are characterized by rapid evolution of technologies, fierce competition, and strong defense of intellectual property. While we believe that our Neoleukin platform and our knowledge, experience, and scientific resources provide us with competitive advantages going forward, we face competition from major pharmaceutical and biotechnology companies, academic institutions, governmental agencies, and public and private research institutions, among others.

The development of next-generation IL-2 or IL-15 agonists for cancer immunotherapy is an area of intense interest within the biotechnology industry. We are aware of several IL-2 or IL-15 agonists in various stages of clinical development, including engineered variants of IL-2 that attempt to improve on aldesleukin's narrow therapeutic window by inhibiting IL-2's natural high-affinity interaction with CD25 using traditional protein engineering approaches including steric inhibition and mutagenesis.

Many of our competitors, either alone or with strategic partners, have substantially greater financial, technical, and human resources than we do. Accordingly, our competitors may be more successful than us in obtaining approval for treatments and achieving widespread market acceptance, rendering our treatments obsolete or non-competitive. Accelerated merger and acquisition activity in the biotechnology and biopharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. These companies also compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites, and patient registration for clinical trials and acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. Our commercial opportunity could be substantially limited in the event that our competitors develop and commercialize products that are more effective, safer, less toxic, more convenient, or less expensive than our comparable products. In geographies that are critical to our commercial success, competitors may also obtain regulatory approvals before us, resulting in our competitors building a strong market position in advance of the entry of our products. We believe the primary factors determining the success of our programs will be the efficacy, safety, and convenience of our product candidates.

Manufacturing

We conduct manufacturing activities for the clinical development of our product candidates under individual purchase orders with third-party contract manufacturing organizations as we do not have a manufacturing facility and currently do not intend to develop one.

The FDA and other health authorities worldwide regulate and inspect equipment, facilities and processes used in manufacturing pharmaceutical products prior to approval. If we or our partners fail to comply with applicable requirements and conditions of product approval, the FDA and/or other global health authorities may seek sanctions, including fines, civil penalties, injunctions, suspension of manufacturing operations, operating restrictions, withdrawal of FDA and/or other global health authorities' approval, seizure or recall of products and criminal prosecution.

Commercial Operations

We do not currently have an organization for the sales, marketing and distribution of pharmaceutical products. We may rely on licensing and co-promotion agreements with strategic partners for the commercialization of our products in the United States and other territories. If we choose to build a commercial infrastructure to support marketing in the United States, such commercial infrastructure could be expected to include a targeted sales force supported by sales management, internal sales support, an internal marketing group and distribution support. To develop the appropriate commercial infrastructure internally, we would have to invest financial and management resources, some of which would have to be deployed prior to any confirmation that NL-201, or any of our other product candidates, will be approved.

Government Regulation

As a biopharmaceutical company that operates and anticipates seeking approval for pharmaceutical product candidates in the United States, we are subject to extensive regulation by the FDA and other federal, state, and local regulatory agencies. The Federal Food, Drug, and Cosmetic Act, or the FDC Act, and its implementing regulations set forth, among other things, requirements for the research, testing, development, manufacture, quality control, safety, effectiveness, approval, labeling, storage, record keeping, reporting, distribution, import, export, advertising and promotion of our products. Our pharmaceutical product candidates must be approved by the FDA before we can commence clinical trials or market those products in the United States.

Although the discussion below focuses on regulation in the United States, we conduct research activities and anticipate seeking approval for, and marketing of, our products in other countries and regions, such as Canada and Australia. Generally, our activities in other countries will be subject to regulation that is similar in nature and scope as that imposed in the United States, although there can be important differences. Additionally, some significant aspects of regulation in Europe are addressed in a centralized way through the European Medicines Agency, or EMA, but country-specific regulation remains essential in many respects. The process of obtaining regulatory marketing approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

FDA Approval Process

The FDA is the main regulatory body that controls pharmaceuticals in the United States, and its regulatory authority is based in the FDC Act. Pharmaceutical products are also subject to other federal and state statutes and regulations. Biological products used for the prevention, treatment, or cure of a disease or condition of a human being are subject to regulation under the FDC Act, except the section of the FDC Act which governs the approval of New Drug Applications, or NDAs. Biological products are approved for marketing under provisions of the Public Health Service Act, or PHSA, via a Biologics License Application, or BLA. However, the application process and requirements for approval of BLAs are very similar to those for NDAs. A failure to comply with any requirements during the product development, approval, or post-approval periods, may lead to administrative or judicial sanctions. These sanctions could include the imposition by the FDA or an institutional review board, or IRB, of a hold on clinical trials, refusal to approve pending marketing applications or supplements, withdrawal of approval, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties or criminal prosecution.

The steps required before a new biological product may be marketed in the United States generally include:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's Good Laboratory Practices regulations;
- submission to the FDA of an Investigational New Drug Application, or IND, which must become effective before human clinical trials may begin;
- approval by an IRB at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled clinical trials in accordance with federal regulations and with current good clinical practices, or GCPs, to establish the safety and efficacy of the investigational drug product for each targeted indication;
- development of manufacturing processes to ensure the product candidate's identity, strength, quality, purity, and potency;
- submission of BLA to the FDA;
- satisfactory completion of an FDA inspection of the manufacturing facilities at which the investigational product is produced to assess compliance with the FDA's Current Good Manufacturing Practice Regulations, or cGMP, and to assure that the facilities, methods and controls are adequate;
- satisfactory completion of FDA inspection of investigator sites; and
- FDA review and approval of the BLA.

With the enactment of the Biologics Price Competition and Innovation Act of 2009, or BPCIA, an abbreviated pathway for the approval of biosimilar and interchangeable biological products was created. The abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as interchangeable based on its similarity to an existing reference product. Notwithstanding minor differences in clinically inactive components, biosimilarity sufficient to reference a prior FDA-approved product requires a high similarity to the reference product and no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, potency, mechanism of action, conditions of use, route of administration, and dosage formulation. Biosimilarity must be shown through analytical studies, animal studies, and at least one clinical trial, absent a waiver by the FDA.

Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after licensure date of the reference product licensed under a BLA. No application for a biosimilar can be submitted for four years from the licensure date of the reference product. However, certain changes and supplements to an approved BLA, and subsequent applications filed by the same sponsor, manufacturer, licensor, predecessor in interest, or other related entity do not qualify for the 12-year exclusivity period.

Preclinical tests include laboratory evaluation of product chemistry, formulation, and toxicity, as well as animal trials to access the characteristics and potential safety and efficacy of the product. The conduct of the preclinical tests must comply with federal regulations and requirements, including Good Laboratory Practices. The results of preclinical testing are submitted to the FDA as part of an IND along with other information, including information about product chemistry, manufacturing and controls, and a proposed clinical trial protocol. Long-term preclinical tests, such as tests of reproductive toxicity and carcinogenicity in animals, may continue after the IND is submitted. A 30-day waiting period after the submission of each IND is required prior to the commencement of clinical testing in humans. If the FDA has neither commented on nor questioned the IND within this 30-day period, the clinical trial proposed in the IND may begin. Clinical trials involve the administration of the investigational drug to patients under the supervision of qualified investigators following GCPs, an international standard meant to protect the rights and health of patients and to define the roles of clinical trial sponsors, administrators and monitors. Clinical trials must be conducted: (i) in compliance with federal regulations; (ii) in compliance with GCPs, an international standard meant to protect the rights and health of patients and to define the roles of clinical trial sponsors, administrators, and monitors; as well as (iii) under protocols that detail the parameters to be used in monitoring safety, and the efficacy criteria to be evaluated. Each protocol involving testing on U.S. patients and subsequent protocol amendments must be submitted to the FDA as part of the IND.

The FDA may order the temporary or permanent discontinuation of a clinical trial at any time, or impose other sanctions, if it believes that the clinical trial either is not being conducted in accordance with FDA regulations or presents an unacceptable risk to the clinical trial patients. The trial protocol and informed consent information for patients in clinical trials must also be submitted to an IRB for approval. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions if it believes that the patients are subject to unacceptable risk. In some cases, clinical trials are overseen by an independent group of qualified experts organized by the trial sponsor, for example, the data safety monitoring board, or DSMB. The suspension or termination of development can occur during any phase of clinical trials if it is determined that the participants or patients are being exposed to an unacceptable health risk.

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

- *Phase 1* — Phase 1 includes the initial introduction of an investigational drug into humans. Phase 1 clinical trials may be conducted in patients with the target disease or condition or healthy volunteers. These trials are designed to evaluate the safety, metabolism, pharmacokinetics and pharmacologic actions of the investigational drug in humans, the side effects associated with increasing doses, and if possible, to gain early evidence on effectiveness. During Phase 1 clinical trials, sufficient information about the investigational product's pharmacokinetics and pharmacological effects may be obtained to permit the design of Phase 2 clinical trials.
- *Phase 2* — Phase 2 includes controlled clinical trials conducted to evaluate the effectiveness of the investigational product for a particular indication(s) in patients with the disease or condition under study, to determine dosage tolerance and optimal dosage, and to identify possible adverse side effects and safety risks associated with the drug. Phase 2 clinical trials are typically well-controlled, closely monitored, and conducted in a limited patient population.
- *Phase 3* — Phase 3 clinical trials are controlled clinical trials conducted in an expanded patient population at geographically dispersed clinical trial sites. They are performed after preliminary evidence suggesting effectiveness of the investigational product has been obtained and are intended to further evaluate dosage, clinical effectiveness and safety, to establish the overall benefit-risk relationship of the product, and to provide an adequate basis for product approval. In most cases, the FDA requires two adequate and well-controlled Phase 3 clinical trials to demonstrate the efficacy of the drug. A single Phase 3 trial may be sufficient in rare instances including (1) where the study is a large multicenter trial demonstrating internal consistency and a statistically very persuasive finding of a clinically meaningful effect on mortality, irreversible morbidity or prevention of a disease with a potentially serious outcome and confirmation of the result in a second trial would be practically or ethically impossible or (2) when in conjunction with other confirmatory evidence.

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

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, a BLA is submitted to the FDA to request market approval for the product in specified indications. The BLA must include the results of all preclinical, clinical, and other testing and a compilation of data relating to the product's pharmacology, chemistry, manufacturing, and controls. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and effectiveness of the investigational drug product to the satisfaction of the FDA. The cost of preparing and submitting a BLA is substantial. The submission of most BLAs is additionally subject to a substantial user fee; there may be some instances in which the user fee is waived.

The FDA will initially review the BLA for completeness before it accepts the BLA for filing. The FDA has 60 days from its receipt of a BLA to determine whether the application will be accepted for filing based on the Agency's threshold determination that it is sufficiently complete to permit substantive review. After the BLA submission is accepted for filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of BLAs. For a new molecular entity, or NME, that is classified as a standard review product, FDA's goal is to review the BLA within ten months of the date the FDA files the BLA; an application for an NME that is classified as a priority review product has a goal for review of six months from the date the FDA files the BLA. A BLA can be classified for priority review when the FDA determines the biologic product has the potential to treat a serious or life-threatening condition and, if approved, would be a significant improvement in safety or effectiveness compared to available therapies. The FDA can extend the review process by three or more additional months to consider certain late-submitted information or information intended to clarify information already provided in the submission.

The FDA does not always achieve its performance goal and its review of BLAs can take significantly longer. The FDA reviews the BLA to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMP. The FDA may refer applications for novel biological products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving a BLA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and are adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect the sponsor and one or more clinical sites to assure compliance with GCPs. After the FDA evaluates the BLA and the manufacturing facilities, it issues either an approval letter or a complete response letter. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing, time or information in order for the FDA to reconsider the application. If, or when, those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the BLA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. The approval process is lengthy and difficult and notwithstanding the submission of any requested additional information, the FDA ultimately may refuse to approve an BLA if applicable regulatory criteria are not satisfied or if the FDA believes additional clinical data or other data and information are required. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than a company interprets the same data.

An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. FDA's approval of a product may be significantly limited to specific disease and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings, or precautions be included in the product labeling. In addition, as a condition of BLA approval, the FDA may require a risk evaluation and mitigation strategy, or REMS, to help ensure that the benefits of the drug outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, restricted distribution, special monitoring, and the use of patient registries. The requirement for REMS can materially affect the potential market and profitability of the drug. Moreover, product approval may require substantial post-approval testing and surveillance to monitor the drug's safety or efficacy. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

Changes to some of the conditions established in an approved application, including changes in indications, labeling, manufacturing processes or facilities, or modification to a REMS, require submission and FDA approval of a new BLA or BLA supplement before the change can be implemented. A BLA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing BLA supplements as it does in reviewing BLAs. Furthermore, should new safety information arise, additional testing, product labeling, or FDA notification may be required.

Sponsors of clinical trials of FDA-regulated products, including biological products, are required to register and disclose certain clinical trial information on the website www.clinicaltrials.gov. Information related to the product, patient population, phase of investigation, trial sites and investigators, and other aspects of a clinical trial are then made public as part of the registration. Sponsors are also obligated to disclose the results of their clinical trials after completion. Disclosure of the results of clinical trials can be delayed in certain circumstances for up to two years after the date of completion of the trial. Competitors may use this publicly available information to gain knowledge regarding the progress of clinical development programs as well as clinical trial design.

Pediatric Information

Under the Pediatric Research Equity Act, or PREA, BLAs or supplements to BLAs must contain data to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant full or partial waivers, or deferrals, for submission of data. Unless otherwise required by regulation, PREA does not apply to any product with orphan product designation except a product with a new active ingredient that is a molecularly targeted cancer product intended for the treatment of an adult cancer and directed at a molecular target determined by FDA to be substantially relevant to the growth or progression of a pediatric cancer.

Fast Track Designation, Accelerated Approval, and Priority Review

A sponsor may seek approval of its product candidate under programs designed to accelerate the FDA's review and approval of BLAs. For example, Fast Track Designation may be granted to a drug intended for treatment of a serious or life-threatening disease or condition that has potential to address unmet medical needs for the disease or condition. The key benefits of fast track designation are more frequent interactions with the FDA and rolling review (submission of portions of an application before the complete marketing application is submitted).

Under Fast Track and the accelerated approval program, the FDA may approve a BLA on the basis of either 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. Post-marketing studies or completion of ongoing studies after marketing approval are required to verify the drug's clinical benefit in relationship to the surrogate endpoint or ultimate outcome in relationship to the clinical benefit.

Based on results of the Phase 3 clinical trial(s) submitted in a BLA, upon the request of an applicant, the FDA may grant the BLA a priority review designation, which sets the target date for FDA action on the application at eight months after the BLA submission. Priority review is granted where there is evidence that the proposed product would be a significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of a serious condition. If criteria are not met for priority review, the application is subject to the standard FDA review period of twelve months after NDA submission. Priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

Additional Controls for Biologics

To help reduce the increased risk of the introduction of adventitious agents, the PHSA emphasizes the importance of manufacturing controls for products whose attributes cannot be precisely defined. The PHSA also provides authority to the FDA to immediately suspend biologics licenses in situations where there exists a danger to public health, to prepare or procure products in the event of shortages and critical public health needs, and to authorize the creation and enforcement of regulations to prevent the introduction or spread of communicable diseases within the United States.

After a BLA is approved, the product may also be subject to official lot release as a condition of approval. As part of the manufacturing process, the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release by the FDA, the manufacturer submits samples of each lot of product to the FDA together with a release protocol showing a summary of the lot manufacturing history and the results of all of the manufacturer's tests performed on the lot. The FDA may also perform certain confirmatory tests on lots of some products, such as viral vaccines, before allowing the manufacturer to release the lots for distribution. In addition, the FDA conducts laboratory research related to the regulatory standards on the safety, purity, potency, and effectiveness of biological products. As with drugs, after approval of a BLA, biologics manufacturers must address any safety issues that arise, are subject to recalls or a halt in manufacturing, and are subject to periodic inspection after approval.

Post-Approval Regulations

After regulatory approval of a biologic is obtained, a company is required to comply with a number of post-approval requirements. For example, as a condition of approval of a BLA, 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, as a holder of an approved BLA, a company is required to report adverse reactions and production problems to the FDA, to provide updated safety and efficacy information, and to comply with requirements concerning advertising and promotional labeling for any of its products. Also, quality control and manufacturing procedures must continue to conform to cGMP after approval to assure and preserve the long-term stability of the drug or biological product. The cGMP requirements apply to all stages of the manufacturing process, including the production, processing, sterilization, packaging, labeling, storage and shipment of the drug product. The FDA periodically inspects manufacturing facilities to assess compliance with cGMP, which imposes extensive procedural and substantive record keeping requirements. In addition, changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon a company and any third-party manufacturers that a company may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our product candidates. Future FDA and state inspections may identify compliance issues at our facilities or at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct.

The FDA may withdraw a product approval if compliance with regulatory standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product or the failure to comply with applicable requirements may result in restrictions on a product, manufacturer or holder of an approved BLA, including withdrawal or recall of the product from the market or other voluntary, FDA-initiated or judicial action that could delay or prohibit further marketing. Further, the failure to maintain compliance with regulatory requirements may result in administrative or judicial actions, such as fines, warning or untitled letters, holds on clinical trials, product recalls or seizures, product detention or refusal to permit the import or export of products, refusal to approve pending applications or supplements, restrictions on marketing or manufacturing, injunctions or civil or criminal penalties.

After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA approval. Newly discovered or developed safety or effectiveness data may require changes to a product's approved labeling, including the addition of new warnings and contraindications, and may require the implementation of other risk management measures. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products under development.

Advertising and Promotion

The FDA and other federal regulatory agencies closely regulate the marketing and promotion of drugs through, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and promotional activities involving the Internet. A product cannot be commercially promoted before it is approved. After approval, product promotion cannot be false or misleading, and product claims must be adequately substantiated. Healthcare providers are permitted to prescribe drugs for "off-label" uses—that is, uses not approved by the FDA and therefore not described in the drug's labeling—because the FDA does not regulate the practice of medicine. However, FDA regulations impose stringent restrictions on manufacturers' communications regarding off-label uses. Broadly speaking, a manufacturer may not promote a drug for off-label use, but may engage in non-promotional, balanced communication regarding off-label use under specified conditions. Failure to comply with applicable FDA requirements and restrictions in this area may subject a company to adverse publicity and enforcement action by the FDA, the U.S. Department of Justice, or DOJ, or the Office of the Inspector General of the Department of Health and Human Services, or HHS, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products.

Enforcement

During all phases of development (pre- and post-marketing), failure to comply with applicable regulatory requirements may result in administrative or judicial sanctions. These sanctions could include the FDA's imposition of a clinical hold on trials, refusal to approve pending applications, withdrawal of an approval, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, product detention or refusal to permit the import or export of products, injunctions, fines, civil penalties or criminal prosecution. Any agency or judicial enforcement action could have a material adverse effect on us.

Comparable European and Other International Government Regulation

In addition to FDA regulations in the United States, we will be subject to a variety of comparable regulations in other jurisdictions governing, among other things, clinical trials 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 trials or marketing of the product in those countries.

Some countries outside of the United States have a similar process that requires the submission of a clinical trial application, or CTA, much like the IND prior to the commencement of human clinical trials. In Europe, for example, a CTA must be submitted to each country's national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the CTA is approved in accordance with a country's requirements, clinical trial development may proceed. To obtain regulatory approval to commercialize a new drug under European Union regulatory systems, we must submit a marketing authorization application, or MAA. The MAA is similar to the NDA, with the exception of, among other things, country-specific document requirements and environmental impact assessments.

For other countries outside of the European Union, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, again, the clinical trials are conducted in accordance with GCPs and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

Australia

Conducting clinical trials for therapeutic drug candidates in Australia is subject to regulation by Australian governmental entities. Approval for inclusion in the Australian Register of Therapeutic Goods, or the ARTG, is required before a pharmaceutical drug product may be marketed in Australia.

Typically, the process of obtaining approval of a new therapeutic drug product for inclusion in the ARTG requires compilation of clinical trial data. Clinical trials conducted using "unapproved therapeutic goods" in Australia, being those which have not yet been evaluated by the Therapeutic Goods Administration, or TGA, for quality, safety and efficacy must occur pursuant to either the Clinical Trial Notification, or CTN, or Clinical Trial Exemption, or CTX, process.

The CTN process broadly involves:

- completion of pre-clinical laboratory and animal testing;
- submission to a Human Research Ethics Committee, or the HREC, of all material relating to the proposed clinical trial, including the trial protocol. The TGA does not review any data relating to the clinical trial;
- the institution or organization at which the trial will be conducted, referred to as the "Approving Authority" gives the final approval for the conduct of the trial at the site, having due regard to the advice from the HREC; and
- CTN trials cannot commence until the trial has been notified to the TGA.

Under the CTX process:

- a sponsor submits an application to conduct a clinical trial to the TGA for evaluation and comment; and
- a sponsor cannot commence a CTX trial until written advice has been received from the TGA regarding the application and approval for the conduct of the trial has been obtained from an ethics committee and the institution at which the trial will be conducted.

In each case, it is required that:

- adequate and well-controlled clinical trials demonstrate the quality, safety and efficacy of the therapeutic product;
- evidence is compiled which demonstrates that the manufacture of the therapeutic drug product complies with the principles of cGMP;
- manufacturing and clinical data is derived to submit to the Australian Committee on Prescription Medicines, which makes recommendations to the TGA as to whether or not to grant approval to include the therapeutic drug product in the ARTG; and
- an ultimate decision is made by the TGA whether to include the therapeutic drug product in the ARTG.

Pre-clinical studies include laboratory evaluation of the therapeutic drug product as well as animal studies to assess the potential safety and efficacy of the drug. The results of the pre-clinical studies form part of the materials submitted to the investigators HREC in the case of a CTN trial and part of the application to the TGA in the case of a CTX trial.

Clinical trials involve administering the investigational product to healthy volunteers or patients under the supervision of a qualified principal investigator. The TGA has developed guidelines for a CTN. Under the CTN process, all material relating to the proposed trial is submitted directly to the HREC of each institution at which the trial is to be conducted. An HREC is an independent review committee set up under guidelines of the Australian National Health and Medical Research Council. The role of an HREC is to ensure the protection of rights, safety and well-being of human subjects involved in a clinical trial by, among other things, reviewing, approving and providing continuing review of trial protocols and amendments, and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects. The TGA is formally notified by submission of a CTN application but does not review the safety of the drug or any aspect of the proposed trial. The approving authority of each institution gives the final approval for the conduct of the clinical trial, having due regard to advice from the HREC. Following approval, responsibility for all aspects of the trial conducted under a CTN application remains with the HREC of each investigator's institution.

The standards for clinical research in Australia are set by the TGA and the National Health and Medical Research Council, and compliance with GCPs is mandatory. Guidelines, such as those promulgated by the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, or ICH, are required across all fields, including those related to pharmaceutical quality, nonclinical and clinical data requirements and study designs. The basic requirements for preclinical data to support a first-in- human study under ICH guidelines are applicable in Australia. Requirements related to adverse event reporting in Australia are similar to those required in other major jurisdictions.

Other Healthcare, Data Protection, and Privacy Laws and Compliance Requirements

In the United States, our activities are potentially subject to additional regulation and oversight under other healthcare laws by various federal, state and local authorities in addition to the FDA, including the Centers for Medicare & Medicaid Services, or CMS, other divisions of the HHS (e.g., the Office of Inspector General), the DOJ, and individual U.S. Attorney offices within the DOJ, and state and local governments. These laws include the federal Anti-Kickback Statute, which prohibits, among other things, any person or entity, from knowingly and willfully offering, paying, soliciting or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or in return for either the referral of an individual, or purchasing, leasing, ordering or arranging for the purchase, lease or order of any good, facility, item or service reimbursable, in whole or part, under Medicare, Medicaid or another federal healthcare program. The term remuneration has been interpreted broadly to include anything of value. The federal Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers, and formulary managers on the other. 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 and practices that involve remuneration that may be alleged to be intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. Our practices may not in all cases meet all of the criteria for protection under a statutory exception or regulatory safe harbor from federal Anti-Kickback Statute liability. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor, however, does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. In addition, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the Affordable Care Act, further strengthened these laws by amending the intent standard under the federal Anti-Kickback Statute and the criminal health care fraud statutes (discussed below), such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the Affordable Care Act codified case law 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 civil False Claims Act (discussed below).

Federal civil and criminal false claims laws, including the False Claims Act, and civil monetary penalties laws prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to, or approval by, the federal government, including the Medicare and Medicaid programs, or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government, including the Medicare and Medicaid programs. As a result of a modification made by the Fraud Enforcement and Recovery Act of 2009, a claim includes "any request or demand" for money or property presented to the U.S. government. Recently, several pharmaceutical and other healthcare companies have been prosecuted under these laws for 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 the product for off-label, and thus, non-covered, uses.In the United States, there are numerous federal and state laws and regulations governing data privacy of personal data and the collection, use, disclosure, and protection of health data, genetic data, consumer data, and children's data.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any money or property owned by, or under the control or custody of, any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up by trick, scheme or device, 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. Also, many states have similar fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

HIPAA was amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, implementing additional regulations and imposing requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes certain HIPAA standards directly applicable to business associates—independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also created four new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, some state laws may more broadly govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways from HIPPA/HITECH and may not have the same effect, thus complicating compliance efforts.

We may be subject to privacy and data security regulations and legal requirements in the United States, Europe, and throughout the world as it relates to collection, use, disclosure, and protection of personal information that may be broader than as is required under HIPAA or comparable state laws to HIPAA. Many of the state laws enable a state attorney general to bring actions and provide private rights of action to consumers as enforcement mechanisms. There is also heightened sensitivity around certain types of health data, which may be subject to additional protections. Compliance with these laws requires a flexible privacy framework as they are constantly evolving. Failure to comply with these laws and regulations could result in government enforcement actions and create liability for us (which could include civil and/or criminal penalties), private litigation, and/or adverse publicity. Federal regulators, state attorneys general, and plaintiffs' attorneys have been active in this space.

Also, as we become more dependent on information technologies to conduct our operations, cyber incidents, including deliberate attacks and attempts to gain unauthorized access to computer systems and networks, may increase in frequency and sophistication, and we may have legal duties to protect that information and, in the event of a security incident, report to affected individuals and government authority.

Other applicable federal, state, and foreign laws related to privacy and data protection, include, without limitation, the following:

- The Federal Trade Commission, or FTC, and state attorneys general enforce consumer protection laws that prohibit unfair and deceptive acts and practices, including Section 5 of the FTC Act, which creates standards for the collection, use, dissemination, and security of health-related and other non-health-related personal information. Individual states have comparable unfair and deceptive acts and practices statutes.
- The California Consumer Privacy Act, or CCPA, came into effect in January 2020 and places increased obligations on businesses, including by requiring covered companies to provide new disclosures to California consumers and provide such consumers certain data protection and privacy rights, including the ability to opt-out of certain sales of personal data. A ballot initiative from privacy rights advocates intended to augment and expand the CCPA called the California Privacy Rights Act, or CPRA, was passed in November 2020 and will take effect in January 2023 (with a look back to January 2022), and modifies the CCPA while also creating a new state agency that will be vested with authority to implement and enforce the CCPA and the CPRA.
- Several states have enacted consumer privacy laws that will take effect in 2023, including: (1) the Virginia Consumer Data Protection Act that gives new data protection rights to Virginia residents and imposes additional obligations on controllers and processors of personal data similar in scope to the CCPA; (2) the Colorado Privacy Act, which is set to take effect on July 1, 2023. As of January 2022, fourteen states have pending legislation under review relating to consumer privacy.
- Domestic laws in all 50 states require businesses to provide notice to customers whose personally identifiable information has been disclosed as a result of a data breach.

- European data protection laws will apply to any clinical trial programs we conduct or research collaborations we enter into in the European Economic Area, or the EEA, the United Kingdom, or the UK, or Switzerland. These include European Union, or EU, General Data Protection Regulation 2016/679, or GDPR, which applies extra-territorially and imposes onerous requirements on controllers (e.g., sponsors) and processors (e.g., contract research organizations, laboratories) of personal data, including, for example: (i) accountability and transparency requirements, and enhanced requirements for obtaining valid consent; (ii) obligations to consider data protection as any new products or services are developed and to limit the amount of personal data processed; (iii) obligations to comply with data protection rights of data subjects; and (iv) reporting of personal data breaches to the supervisory authority without undue delay (and no later than 72 hours). The GDPR and comparable UK and Swiss law also prohibits the international transfer of personal data from the EEA/UK/Switzerland to countries outside of those jurisdictions unless made to a country deemed to have adequate data privacy laws by the European Commission (or as applicable under UK/Swiss authority) or where a data transfer mechanism has been put in place. Further, the GDPR provides that countries in the EEA may establish their own laws and regulations further restricting the processing of certain personal data, including genetic data, biometric data, and health data.
- In Canada, the Personal Information Protection and Electronic Documents Act, or PIPEDA, and similar provincial laws may impose obligations with respect to processing personal information, including health-related information. PIPEDA requires companies to obtain an individual's consent when collecting, using or disclosing that individual's personal information.
- In Australia, the Privacy Act of 1988 is the primary federal legislation applying to protection of privacy in Australia, applicable to both private and public sectors at the Commonwealth level and outlines Data Subject's rights, and is supplemented by TGA (Therapeutic Goods Administration).

Additionally, the federal Physician Payments Sunshine Act within the Affordable Care Act, and its implementing regulations, require that certain manufacturers of drugs, devices, biological and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) report annually to CMS information related to certain payments or other transfers of value made or distributed to physicians, physician assistants, certain types of advance practice nurses and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians, physician assistants, certain types of advance practice nurses and teaching hospitals, and applicable manufacturers and group purchasing organizations to report annually certain ownership and investment interests held by physicians and their immediate family members and payments or other "transfers of value" to such physician owners and their immediate family members.

In order to distribute products commercially, we must comply with state laws that require the registration of manufacturers and wholesale distributors of pharmaceutical products in a state, including, in some states, manufacturers and distributors who ship products into the state even if such manufacturers or distributors have no place of business within the state. Some states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that require manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain. Several local, state and foreign governments have enacted legislation requiring pharmaceutical companies to, among other things, establish compliance programs, file periodic reports with the state or foreign government, make periodic public disclosures on sales, marketing, pricing, clinical trials and other activities, and/ or register their sales representatives, as well as to prohibit pharmacies and other healthcare entities from providing specified physician prescribing data to pharmaceutical companies for use in sales and marketing, and to prohibit other specified sales and marketing practices. In addition, our future commercial activities may also be subject to federal and state consumer protection and unfair competition laws.

If our operations are found to be in violation of any of the federal and state healthcare laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including without limitation, civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion from participation in government programs, such as Medicaid and Medicare, integrity obligations, injunctions, as well as reputational harm, administrative burdens, diminished profits and future earnings and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our products are sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

Coverage, Reimbursement, and Pricing

Significant uncertainty exists as to the coverage and reimbursement status of any drug products for which we obtain regulatory approval. In the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend, in part, on the extent that third-party payors provide coverage, and establish adequate reimbursement levels for such drug products. In the United States, third-party payors include federal healthcare programs, state healthcare programs, managed care providers, private health insurers, and other organizations. The process for determining whether a third-party payor will provide coverage for a drug product may be separate from the process for setting the price of a drug product or for establishing the reimbursement rate that such a payor will pay for the drug product. Third-party payors may limit coverage to specific drug products on an approved list, also known as a formulary, which might not include all of the FDA-approved drugs for a particular indication. Third-party payors are increasingly challenging the price, examining the medical necessity and reviewing the cost-effectiveness of drug products and medical services, in addition to questioning their safety and efficacy. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain FDA approvals. NL-201 or our future product candidates may not be considered medically necessary or cost-effective. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a drug product does not assure that other payors will also provide coverage for the drug product. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. If a drug product is reimbursed under a governmental healthcare program, such as Medicare, Medicaid or TRICARE, additional laws and program requirements will apply.

Different pricing and reimbursement schemes exist in other countries. In the European Union, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national healthcare systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed upon. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular product candidate to currently available therapies. Other member states allow companies to fix their own prices for drugs, but monitor and control company profits. The downward pressure on healthcare costs in general, particularly prescription drugs, has become more intense. As a result, increasingly high barriers are being erected to the entry of new products. The European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product, or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. We may face competition for our product candidates from lower-priced products in foreign countries that have placed price controls on pharmaceutical products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, an increasing emphasis on managed care in the United States has increased and will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Healthcare Reform

In March 2010, President Obama signed the Affordable Care Act, which substantially changed healthcare financing and the delivery by both governmental and private insurers, and significantly impacted the pharmaceutical industry. The Affordable Care Act impacts existing government healthcare programs and requires the development of new programs. For example, the Affordable Care Act provides for Medicare payment for performance initiatives and improvements to the physician quality reporting system and feedback program.

Among the Affordable Care Act's provisions of importance to the pharmaceutical industry are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biological products apportioned among these entities according to their market share in some government healthcare programs, that began in 2011;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program, retroactive to January 1, 2010, 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 AMP;
- expansion of healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;

- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer point-of-sale discounts, now 7% off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to 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;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- a requirement to report annually specified financial arrangements with physicians and teaching hospitals, as defined in the Affordable Care Act and its implementing regulations, including reporting information related to "payments or other transfers of value" made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, and applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by physicians (as defined above) and their immediate family members and payments or other "transfers of value" to such physician owners and their immediate family members;
- a requirement to annually report drug samples that manufacturers and distributors provide to licensed practitioners, pharmacies of hospitals and other healthcare entities; and
- a Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. On August 2, 2011, the President signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend proposals in spending reductions to Congress. The Joint Select Committee did not achieve its targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, triggering the legislation's automatic reductions to several government programs. These reductions include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments, will stay in effect through 2029 unless additional Congressional action is taken. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, 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. Furthermore, there has been heightened governmental scrutiny recently over the manner in which manufacturers set prices for their marketed products. For example, there have been several recent Congressional inquiries and proposed bills designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. These new laws and initiatives may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on our future customers and accordingly, our financial operations.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of Affordable Care Act, as well as efforts by the Trump administration to repeal or replace certain aspects of the Affordable Care Act, or ACA. Since January 2017, President Trump signed two executive orders and other directives designed to delay, circumvent, or loosen certain requirements mandated by the Affordable Care Act. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed repeal legislation, the Tax Cuts and Jobs Act of 2017 includes 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". In November 2020, the United States Supreme Court held oral arguments on the Fifth Circuit U.S. Court of Appeals decision that held that the individual mandate is unconstitutional. It is uncertain how the United States Supreme Court will rule on this case or how healthcare measures of the Biden administration will impact the ACA and our business. Congress may consider other legislation to repeal or replace elements of the ACA.

We cannot predict what healthcare reform initiatives may be adopted in the future. However, we anticipate that Congress, state legislatures, and third-party payors may continue to review and assess alternative healthcare delivery and payment systems and may in the future propose and adopt legislation or policy changes or implementations effecting additional fundamental changes in the healthcare delivery system. We also expect ongoing initiatives to increase pressure on drug pricing. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payors.

Anti-Corruption Legislation

The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with accounting provisions requiring us to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Human Capital Resources

Employees

As of December 31, 2021, we had 91 employees, of whom 25 hold Ph.D. degrees or M.D. degrees and all of which are full time employees. We have no collective bargaining agreements with our employees and have not experienced any work stoppages. We believe that relations with our employees are good.

Diversity & Inclusion

We are committed to creating and maintaining a workplace free from discrimination or harassment on the basis of color, race, sex, national origin, ethnicity, religion, age, disability, sexual orientation, gender identification or expression or any other status protected by applicable law. Our management team and employees are expected to exhibit and promote honest, ethical and respectful conduct in the workplace. All of our employees must adhere to a code of conduct that sets standards for appropriate behavior and are required annual training to prevent, identify, report, and stop any type of discrimination and harassment. Recruitment, hiring, development, training, compensation, and advancement at the Company is based on qualifications, performance, skills and experience without regard to gender, race and ethnicity.

Competitive Pay & Benefits

We strive to provide pay, comprehensive benefits, and services that help meet the varying needs of our employees. Our total rewards package includes competitive pay; comprehensive healthcare benefits package for employees, with family member healthcare benefits; paid leave and paid holidays; family medical leave and flexible work schedules. In addition, we offer every full-time employee the benefit of equity ownership in the company through stock option grants and our employee stock purchase plan. We also sponsor a 401(k) plan that allows full-time employees to contribute a portion of their salary, subject to statutory limits. We make matching cash contributions up to a pre-defined annual maximum contribution per employee per year.

Employee Development & Training

We focus on attracting, retaining, and cultivating talented individuals. We emphasize employee development and training by providing access to in house development and training sessions. Employees are encouraged to attend scientific, clinical, and technological meetings and conferences and have access to the broad resources they need to be successful.

Safety

The safety, health and wellness of our employees is a top priority. In response to the COVID-19 pandemic, we have implemented safety protocols, which are reviewed regularly and revised from time to time based on local and federal guidelines. Since March of 2020, we have made accommodations, including reducing the number and density of people in our facilities, requirements for the wearing of masks and for social distancing, increased cleaning procedures and readily available hand sanitizer. These protocols are designed to comply with health and safety standards as required by federal, state, and local government agencies, taking into consideration guidelines of the Centers for Disease Control and Prevention and other public health authorities. In addition, we have provided work-at-home arrangements for employees who are able to do so and require that employees be fully vaccinated and asymptomatic if they are working on site.

Corporate Information

On August 8, 2019, Former Neoleukin, completed its merger with Aquinox Pharmaceuticals, Inc., or Aquinox, in accordance with the terms of the Agreement and Plan of Merger dated August 5, 2019, or the Merger Agreement by and among Aquinox, Former Neoleukin and Apollo Sub, Inc., a wholly-owned subsidiary of Aquinox. Pursuant to the Merger Agreement, Apollo Sub, Inc. merged with and into Former Neoleukin, with Former Neoleukin surviving the Merger as a wholly-owned subsidiary of Aquinox, referred to herein as the Merger. Upon completion of the Merger, Aquinox was renamed Neoleukin Therapeutics, Inc. and Former Neoleukin was renamed Neoleukin Corporation.

On July 31, 2020, we sold all issued and outstanding capital stock of our Canadian subsidiary, Aquinox Pharmaceuticals (Canada) Inc., or Aquinox Canada, to an unrelated third party. On December 31, 2020, Neoleukin Corporation was merged into Neoleukin Therapeutics, Inc. As a result of these transactions, we have consisted of a single operating company since December 31, 2020.

We make available free of charge on our website our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports as soon as reasonably practicable after we electronically file or furnish such materials to the Securities and Exchange Commission, or SEC. The reports are also available at www.sec.gov. Our website address is www.neoleukin.com. The information contained on, or that can be accessed through, our website is not part of, and is not incorporated by reference into, this report.

Neoleukin and our other trademarks, service marks, or trade names appearing in this Annual Report on Form 10-K are the property of Neoleukin Therapeutics, Inc. Other trademarks, service marks, or trade names appearing in this Annual Report on Form 10-K are the property of their respective owners.

Item 1A. Risk Factors

Summary of Risk Factors

An investment in our common stock involves various risks, and prospective investors are urged to carefully consider the matters discussed in the section titled "Risk Factors" prior to making an investment in our common stock. These risks include, but are not limited to, the following:

- We will require substantial additional capital to finance our operations which may not be available to us on acceptable terms, or at all. If we fail to obtain necessary financing, we may be unable to complete the development and potential commercialization of our product candidates.
- We have incurred significant losses in every quarter since our inception and anticipate that we will continue to incur significant losses in the future.
- We have a limited operating history, which may make it difficult for you to evaluate the success of our business to date and to assess our future viability.
- We currently have no source of product revenue and may never become profitable.
- Our product candidates are in early stages of development and may fail in development or suffer delays that materially and adversely affect their commercial viability. If we are unable to complete development of, or commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.
- Our business is heavily dependent on the success of our Neoleukin platform and of our most advanced product candidate, NL-201. Existing and future preclinical studies and clinical trials of our product candidates may not be successful, and if we are unable to commercialize these product candidates or experience significant delays in doing so, our business will be materially harmed.
- Our clinical trials or those of any future collaborators may reveal significant adverse events not seen in our preclinical studies and may result in a safety profile that could inhibit regulatory approval or market acceptance of any of our product candidates.
- If we do not achieve our projected development goals in the timeframes we announce and expect, the commercialization of our products may be delayed and, as a result, our stock price may decline.
- Our approach to the discovery and development of our therapeutic treatments is based on *de novo* protein design technology which is unproven and may not result in marketable products.
- We rely on and expect to continue to rely on third parties to conduct certain of our preclinical studies and clinical trials. If those third parties do not perform as contractually required, fail to satisfy legal or regulatory requirements, miss expected deadlines or terminate the relationship, our development program could be delayed with potentially material and adverse effects on our business, financial condition, results of operations, and prospects.
- We rely on and expect to continue to rely on third-party manufacturers and suppliers to supply components of our product candidates. The loss of our third-party manufacturers or suppliers, or our or their failure to comply with applicable regulatory requirements or to supply sufficient quantities at acceptable quality levels or prices, or at all, would materially and adversely affect our business.
- The continued impact of the novel strain of coronavirus, SARS-CoV-2, which causes COVID-19 disease, could adversely impact our business, including our preclinical development activities and clinical trial activities.
- If we are not able to obtain, maintain, and enforce patent protection and other intellectual property rights for our product candidates, our Neoleukin platform technology, or other proprietary technologies we may develop, development and commercialization of our product candidates may be adversely affected.

Risk Factors

You should carefully consider the following risk factors, in addition to the other information contained in this Annual Report on Form 10-K and the information incorporated by reference herein. If any of the events described in the following risk factors occurs, our business, operating results and financial condition could be adversely affected. This Annual Report on Form 10-K also contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in the forward-looking statements as a result of factors that are described below and elsewhere in this Annual Report on Form 10-K.

Risks Related to Our Financial Position and Capital Needs

We will require substantial additional capital to finance our operations which may not be available to us on acceptable terms, or at all. If we fail to obtain necessary financing, we may be unable to complete the development and potential commercialization of our product candidates.

The development of biopharmaceutical product candidates is capital-intensive. If our product candidates enter and advance through preclinical studies and clinical trials, we will need substantial additional funds to expand or create our development, regulatory, manufacturing, marketing, and sales capabilities. We have used substantial funds to develop our technology and product candidates and will require significant funds to conduct further research and development and preclinical testing and clinical trials of our product candidates, to seek regulatory approvals for our product candidates and to manufacture and market products, if any, which are approved for commercial sale. In addition, we expect to continue incurring costs associated with operating as a public company.

Preclinical studies and clinical trials for our product candidates will require substantial funds to complete. As of December 31, 2021, we had approximately $142.5 million in cash and cash equivalents. We expect to incur substantial expenditures in the foreseeable future as we seek to advance NL-201 and any future product candidates through preclinical and clinical development, the regulatory approval process and, if approved, commercial launch activities. Based on our current operating plan, we believe that our available cash and cash equivalents will be sufficient to fund our operating expenses and capital expenditure requirements into the second half of 2023. However, our future capital requirements and the period for which we expect our existing resources to support our operations, fund expansion, develop new or enhanced products, or otherwise respond to competitive pressures, may vary significantly from what we expect, and we may need to seek additional funds sooner than planned. Our monthly spending levels vary based on new and ongoing research and development and other corporate activities. Because the length of time and activities associated with successful research and development of our product candidates is highly uncertain, we are unable to estimate the actual funds we will require for development and any marketing and commercialization activities for approved products. Our future funding requirements, both near and long-term, will depend on many factors, including, but not limited to:

- the timing, cost and progress of preclinical and clinical development activities;
- the number and scope of preclinical and clinical programs we decide to pursue;
- the progress of the development efforts of parties with whom we have entered or may in the future enter into collaborations and/or research and development agreements;
- the timing and amount of milestone and other payments we may receive or make under our collaboration agreements;
- our ability to maintain our current licenses and to establish new collaboration arrangements;
- the costs involved in prosecuting and enforcing patent and other intellectual property claims;
- the costs of manufacturing our product candidates by third parties;
- the cost of regulatory submissions and timing of regulatory approvals;
- the potential delays in our preclinical studies, our development programs and our ongoing and planned clinical trial activities due to the effects of the COVID-19 pandemic;
- the cost of commercialization activities if our product candidates or any future product candidates are approved for sale, including marketing, sales and distribution costs; and
- our efforts to enhance operational systems and hire additional personnel, including personnel to support development of our product candidates.

If we are unable to obtain funding on a timely basis or on acceptable terms, we may have to delay, reduce or terminate our research and development programs and preclinical studies or clinical trials, limit strategic opportunities or undergo reductions in our workforce or other corporate restructuring activities. We do not expect to realize revenue from sales of commercial products or royalties from licensed products in the foreseeable future, if at all, and, in no event, before our product candidates are clinically tested, approved for commercialization and successfully marketed.

We will be required to seek additional funding in the future and currently intend to do so through additional collaborations and/or licensing agreements, public or private equity offerings or debt financings, credit or loan facilities, or a combination of one or more of these funding sources. If we raise additional funds by issuing equity securities, our stockholders will suffer dilution and the terms of any financing may adversely affect the rights of our stockholders. In addition, as a condition to providing additional funds to us, future investors may demand, and may be granted, rights superior to those of existing stockholders. Our future debt financings, if available, are likely to involve restrictive covenants limiting our flexibility in conducting future business activities, and, in the event of insolvency, debt holders would be repaid before holders of our equity securities received any distribution of our corporate assets. If we raise additional funds through licensing or collaboration arrangements with third parties, we may have to relinquish valuable rights to our product candidates or grant licenses on terms that are not favorable to us. We also could be required to seek collaborators for product candidates at an earlier stage than otherwise would be desirable or relinquish our rights to product candidates or technologies that we otherwise would seek to develop or commercialize ourselves. Failure to obtain capital when needed on acceptable terms may force us to delay, limit or terminate our product development and commercialization of our current or future product candidates, which could have a material and adverse effect on our business, financial condition, results of operations, and prospects.

We have incurred significant losses in every quarter since our inception and anticipate that we will continue to incur significant losses in the future.

We are a biotechnology company with a limited operating history of developing next generation immunotherapies for cancer, inflammation, and autoimmunity using *de novo* protein design technology. Investment in biotechnology is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate effect or an acceptable safety profile, gain regulatory approval or become commercially viable. We do not have any products approved by regulatory authorities for marketing or commercial sale, we have not generated any revenue from product sales to date, and all of our product candidates are in early clinical or preclinical development. We continue to incur significant expenses related to our ongoing operations. As a result, we are not profitable and have incurred losses in every reporting period since our inception in 2003. For the years ended December 31, 2021 and 2020, we reported a net loss of $60.7 million and $33.3 million, respectively. As of December 31, 2021, we had an accumulated deficit since inception of $393.5 million.

We expect to continue to incur significant expenses and operating losses for the foreseeable future as we seek to identify, acquire and conduct research and development of future product candidates, and potentially begin to commercialize any future products that may achieve regulatory approval. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our financial condition. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenues. Our prior losses and expected future losses have had, and will continue to have, an adverse effect on our financial condition. If any of our future product candidates fail in clinical trials or do not gain regulatory approval, or if approved, fails to achieve market acceptance, we may never become profitable. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods.

We have a limited operating history as a company developing therapies using* de novo *protein design technology, which may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

Since our acquisition of the former Neoleukin Therapeutics, Inc., our operations to date have been primarily limited to organizing and staffing our company, acquiring product and technology rights, discovering and developing novel *de novo* proteins, undertaking preclinical studies and early clinical development activities, and, prior to the merger, developing small molecule drug candidates and conducting clinical trials of rosiptor. We have not yet obtained regulatory approval for any product candidate. Consequently, evaluating our performance, viability or possibility of future success will be more difficult than if we had a longer operating history or approved products on the market.

We currently have no source of product revenue and may never become profitable.

To date, we have not generated any revenues from commercial product sales, or otherwise. Our ability to generate revenue from product sales and achieve profitability will depend upon our ability, alone or with any future collaborators, to successfully commercialize any products that we may develop, in-license, or acquire in the future. Even if we can successfully achieve regulatory approval for any future product candidates, we do not know when any of these products will generate revenue from product sales for us, if at all. Our ability to generate revenue from any of our future product candidates also depends on several additional factors, including our or any future collaborators' ability to:

- complete development activities, including the necessary clinical trials;
- complete and submit Biologics License Applications, or BLAs, to the U.S. Food and Drug Administration, or FDA, and obtain regulatory approval for indications for which there is a commercial market;
- complete and submit applications to, and obtain regulatory approval from, foreign regulatory authorities;
- set a commercially viable price for our products;
- establish and maintain supply and manufacturing relationships with third parties, and ensure adequate and legally compliant manufacturing of bulk drug substances and drug products to maintain that supply;
- develop a commercial organization capable of sales, marketing and distribution for any products for which we obtain marketing approval and intend to sell ourselves in the markets in which we choose to commercialize on our own;
- find suitable distribution partners to help us market, sell, and distribute our approved products in other markets;
- obtain coverage and adequate reimbursement from third-party payors, including government and private payors;
- achieve market acceptance for our products, if any;
- establish, maintain and protect our intellectual property rights; and
- attract, hire, and retain qualified personnel.

In addition, because of the numerous risks and uncertainties associated with biological product development, any future product candidates may not advance through development or achieve the endpoints of applicable clinical trials. Therefore, we are unable to predict the timing or amount of increased expenses, or when or if we will be able to achieve or maintain profitability. In addition, our expenses could increase beyond expectations if we decide, or are required by the FDA or foreign regulatory authorities, to perform studies or trials in addition to those that we currently anticipate. Even if we can complete the development and regulatory process for any future product candidates, we anticipate incurring significant costs associated with commercializing these products.

Even if we can generate revenues from the sale of any future product candidates that may be approved, we may not become profitable and may need to obtain additional funding to continue operations. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce our operations.

We will require additional capital to finance our operations which may not be available to us on acceptable terms, or at all. If we fail to obtain necessary financing, we may be unable to complete the development and potential commercialization of future product candidates.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is expensive. Our operations have consumed substantial amounts of cash since inception. If we identify and advance any current or future product candidates into clinical trials and launch and commercialize any product candidates for which we receive regulatory approval, we expect research and clinical development expenses, and our selling, general and administrative expenses to increase substantially. In connection with our ongoing activities, we believe that our existing cash and cash equivalents will be sufficient to fund our operating requirements for at least the next 12 months. However, circumstances may cause us to consume capital more rapidly than we anticipate. We will likely require additional capital for the further development and potential commercialization of future product candidates and may also need to raise additional funds sooner to pursue a more accelerated development of future product candidates.

If we need to secure additional financing, fundraising efforts may divert our management from our day-to-day activities, which may adversely affect our ability to develop and commercialize future product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. If we do not raise additional capital when required or on acceptable terms, we may need to:

- significantly delay, scale back or discontinue clinical trials related to the development or commercialization of any of our current or future product candidates or cease operations altogether;
- seek strategic alliances for research and development programs at an earlier stage than we would otherwise desire or on terms less favorable than might otherwise be available; or
- relinquish, or license on unfavorable terms, our rights to any future product candidates that we otherwise would seek to develop or commercialize ourselves.

If we need to conduct additional fundraising activities and we do not raise additional capital in sufficient amounts or on terms acceptable to us, we may be prevented from pursuing development and commercialization efforts, which will have a material adverse effect on our business, operating results and prospects.

Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement and involves risks and uncertainties, and actual results could vary as a result of a number of factors, including the factors discussed elsewhere in this "Risk Factors" section. We have based this estimate on assumptions that may prove to be wrong, and we could spend our available capital resources sooner than we currently expect. Our future funding requirements, both near and long-term, will depend on many factors, including, but not limited to:

- our ability to identify additional product candidates for development;
- if we in-license or acquire product candidates from third parties, the cost of in-licensing or acquisition;
- the initiation, progress, timing, costs and results of clinical trials for any future product candidates;
- the clinical development plans we establish for NL-201 and any future product candidates;
- the achievement of milestones and our obligation to make milestone payments under our present or any future in-licensing agreements;
- the number and characteristics of product candidates that we discover, or in-license and develop;
- the outcome, timing and cost of regulatory review by the FDA and comparable foreign regulatory authorities, including the potential for the FDA or comparable foreign regulatory authorities to require that we perform more studies than those that we currently expect;
- the cost to establish, maintain, expand, and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with licensing, preparing, filing, prosecuting, defending, and enforcing any patent claims and maintaining and enforcing other intellectual property rights;
- the effects of the COVID-19 pandemic on our business and financial results;
- the effect of competing technological and market developments;
- the costs and timing of the implementation of commercial-scale outsourced manufacturing activities; and
- the costs and timing of establishing sales, marketing, distribution, and pharmacovigilance capabilities for any product candidates for which we may receive regulatory approval in territories where we choose to commercialize products on our own.

If we are unable to expand our operations or otherwise capitalize on our business opportunities due to a lack of capital, our business, results of operations, financial condition and cash flows, and future prospects could be materially adversely affected.

Risks Related to Discovery, Development, and Commercialization

Our product candidates are in early stages of development and may fail in development or suffer delays that materially and adversely affect their commercial viability. If we are unable to complete development of, or commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed.

We are in the early stages of our development efforts. We have no products on the market and all of our product candidates, including NL-201, are still in early clinical, preclinical or drug discovery stages, and we may not ever obtain regulatory approval for any of our product candidates. We have limited experience in conducting and managing the clinical trials necessary to obtain regulatory approvals, including approval by the FDA. Before obtaining regulatory approval for the commercial distribution of our product candidates, we or an existing or future collaborator must conduct extensive preclinical tests and clinical trials to demonstrate the safety and efficacy in humans of our product candidates. Additionally, we have a portfolio of targets and programs that are in earlier stages of discovery and preclinical development and may never advance to clinical-stage development. If we do not receive regulatory approvals for clinical testing and commercialization of our product candidates, we may not be able to continue our operations.

We may not have the financial resources to continue development of, or to enter into collaborations for, a product candidate if we experience any issues that delay clinical trials or delay and/or prevent regulatory approval of, or our ability to commercialize, product candidates, including:

- preclinical study results may show the product candidate to be less effective than desired or to have harmful or problematic side effects, which could cause us to delay or even abandon clinical testing;
- negative or inconclusive results from our clinical trials or the clinical trials of others for product candidates similar to ours, leading to a decision or requirement to conduct additional preclinical testing or clinical trials or abandon a program;
- product-related side effects experienced by patients in our clinical trials or by individuals using drugs or therapeutic biologics similar to our product candidates;
- our third-party manufacturers' inability to successfully manufacture our products or to meet regulatory specifications;
- inability of any third-party contract manufacturer to scale up manufacturing of our product candidates and those of our collaborators to supply the needs of clinical trials or commercial sales;
- delays in submitting INDs or comparable foreign applications or delays or failures in obtaining the necessary approvals from regulators to commence a clinical trial, or a suspension or termination of a clinical trial once commenced;
- conditions imposed by the FDA, the European Medicines Agency, or EMA, or other applicable regulatory authorities regarding the scope or design of our clinical trials;
- delays in enrolling patients in our clinical trials;
- high drop-out rates of our clinical trial patients;
- inadequate supply or quality of product candidate components or materials or other supplies necessary for the conduct of our clinical trials;
- inability to obtain alternative sources of supply for which we have a single source for product candidate components or materials;
- greater than anticipated costs of our clinical trials;
- manufacturing costs, formulation issues, pricing or reimbursement issues or other factors that no longer make a product candidate economically feasible;
- harmful side effects or inability of our product candidates to meet efficacy endpoints during clinical trials;
- failure to demonstrate a benefit-risk profile acceptable to the FDA, EMA or other applicable regulatory authorities;
- unfavorable inspection and review by the FDA, EMA or other applicable regulatory authorities of one or more clinical trial sites or manufacturing facilities used in the testing and manufacture of any of our product candidates;

- failure of our third-party contractors or investigators to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner, or at all;
- delays and changes in regulatory requirements, policy, and guidelines, including the imposition of additional regulatory oversight around clinical testing generally or with respect to our technology in particular; or
- varying interpretations of our data by the FDA, EMA or other applicable regulatory authorities.

We or our future partners' inability to complete development of, or commercialize our product candidates, or significant delays in doing so due to one or more of these factors, could have a material and adverse effect on our business, financial condition, results of operations, and prospects.

Further, cancer therapies are sometimes characterized as first-line, second-line, or third-line, and the FDA often approves new therapies initially only for advanced cancers, i.e. third-line or beyond. When cancer is detected early enough, first-line therapy, usually chemotherapy, surgery, radiation therapy, immunotherapy, hormone therapy, or a combination of these, is sometimes adequate to cure the cancer or prolong life without a cure. Second- and third-line therapies are administered to patients when prior therapy is not effective. Our current phase 1 clinical trial for NL-201 is in patients who have received one or more prior treatments, and we expect that to be the case for future clinical trials of NL-201. Subsequently, for those of our products that prove to be sufficiently beneficial, if any, we would expect to seek approval in earlier lines of therapy. Any product candidates we develop, even if approved, may not be successfully approved for earlier lines of therapy, and, prior to any such approvals, we will likely have to conduct additional clinical trials, which are often very lengthy, expensive, and have a significant risk of failure.

Our business is heavily dependent on the success of our Neoleukin platform and of our most advanced product candidate, NL-201. Existing and future preclinical studies and clinical trials of our product candidates may not be successful, and if we are unable to commercialize these product candidates or experience significant delays in doing so, our business will be materially harmed.

Our business is heavily dependent on our ability to obtain regulatory approval of, and then successfully launch and commercialize, our product candidates. We have invested a significant portion of our efforts and financial resources in the development of our proprietary system of advanced computational algorithms and methods for the design of functional *de novo* proteins, which we refer to as our Neoleukin platform, with an initial focus on key cytokine mimetics, which we refer to as Neoleukin *de novo* cytokine mimetics. Our lead product candidate, NL-201, is a Neoleukin *de novo* protein derived from our Neoleukin platform. However, NL-201 and our other product candidates are still in early stages of development. Our ability to generate commercial product revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our lead product candidates. Our product candidates may not be successful in clinical trials or receive regulatory approval. Even if they are successful in clinical trials, regulatory authorities may not complete their review in a timely manner, or additional delays may result if an FDA Advisory Committee or other regulatory authority recommends non-approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory authority policy during the period of product development, clinical trials, and the review process. Regulatory authorities may approve a product candidate for targets, disease indications or patient populations that are not as broad as we intended or desired, approve more limited indications than requested, or require distribution restrictions or strong safety language, such as contraindications or boxed warnings. Regulatory authorities may also require Risk Evaluation and Mitigation Strategies, or REMS, or the performance of costly post-marketing clinical trials. Even if we successfully obtain regulatory approvals to market our product candidates, our revenues will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval and have commercial rights. If the markets for patient subsets that we are targeting are not as significant as we estimate, we may not generate significant revenues from sales of such products, if approved.

We plan to seek regulatory approval to commercialize our product candidates both in the United States and in selected foreign countries. In order to market and sell our product candidates in the European Union and many other jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. The approval procedure varies among countries and can involve additional testing. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We may be required to expend significant resources to obtain regulatory approval, which may not be on a timely basis or successful at all, and to comply with ongoing regulations in these jurisdictions.

The success of our Neoleukin platform, NL-201, and our other product candidates will depend on many factors, including the following:

- successful completion of necessary preclinical studies to enable the initiation of clinical trials;
- successful enrollment of patients in, and the completion of, our clinical trials;
- obtaining adequate financing to perform the expensive clinical development programs anticipated for approval;
- receiving required regulatory authorizations for the development and approvals for the commercialization of our product candidates;
- establishing and maintaining arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and non-patent exclusivity for our product candidates and their components;
- enforcing and defending our intellectual property rights and claims;
- achieving desirable therapeutic properties for our product candidates' intended indications;
- launching commercial sales of our product candidates, if and when approved, whether alone or in collaboration with third parties;
- acceptance of our product candidates, if and when approved, by patients, the medical community and third-party payors;
- achieving appropriate reimbursement, pricing, and payment coverage for our product candidates;
- effectively competing with other therapies, including those that are currently in development; and
- maintaining an acceptable safety profile of our product candidates through clinical trials and following regulatory approval.

If we do not achieve any one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business.

Our current or future clinical trials or those of any future collaborators may reveal significant adverse events not seen in our preclinical studies and may result in a safety profile that could inhibit regulatory approval or market acceptance of any of our product candidates.

If significant adverse events or other side effects are observed in any of our clinical trials, we may have difficulty recruiting patients to our clinical trials, patients may drop out of our trials, we may be required to pause, delay, or abandon the trials or our development efforts of one or more product candidates altogether, we may be required to have more restrictive labeling, or we may experience the delay or denial of regulatory approval by the FDA, EMA or other applicable regulatory authorities. We, the FDA, EMA or other applicable regulatory authorities, or IRB, may suspend clinical trials of a product candidate at any time for various reasons, including a belief that subjects or patients in such trials are being exposed to unacceptable health risks or adverse side effects. Some potential therapeutics developed in the biotechnology industry that initially showed therapeutic promise in early-stage trials have later been found to cause side effects that prevented their further development. Even if the side effects do not preclude the product candidate from obtaining or maintaining marketing approval, undesirable side effects may inhibit market acceptance of the approved product due to its tolerability versus other therapies. NL-201 was designed to mimic the therapeutic activity of the cytokine interleukin-2, or IL-2, and interleukin-15, or IL-15, while limiting the toxicity cause by the preferential binding of native IL-2 and native IL-15 to cells that co-express the alpha subunit known as CD25. However, it is possible NL-201 will demonstrate significant adverse events similar to, or in addition to, those associated with IL-2 and IL-15, such as vascular leak syndrome, hypotension, impaired kidney and liver function, and mental status changes. Therapies involving cytokines have been known to cause side effects such as neurotoxicity and cytokine release syndrome.

Further, *de novo* proteins are a new class of therapeutics that have not been previously tested in humans. *De novo* proteins can be substantially different from all known proteins and as a result, it is unknown to what extent, if any, these *de novo* proteins will produce immunologic reactions in patients. Immunologic reactions could substantially limit the effectiveness of the treatment, the duration of treatment, or represent safety risks.

Additionally, if any of our product candidates receives marketing approval, the FDA could require us to adopt a REMS to ensure that the benefits of the product outweigh its risks, which may include, among other things, a Medication Guide outlining the risks of the product for distribution to patients and a communication plan to health care practitioners. Furthermore, if we or others later identify undesirable side effects caused by any of our products, several potentially significant negative consequences could result, including:

- regulatory authorities may suspend or withdraw approvals of such product;
- regulatory authorities may require additional warnings on the label of such product;
- we may be required to change the way such a product is administered or conduct additional clinical trials;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these developments could materially harm our business, financial condition and prospects.

If we do not achieve our projected development goals in the timeframes we announce and expect, the commercialization of our products may be delayed and, as a result, our stock price may decline.

From time to time, we estimate the timing of the anticipated accomplishment of various scientific, clinical, regulatory and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of scientific studies and clinical trials and the submission of regulatory filings. From time to time, we may publicly announce the expected timing of some of these milestones. All of these milestones are and will be based on numerous assumptions. The actual timing of these milestones can vary dramatically compared to our estimates, in some cases for reasons beyond our control. If we do not meet these milestones as publicly announced, or at all, the commercialization of our products may be delayed or never achieved and, as a result, our stock price may decline.

Our approach to the discovery and development of our therapeutic treatments is based on novel de novo protein design technology that are unproven and may not result in marketable products.

The success of our business depends primarily upon our ability to discover, develop, and commercialize a pipeline of product candidates using our Neoleukin platform. Unlike traditional protein-based therapeutics that modify native proteins, our Neoleukin platform designs new proteins from the ground up. Our platform uses advanced computational algorithms and methods to design functional *de novo* proteins that are hyper-stable, modifiable, and are designed to optimize desired intermolecular interactions and eliminate undesirable interactions. While we believe this approach will enable us to develop product candidates that may offer unique therapeutic benefits, the scientific basis of our efforts to develop product candidates using our Neoleukin platform is ongoing and may not result in viable product candidates.

While we have had favorable preclinical study results related to NL-201, we are still in the early stages of product development of NL-201. Our approach may be unsuccessful in moving NL-201 through clinical development, discovering additional product candidates, and NL-201 or any product candidates that we are currently developing may be shown to have harmful side effects or may have other characteristics that may necessitate additional clinical testing or make the product candidates unmarketable or unlikely to receive marketing approval. If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations.

To date, NL-201 is our only product candidate currently being tested in a clinical trial, and testing is in the early stages. We have not tested any of our other product candidates in any clinical trials. We may ultimately discover that our Neoleukin platform and any product candidates resulting therefrom do not possess certain properties required for therapeutic effectiveness. Our product candidates may also be unable to remain stable in the human body for the period of time required for the drug to reach the target tissue, or they may trigger immune responses that inhibit the activity of the product candidate or that cause adverse side effects in humans. We may spend substantial funds attempting to mitigate these properties and may never succeed in doing so. In addition, product candidates based on our Neoleukin platform may demonstrate different chemical and pharmacological properties in patients than they do in laboratory studies. Our Neoleukin platform and any product candidates resulting therefrom may not demonstrate the same chemical and pharmacological properties in humans and may interact with human biological systems in unforeseen, ineffective, or harmful ways.

The regulatory approval process for novel product candidates such as ours can be more expensive and take longer than for other, better known or extensively studied product candidates. Because the FDA has no prior experience with *de novo* proteins as therapeutics, we anticipate that this may increase the complexity, uncertainty and length of the regulatory approval process for our product candidates. We or any future partners may be required to perform additional or unanticipated clinical trials to obtain approval or be subject to post-marketing testing requirements to maintain regulatory approval. If the products resulting from our Neoleukin platform and research programs prove to be ineffective, unsafe, or commercially unviable, our Neoleukin platform and pipeline would have little, if any, value, which would have a material and adverse effect on our business, financial condition, results of operations, and prospects.

Preclinical and clinical development involve a lengthy and expensive process, with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our current product candidates or any future product candidates.

All of our product candidates are in early clinical, preclinical or earlier development and their risk of failure is high. It is impossible to predict when or if any of our product candidates will receive regulatory approval. To obtain the requisite regulatory approvals to commercialize any product candidates, we must demonstrate through extensive preclinical studies and lengthy, complex, and expensive clinical trials that our product candidates are safe and effective in humans. Clinical testing can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the success of later-stage clinical trials. The design of a clinical trial can determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We may be unable to establish clinical endpoints that applicable regulatory authorities would consider clinically meaningful, and a clinical trial can fail at any stage of testing, and we have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval. Differences in trial design between early-stage clinical trials and later-stage clinical trials make it difficult to extrapolate the results of earlier clinical trials to later clinical trials. Moreover, clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in clinical trials have nonetheless failed to obtain marketing approval of their products. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or to unfavorable safety profiles, notwithstanding promising results in earlier trials, and we could face similar setbacks. There is typically a high rate of failure of product candidates proceeding through clinical trials. Most product candidates that commence clinical trials are never approved as products and there can be no assurance that any of our current or future clinical trials will ultimately be successful or support clinical development of our current or any of our future product candidates.

Commencement of our future clinical trials is subject to finalizing the trial design and receiving approval from the FDA to proceed with clinical testing or similar approval from the EMA or other comparable foreign regulatory authorities. Even after we submit our IND or comparable submissions in other jurisdictions, the FDA, EMA, or comparable foreign regulatory authorities could disagree that we have satisfied their requirements to commence our clinical trials or disagree with our study design, which may require us to complete additional preclinical studies or amend our protocols or impose stricter conditions on the commencement of clinical trials.

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

We or any collaborators may experience delays in initiating or completing clinical trials or may experience numerous unforeseen events during, or as a result of, any future clinical trials that we may conduct that could delay or prevent our ability to receive marketing approval or commercialize NL-201 or any future product candidates, including:

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

- clinical trials of any product candidates may fail to show safety or efficacy, produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional preclinical studies or clinical trials or we may decide to abandon product development programs;
- the number of subjects required for clinical trials of any product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, or subjects may drop out of these clinical trials or fail to return for post-treatment follow-up at a higher rate than we anticipate;
- 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, or may deviate from the clinical trial protocol or drop out of the trial, which may require that we add new clinical trial sites or investigators;
- we may elect to, or regulators, IRBs, or ethics committees may require that we or our investigators, suspend or terminate clinical research or trials for various reasons, including noncompliance with regulatory requirements or a finding that the participants in our trials are being exposed to unacceptable health risks;
- the cost of clinical trials of any of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate to initiate or complete a given clinical trial;
- we may be unable to obtain or manufacture sufficient quantities of our product candidates for use in clinical trials;
- reports from clinical testing of other therapies may raise safety or efficacy concerns about our product candidates; and
- we may fail to establish an appropriate safety profile for a product candidate based on clinical or preclinical data for such product candidate as well as data emerging from other molecules in the same class as our product candidate.

We could also encounter delays if a clinical trial is suspended or terminated by us, the IRBs of the institutions in which such trials are being conducted, or the FDA, EMA or other regulatory authorities, or if a clinical trial is recommended for suspension or termination by the Data Safety Monitoring Board, or the DSMB, for such trial. A suspension or termination may be imposed due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA, EMA, or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product or treatment, failure to establish or achieve clinically meaningful trial endpoints, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. For example, our IND for NL-201 was initially placed on clinical hold. Even though the FDA removed the clinical hold on the IND for NL-201, NL-201 could be put on clinical hold again, and other future product candidates may be subject to clinical holds in the future. Clinical studies may also be delayed or terminated as a result of ambiguous or negative interim results. Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates. Further, the FDA, EMA, or other regulatory authorities may disagree with our clinical trial design and our interpretation of data from clinical trials, or may change the requirements for approval even after they have reviewed and commented on the design for our clinical trials.

Our product development costs will increase if we experience delays in clinical testing or obtaining marketing approvals. We do not know whether any of our clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates and may allow our competitors to bring products to market before we do, potentially impairing our ability to successfully commercialize our product candidates and harming our business and results of operations. Any delays in our clinical development programs may harm our business, financial condition, and results of operations significantly.

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

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, the number and location of clinical sites we enroll, the proximity of patients to clinical sites, the eligibility and exclusion criteria for the trial, the design of the clinical trial, the inability to obtain and maintain patient consents, the risk that enrolled participants will drop out before completion, competing clinical trials, and clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new drugs or therapeutic biologics that may be approved for the indications being investigated by us. The COVID 19 pandemic may also delay clinical trials if there are inadequate clinical resources for sites to safely conduct clinical research. Furthermore, we expect to rely on our collaborators, CROs, and clinical trial sites to ensure the proper and timely conduct of our future clinical trials, including the patient enrollment process, and we have limited influence over their performance. Additionally, we could encounter delays if treating physicians encounter unresolved ethical issues associated with enrolling patients in future clinical trials of our product candidates in lieu of prescribing existing treatments that have established safety and efficacy profiles.

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

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

From time to time, we may publish preliminary or topline data from our clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the more complete data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the interim or preliminary results that we report may differ from future results of the same studies or clinical trials, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Preliminary or topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary or topline data we previously published. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. As a result, interim, preliminary and topline data should be viewed with caution until the final data are available. Adverse differences between interim, preliminary, or topline data and final data could significantly harm our reputation and business prospects.

Failure to obtain regulatory approval in international jurisdictions would prevent any future product candidates from being marketed outside the United States.

In order to market and sell our products in the European Union and other jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. We may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. A failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory approval process in others. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market. If we are unable to obtain approval of any of our future product candidates by regulatory authorities in the European Union or another jurisdiction, the commercial prospects of that product candidate may be significantly diminished and our business prospects could decline.

Recently enacted and future legislation, including potentially unfavorable pricing regulations or other healthcare reform initiatives, may increase the difficulty and cost for us to obtain marketing approval of, and commercialization of, our future product candidates and affect the prices we may obtain.

The regulations that govern, among other things, marketing approvals, coverage, pricing and reimbursement for new drug products vary from country to country. In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our future product candidates, restrict or regulate post-approval activities and affect our ability to successfully sell any product candidates for which we obtain marketing approval.

In the United States in recent years, Congress has considered reductions in Medicare reimbursement for drugs administered by physicians. The Centers for Medicare and Medicaid Services, or CMS, the agency that administers the Medicare program, also has the authority to revise reimbursement rates and to implement coverage restrictions for drugs. Cost reduction initiatives and changes in coverage implemented through legislation or regulation could decrease utilization of, and reimbursement for, any approved products, which in turn could affect the price we can receive for those products. For example, on September 9, 2021, the Biden administration published a wide-ranging list of policy proposals, most of which would need to be carried out by Congress, to reduce drug prices and drug payment. The HHS plan includes, among other reform measures, proposals to lower prescription drug prices, including by allowing Medicare to negotiate prices and disincentivizing price increases, and to support market changes that strengthen supply chains, promote biosimilars and generic drugs, and increase price transparency. Many similar proposals, including the plans to give Medicare Part D authority to negotiate drug prices, require drug manufacturers to pay rebates on drugs whose prices increase greater than the rate of inflation, and cap out-of-pocket costs, have already been included in policy statements and legislation currently being considered by Congress. It is unclear to what extent these and other statutory, regulatory, and administrative initiatives will be enacted and implemented, and to what extent these or any future legislation or regulations by the Biden administration will have on our business or future product candidates. While Medicare regulations apply only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in establishing their own coverage polices and reimbursement rates. Therefore, any reduction in reimbursement that results from federal legislation or regulation may result in a similar reduction in payments from private payors.

In March 2010, President Obama signed into law the Affordable Care Act in an effort to, among other things, broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on pharmaceutical and medical device manufacturers and impose additional health policy reforms. The Affordable Care Act, among other things, also expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program imposed a significant annual, nondeductible fee on companies that manufacture or import certain branded prescription drug products, and enacted substantial provisions affecting compliance , which may affect our business practices with healthcare practitioners. Certain provisions of the Affordable Care Act have been subject to judicial and Congressional challenges to repeal or replace certain aspects of the Affordable Care Act.On June 17, 2021, the U.S. Supreme Court dismissed a challenge on procedural grounds that argued that the Affordable Care Act is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Thus, the Affordable Care Act will remain in effect in its current form. It is possible that the Affordable Care Act will be subject to judicial or Congressional challenges in the future. It is uncertain how any such challenges and the healthcare measures of the Biden administration will impact the Affordable Care Act and our business, prospects, financial condition or results of operations.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. On August 2, 2011, the President signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee did not achieve a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic, unless additional Congressional action is taken. The Medicare reductions phase back in starting with a 1% reduction in effect from April 1, 2022 to June 30, 2022 before increasing to the full 2% reduction. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, 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 a material adverse effect on our customers and accordingly, our financial operations. Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. Furthermore, there has been heightened governmental scrutiny recently over the manner in which manufacturers set prices for their marketed products. For example, there have been several recent Congressional inquiries and proposed bills designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer's patient programs, and reform government program reimbursement methodologies for drug products. We cannot be sure whether additional legislative changes will be enacted, or whether existing regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our future product candidates, if any, may be.

In the United States, the European Union and other potentially significant markets for our future product candidates, government authorities and third-party payors are increasingly attempting to limit or regulate the price of medical products and services, particularly for new and innovative products and therapies, which has resulted in lower average selling prices. Furthermore, the increased emphasis on managed healthcare in the United States and on country and regional coverage, pricing and reimbursement controls in the European Union will put additional pressure on product coverage, pricing, reimbursement and utilization, which may adversely affect our business, results of operations, financial condition and cash flows and future prospects. These pressures can arise from various sources, including but not limited to, rules and practices of managed care groups, judicial decisions and governmental laws and regulations related to Medicare, Medicaid and healthcare reform, pharmaceutical reimbursement policies and pricing in general.

Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product candidate in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, which could negatively impact the revenues we are able to generate from the sale of the product in that particular country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates even if our product candidates obtain marketing approval.

Laws and regulations governing international operations may preclude us from developing, manufacturing and selling certain product candidates outside of the United States and require us to develop and implement costly compliance programs.

As we expand our operations outside of the United States, we must comply with numerous laws and regulations in each jurisdiction in which we plan to operate. We must also comply with U.S. laws applicable to the foreign operations of U.S. businesses and individuals, such as the Foreign Corrupt Practices Act, or FCPA. The creation and implementation of international business practices compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required.

The FCPA prohibits any U.S. individual or business from paying, offering, authorizing payment or offering anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring us to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. The anti-bribery provisions of the FCPA are enforced primarily by the U.S. Department of Justice. The SEC is involved with enforcement of the books and records provisions of the FCPA.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. Our expanding presence outside the United States will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside the United States, which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial penalties, including suspension or debarment from government contracting. Violation of the FCPA can result in significant civil and criminal penalties. Indictment alone under the FCPA can lead to suspension of the right to do business with the U.S. government until the pending claims are resolved. Conviction of a violation of the FCPA can result in long-term disqualification as a government contractor. The termination of a government contract or relationship as a result of our failure to satisfy any of our obligations under laws governing international business practices would have a negative impact on our operations and harm our reputation and ability to procure government contracts. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

Even if we are able to commercialize our future product candidates, the products may not receive coverage and adequate reimbursement from third-party payors, which could harm our business.

Our ability to commercialize any products successfully will depend, in part, on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government authorities, private health insurers, health maintenance organizations and third-party payors. Patients who are prescribed medications for the treatment of their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their prescription drugs. Coverage and adequate reimbursement from government healthcare programs, such as Medicare and Medicaid, and private health insurers are critical to new product acceptance. Patients are unlikely to use our future product candidates unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our product candidates. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. As a result, government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. 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. Third-party payors may also seek additional clinical evidence, beyond the data required to obtain marketing approval, demonstrating clinical benefits and value in specific patient populations before covering our products for those patients. We cannot be sure that coverage and adequate reimbursement will be available for any product that we commercialize and, if reimbursement is available, what that level of reimbursement will be. Coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If coverage and reimbursement are not available or are available only at limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, obtaining coverage does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sales and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may only be temporary. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used. Reimbursement rates may also be based in part on existing reimbursement amounts for lower cost drugs or may be bundled into the payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Coverage and reimbursement for drug products can differ significantly from payor to payor. As a result, the coverage and reimbursement determination process is often a time-consuming and costly process with no assurance that coverage and adequate reimbursement will be obtained or applied consistently. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own coverage and reimbursement policies. Our inability to promptly obtain coverage and profitable reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

We have never marketed a drug before. If we are able to identify and develop or acquire a product candidate that is ultimately approved for sale but are unable to establish an effective sales force and marketing infrastructure or enter into acceptable third-party sales and marketing or licensing arrangements, we may be unable to generate any revenue.

We do not currently have an infrastructure for the sales, marketing and distribution of pharmaceutical drug products and the cost of establishing and maintaining such an infrastructure may exceed the cost-effectiveness of doing so. In addition, NL-201 is our only product candidate in clinical development, and such clinical development is in the early stages. If we are able to successfully advance NL-201 through clinical development or to identify and establish other product candidates and advance them through clinical development, in order to market any products that may ultimately be approved by the FDA and comparable foreign regulatory authorities, we must build our sales, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. If we are unable to establish adequate sales, marketing, and distribution capabilities, whether independently or with third parties, we may not be able to generate product revenue and may not become profitable. We will be competing with many companies that have extensive and well-funded sales and marketing operations. Without an internal commercial organization or the support of a third party to perform sales and marketing functions, we may be unable to compete successfully against these more established companies.

Even if we are able to effectively hire a sales force and develop a marketing and sales infrastructure, our sales force and marketing team may not be successful in commercializing our product candidates, which would negatively affect our ability to generate revenue.

We may not be successful in our efforts to use our Neoleukin platform to expand our pipeline of product candidates and develop marketable products.

The success of our business depends in part upon our ability to discover, develop, and commercialize products based on our Neoleukin platform, which may fail to identify other potential product candidates for clinical development for a number of reasons. Our research methodology may be unsuccessful in identifying potential product candidates or our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval. If any of these events occur, we may be forced to abandon our development efforts for a program or for multiple programs, which would materially harm our business and could potentially cause us to cease operations. Research programs to identify new product candidates require substantial technical, financial, and human resources.

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

Because we have limited financial and managerial resources, we focus our research and development efforts on our lead product candidate, NL-201, with initial indications including renal cell carcinoma and melanoma. As a result, we may forgo or delay pursuit of opportunities with other product candidates that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable product candidates. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other 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.

We face substantial competition, including companies developing novel treatments and technology platforms in oncology. If these companies develop technologies or product candidates more rapidly than we do or their technologies are more effective, our ability to develop and successfully commercialize product candidates may be adversely affected.

The development and commercialization of drugs is highly competitive. Our product candidates, if approved, will face significant competition and our failure to effectively compete may prevent us from achieving significant market penetration. Most of our competitors have significantly greater resources than we do and we may not be able to successfully compete. We compete with a variety of multinational biopharmaceutical companies, specialized biotechnology companies, and emerging biotechnology companies, as well as with technologies and product candidates being developed at academic institutions, governmental agencies, and other public and private research institutions. Our competitors have developed, are developing, or will develop product candidates and processes competitive with our product candidates and processes. Competitive therapeutic treatments include those that have already been approved and accepted by the medical community and any new treatments, including those based on novel technology platforms that enter the market. We believe that a significant number of products are currently under development, and may become commercially available in the future, for the treatment of conditions for which we are trying, or may try, to develop product candidates. There is intense and rapidly evolving competition in the biotechnology, biopharmaceutical, and interleukin and immunoregulatory therapeutics fields. Competition from many sources exists or may arise in the future. Our competitors include larger and better funded biopharmaceutical, biotechnological, and therapeutics companies, including companies focused on oncology therapeutics, as well as numerous small companies.

Moreover, we also compete with current and future therapeutics developed at universities and other research institutions. Some of these companies are well-capitalized and, in contrast to us, have significant clinical experience, and may include our future partners. In addition, these companies compete with us in recruiting scientific and managerial talent.

Our success will depend partially on our ability to develop and commercialize therapeutics that are safer and more effective than competing products. Our commercial opportunity and success will be reduced or eliminated if competing products are safer, more effective, or less expensive than the therapeutics we develop.

Our lead product candidate, NL-201, is under development for the treatment of advanced solid tumors, including melanoma and renal cell carcinoma. If approved, it would face competition from approved advanced melanoma and renal cell carcinoma treatments, including multiple checkpoint inhibitors, tyrosine kinase inhibitors, VEGF inhibitors, recombinant human IL-2, and several chemotherapy drugs or combinations. Further, we are aware of several IL-2 or IL-15 agonists in various stages of clinical and preclinical development.

Many of our competitors have significantly greater financial, technical, manufacturing, marketing, sales, and supply resources or experience than we have. If we successfully obtain approval for any product candidate, we will face competition based on many different factors, including the safety and effectiveness of our products, the ease with which our products can be administered and the extent to which patients accept relatively new routes of administration, the timing and scope of regulatory approvals for these products, the availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage, and patent position. Competing products could present superior treatment alternatives, including by being more effective, safer, less expensive, or marketed and sold more effectively than any products we may develop. Competitive products may make any products we develop obsolete or noncompetitive before we recover the expense of developing and commercializing our product candidates. Such competitors could also recruit our employees, which could negatively impact our level of expertise and our ability to execute our business plan.

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

Our product candidates may face competition from other products that are the same as or similar to ours. If the FDA or comparable foreign regulatory authorities approve biosimilar versions of our product candidates, or such authorities do not grant our products appropriate periods of regulatory exclusivity, the sales of our products could be adversely impacted.

The Biologics Price Competition and Innovation Act of 2009, or the BPCIA, was enacted as part of the Affordable Care Act to establish an abbreviated pathway for the approval of biosimilar biological products (both highly similar and interchangeable biosimilar biological products. The regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on its similarity to an approved biologic. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after the first licensure date of the reference product licensed under a BLA. The law is complex and some provisions are still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty.

A biological product submitted for licensure under a BLA is eligible for a period of exclusivity that commences on the date of its licensure, unless its date of licensure is not considered a date of first licensure because it falls within an exclusion under the PBCIA. Our biological product candidates may qualify for the BPCIA's 12-year period of exclusivity, but there is a risk that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for biosimilar competition sooner than anticipated. There is also a risk that this exclusivity could be shortened due to congressional action or otherwise, potentially creating the opportunity for generic competition sooner than anticipated. For example, there have been efforts to decrease this period of exclusivity to a shorter timeframe—future proposed budgets, international trade agreements, and other arrangements or proposals may affect periods of exclusivity. Most states have enacted substitution laws that permit substitution of only interchangeable biosimilars. The extent to which a highly similar biosimilar, once approved, will be substituted for any one of the reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

If we decide to pursue accelerated approval for any of our product candidates, it may not lead to a faster development or regulatory review or approval process and does not increase the likelihood that our product candidates will receive marketing approval. If we are unable to obtain approval under an accelerated pathway, we may be required to conduct additional clinical trials beyond those that we contemplate, which could increase the expense of obtaining, reduce the likelihood of obtaining and/or delay the timing of obtaining, necessary marketing approvals.

In the future, we may decide to pursue accelerated approval for one or more of our product candidates. Under the FDA's accelerated approval program, the FDA may approve a drug for a serious or life-threatening disease or condition that provides a meaningful advantage over available therapies 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. For drugs granted accelerated approval, post-marketing confirmatory trials are required to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. These confirmatory trials must be completed with due diligence, and the FDA may require that the trial be designed, initiated, and/or fully enrolled prior to approval. If we were to pursue accelerated approval for a product candidate for a disease or condition, we would do so on the basis that there is no available therapy for that disease or condition. If any of our competitors were to receive full approval on the basis of a confirmatory trial for a drug for a disease or condition for which we are seeking accelerated approval before we receive accelerated approval, the disease or condition would no longer qualify as one for which there is no available therapy, and accelerated approval of our product candidate would not occur. Many cancer therapies rely on accelerated approval, and the treatment landscape can change quickly as the FDA converts accelerated approvals to full approvals on the basis of successful confirmatory trials.

Moreover, the FDA may withdraw approval of any product candidate approved under the accelerated approval pathway if, for example:

- the trial or trials required to verify the predicted clinical benefit of our product candidate fail to verify such benefit or do not demonstrate sufficient clinical benefit to justify the risks associated with such product;
- other evidence demonstrates that our product candidate is not shown to be safe or effective under the conditions of use;
- we fail to conduct any required post-approval trial of our product candidate with due diligence; or
- we disseminate false or misleading promotional materials relating to the relevant product candidate.

Risks Related to Our Reliance on Third Parties

We rely on and expect to continue to rely on third parties to conduct certain of our preclinical studies and clinical trials. If those third parties do not perform as contractually required, fail to satisfy legal or regulatory requirements, miss expected deadlines or terminate the relationship, our development program could be delayed with potentially material and adverse effects on our business, financial condition, results of operations, and prospects.

We currently rely and intend to continue to rely in the future on third-party clinical investigators, CROs, clinical data management organizations, and consultants to assist or provide the design, conduct, supervision, and monitoring of preclinical studies and clinical trials of our product candidates. Because we rely on and intend to continue to rely on these third parties and will not have the ability to conduct all preclinical studies or clinical trials independently, we will have less control over the timing, quality, and other aspects of preclinical studies and clinical trials than we would have had we conducted them on our own. Although we have agreements governing the activities of third parties, these investigators, CROs, and consultants will not be our employees, and we will have limited control over the amount of time and resources that they dedicate to our programs. These third parties may have contractual relationships with other entities, some of which may be our competitors, which may draw time and resources from our programs. The third parties with which we may contract might not be diligent, careful, or timely in conducting our preclinical studies or clinical trials, resulting in the preclinical studies or clinical trials being delayed or unsuccessful.

If we cannot contract with acceptable third parties on commercially reasonable terms, or at all, or if these third parties do not carry out their contractual duties, satisfy legal and regulatory requirements for the conduct of preclinical studies or clinical trials or meet expected deadlines, our clinical development programs could be delayed and otherwise adversely affected. In all events, we will be responsible for ensuring that each of our preclinical studies and clinical trials are conducted in accordance with the general investigational plan and protocols for the trial as well as applicable legal and regulatory requirements. The FDA generally requires preclinical studies to be conducted in accordance with Good Laboratory Practices, or GLPs, and clinical trials to be conducted in accordance with Good Clinical Practices, or GCPs, including for designing, conducting, recording, and reporting the results of preclinical studies and clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity, and confidentiality of clinical trial participants are protected. Our reliance on third parties that we do not control will not relieve us of these responsibilities and requirements. If we or any of our third-party service providers fail to comply with applicable GCPs or other regulatory requirements, we or they may be subject to enforcement or other legal actions, the data generated in our trials may be deemed unreliable, and the FDA or comparable foreign regulatory authorities may require us to perform additional studies. Any adverse development or delay in our preclinical studies or clinical trials as a result of our reliance on third parties could have a material and adverse effect on our business, financial condition, results of operations, and prospects.

If any of our relationships with these third-party CROs or others terminate, we may not be able to enter into arrangements with alternative CROs or other third parties or to do so on commercially reasonable terms. Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO begins work. As a result, delays may occur, which can materially impact our ability to meet our desired clinical development timelines.

We rely on and expect to continue to rely on third-party manufacturers and suppliers to supply components of our product candidates. The loss of our third-party manufacturers or suppliers, or our or their failure to comply with applicable regulatory requirements or to supply sufficient quantities at acceptable quality levels or prices, or at all, would materially and adversely affect our business.

We do not own or operate facilities for drug manufacturing, storage, distribution, or quality testing. We currently rely, and expect to continue to rely, on third-party contract manufacturers to manufacture bulk drug substances, drug products, raw materials, samples, components, or other materials and reports, and conduct fill-finish services. Reliance on third-party manufacturers may expose us to different risks than if we were to manufacture product candidates ourselves. Our third-party manufacturers may prioritize another customer's needs in front of ours, especially in the event of a global pandemic. Additionally, raw materials and components used in the manufacturing process, particularly those for which we have no other source or supplier, may not be available or may not be suitable or acceptable for use due to material or component defects, may be in short supply, and may significantly increase in price. There can be no assurance that our preclinical and clinical development product supplies will not be limited, available at acceptable prices. In particular, any replacement of our manufacturer could require significant effort and expertise because there may be a limited number of qualified replacements.

The manufacturing process for a product candidate is subject to review by the FDA, EMA, or other applicable regulatory authorities. We, and our suppliers and manufacturers, must meet applicable manufacturing requirements and undergo rigorous facility and process validation tests required by regulatory authorities in order to comply with regulatory standards, such as current Good Manufacturing Practices, or cGMPs. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the FDA and foreign regulatory authorities. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA, EMA or other applicable regulatory authorities, we may not be able to rely on their manufacturing facilities for the manufacture of elements of our product candidates and approval may be delayed. Moreover, although we do not control the manufacturing process at our contract manufacturers and are completely dependent on them for compliance with current regulatory requirements, we are responsible for ensuring that our products comply with regulatory requirements. If any of our manufacturers fails to comply with such requirements or to perform its obligations in relation to quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, we may be forced to enter into an agreement with another third party, which we may not be able to do on reasonable terms, if at all. In some cases, the technical skills or technology required to manufacture our product candidates may be unique or proprietary to the original manufacturer and we may have difficulty transferring such to another third party. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to enable us, or to have another third party, manufacture our product candidates. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines; and we may be required to repeat some of the development program. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget.

We expect to continue to rely on third-party manufacturers if we receive regulatory approval for any product candidate. To the extent that we have existing, or enter into future, manufacturing arrangements with third parties, we will depend on these third parties to perform their obligations in a timely manner consistent with contractual and regulatory requirements, including those related to quality control and assurance. Any manufacturing facilities used to produce our products will be subject to periodic review and inspection by the FDA, EMA, or other applicable regulatory authorities, including for continued compliance with cGMP requirements, quality control, quality assurance, and corresponding maintenance of records and documents. If we are unable to obtain or maintain third-party manufacturing for product candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our product candidates successfully. Our or a third party's failure to execute on our manufacturing requirements, comply with cGMPs, or maintain a compliance status acceptable to the FDA, EMA, or other applicable regulatory authorities could adversely affect our business in a number of ways, including:

- an inability to initiate or continue clinical trials of product candidates under development;
- delay in submitting regulatory applications, or receiving regulatory approvals, for product candidates;
- loss of the cooperation of future collaborators;
- subjecting third-party manufacturing facilities to additional inspections by regulatory authorities;
- requirements to cease distribution or to recall batches of our product candidates; and
- in the event of approval to market and commercialize a product candidate, an inability to meet commercial demands for our products.

Additionally, our contract manufacturers may experience manufacturing difficulties due to resource constraints or as a result of labor disputes or unstable political environments. For example, the outbreak of COVID-19 has spread across the globe and has resulted in extended shutdowns of businesses in the United States, Canada and many other countries and has had ripple effects to businesses around the world. Global health concerns, such as the COVID-19 pandemic, could also result in adverse effects to our manufacturing operations, including our ability to source raw materials and reagents. If our contract manufacturers were to encounter any of these difficulties, our ability to provide our product candidates to patients in preclinical and clinical trials, or to provide product for treatment of patients once approved, would be jeopardized.

Our third-party manufacturers may encounter difficulties in production. If we or any of our third-party manufacturers encounter such difficulties, our ability to provide supply of our product candidates for clinical trials, our ability to obtain marketing approval, or our ability to provide supply of our products for patients, if approved, could be delayed or stopped.

Our product candidates are biopharmaceuticals, and the process of manufacturing biopharmaceuticals is complex, time-consuming, highly regulated, and subject to multiple risks. Our contract manufacturers must comply with legal requirements, cGMPs, and guidelines for the bulk manufacturing, fill-finish services, packaging, and storage of biopharmaceuticals used in clinical trials and, if approved, marketed products. Our contract manufacturers may have limited experience in the manufacturing of cGMP batches.

Manufacturing biopharmaceuticals is highly susceptible to product loss due to contamination, equipment failure, improper installation or operation of equipment, vendor or operator error, inconsistency in yields, variability in product characteristics, and difficulties in scaling the production process. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects, and other supply disruptions. If microbial, viral, or other contaminations are discovered at our third-party manufacturers' facilities, such facilities may need to be closed for an extended period of time to investigate and remedy the contamination, which could delay clinical trials and adversely harm our business. Moreover, if the FDA determines that our third-party manufacturers' facilities are not in compliance with FDA laws and regulations, including those governing cGMPs, the FDA may deny approval of our application until the deficiencies are corrected or we replace the manufacturer in our application with a manufacturer that is in compliance.

In addition, there are risks associated with large scale manufacturing for clinical trials or commercial scale including, among others, cost overruns, potential problems with process scale-up, process reproducibility, stability issues, compliance with cGMPs, lot consistency and timely availability of raw materials. For example, certain resins used in the manufacture of biopharmaceuticals have recently experienced limited availability. Even if we obtain regulatory approval for any of our product candidates, there is no assurance that manufacturers will be able to manufacture the approved product, or provide fill-finish services, to specifications acceptable to the FDA, EMA, or other applicable regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product or to meet potential future demand. If our manufacturers are unable to produce sufficient quantities for clinical trials or for commercialization, commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations, and prospects.

Scaling up a biopharmaceutical manufacturing process is a difficult and uncertain task, and our third-party manufacturers may not have the necessary capabilities to complete the implementation, manufacturing, and development process. If we are unable to adequately validate or scale-up the manufacturing process at our current manufacturers' facilities, we will need to transfer to another manufacturer and complete the manufacturing validation process, which can be lengthy. If we are able to adequately validate and scale-up the manufacturing process for our product candidates with a contract manufacturer, we will still need to negotiate with such contract manufacturer an agreement for commercial supply and it is not certain we will be able to come to agreement on terms acceptable to us.

We cannot assure you that any stability or other issues relating to the manufacture of any of our product candidates or products will not occur in the future. Our *de novo* protein product candidates may not demonstrate sufficient long-term stability to support a BLA filing or obtain approval, or the product shelf life may be limited by stability results. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants, or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. If our third-party manufacturers were to encounter any of these difficulties, our ability to provide any product candidates to patients in planned clinical trials and products to patients, once approved, would be jeopardized. Any delay, interruption or other issues that arise in the manufacture, fill- finish, packaging, or storage of clinical trial supplies could delay the completion of planned clinical trials, increase the costs associated with maintaining clinical trial programs and, depending upon the period of delay, require us to commence new clinical trials at additional expense or terminate clinical trials completely. Any adverse development affecting clinical or commercial manufacturing of our product candidates or products may result in shipment delays, inventory shortages, lot failures, product withdrawals or recalls, or other interruptions in the supply of our product candidates or products. We may also have to take inventory write-offs and incur other charges and expenses for product candidates or products that fail to meet specifications, undertake costly remediation efforts or seek more costly manufacturing alternatives. Accordingly, failures or difficulties faced at any level of our supply chain could adversely affect our business and delay or impede the development and commercialization of any of our product candidates or products, if approved, and could have an adverse effect on our business, prospects, financial condition, and results of operations.

As part of our process development efforts, we also may make changes to the manufacturing processes at various points during development, for various reasons, such as controlling costs, achieving scale, decreasing processing time, increasing manufacturing success rate or other reasons. Such changes carry the risk that they will not achieve their intended objectives, and any of these changes could cause our product candidates to perform differently and affect the results of our ongoing clinical trials or future clinical trials. In some circumstances, changes in the manufacturing process may require us to perform *ex vivo* comparability studies and to collect additional data from patients prior to undertaking more advanced clinical trials. For instance, changes in our process during the course of clinical development may require us to show the comparability of the product used in earlier clinical phases or at earlier portions of a trial to the product used in later clinical phases or later portions of the trial.

We may, in the future, seek to enter into collaborations with other third parties for the discovery, development and commercialization of our product candidates. If our collaborators cease development efforts under our collaboration agreements, or if any of those agreements are terminated, these collaborations may fail to lead to commercial products, and we may never receive milestone payments or future royalties under these agreements.

We expect a significant portion of our future revenue and cash resources to be derived from collaboration agreements or other similar agreements into which we may enter in the future for research, development, and commercialization of other therapeutic technologies or product candidates. Biopharmaceutical companies are our likely future collaborators for any marketing, distribution, development, licensing, or broader collaboration arrangements. If we fail to enter into future collaborations on commercially reasonable terms, or at all, or such collaborations are not successful, we may not be able to execute our strategy to develop certain targets, product candidates, or disease areas that we believe could benefit from the resources of either larger biopharmaceutical companies or those specialized in a particular area of relevance.

Revenue from research and development collaborations depends upon continuation of the collaborations, payments for research and development services, and resulting options to acquire any licenses of successful product candidates, and the achievement of milestones, contingent payments, and royalties, if any, derived from future products developed from our research. If we are unable to successfully advance the development of our product candidates or achieve milestones, revenue and cash resources from milestone payments under our collaboration agreements will be substantially less than expected.

With respect to future collaboration agreements, we expect to have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Moreover, 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 may 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 pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on preclinical studies or clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial, or abandon a product candidate, repeat or conduct new clinical trials, or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- collaborators with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to litigation or potential liability;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our product candidates or that result in costly litigation or arbitration that diverts management attention and resources; and
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

As a result of the foregoing, our current and any future collaboration agreements may not lead to development or commercialization of our product candidates in the most efficient manner or at all. If a collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated. Any failure to successfully develop or commercialize our product candidates pursuant to our current or any future collaboration agreements could have a material and adverse effect on our business, financial condition, results of operations, and prospects.

Moreover, to the extent that any of our future collaborators were to terminate a collaboration agreement, we may be forced to independently develop these product candidates, including funding preclinical studies or clinical trials, assuming marketing and distribution costs and defending intellectual property rights, or, in certain instances, abandon product candidates altogether, any of which could result in a change to our business plan and have a material adverse effect on our business, financial condition, results of operations, and prospects.

We may have conflicts with our collaborators that could delay or prevent the development or commercialization of our product candidates.

We may have conflicts with our collaborators, such as conflicts concerning the interpretation of preclinical or clinical data, the achievement of milestones, the interpretation of contractual obligations, payments for services, development obligations or the ownership of intellectual property developed during our collaboration. If any conflicts arise with any of our collaborators, such collaborator may act in a manner that is adverse to our best interests. Any such disagreement could result in one or more of the following, each of which could delay or prevent the development or commercialization of our product candidates, and in turn prevent us from generating revenues: unwillingness on the part of a collaborator to pay us milestone payments or royalties we believe are due to us under a collaboration, which could require us to raise additional capital; uncertainty regarding ownership of intellectual property rights arising from our collaborative activities, which could prevent us from entering into additional collaborations; unwillingness by the collaborator to cooperate in the development or manufacture of the product, including providing us with product data or materials; unwillingness on the part of a collaborator to keep us informed regarding the progress of its development and commercialization activities or to permit public disclosure of the results of those activities; initiating of litigation or alternative dispute resolution options by either party to resolve the dispute; or attempts by either party to terminate the agreement.

We may not successfully engage in strategic transactions, including any additional collaborations we seek, which could adversely affect our ability to develop and commercialize product candidates, impact our cash position, increase our expenses, and present significant distractions to our management.

From time to time, we may consider strategic transactions, such as additional collaborations, acquisitions of companies, asset purchases, and out- or in-licensing of product candidates or technologies that we believe will complement or augment our existing business. In particular, we will evaluate and, if strategically attractive, seek to enter into additional collaborations, including with major biotechnology or biopharmaceutical companies. The competition for collaborators is intense, and the negotiation process is time-consuming and complex. Any new collaboration may be on terms that are not optimal for us, and we may not be able to maintain any new collaboration if, for example, development or approval of a product candidate is delayed, sales of an approved product candidate do not meet expectations or the collaborator terminates the collaboration. In addition, a significant number of recent business combinations among large pharmaceutical companies has resulted in a reduced number of potential future strategic partners. Our collaborators may consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. Our ability to reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the strategic partner's resources and expertise, the terms and conditions of the proposed collaboration, and the proposed strategic partner's evaluation of a number of factors. These factors may include the design or results of clinical trials, the likelihood of approval by the FDA, EMA, or other applicable regulatory authorities, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. Moreover, if we acquire assets with promising markets or technologies, we may not be able to realize the benefit of acquiring such assets if we are not able to successfully integrate them with our existing technologies. We may encounter numerous difficulties in developing, testing, manufacturing, and marketing any new products resulting from a strategic acquisition that delay or prevent us from realizing their expected benefits or enhancing our business.

We cannot assure you that following any such collaboration, or other strategic transaction, we will achieve the expected synergies to justify the transaction. For example, such transactions may require us to incur non-recurring or other charges, increase our near- and long-term expenditures and pose significant integration or implementation challenges or disrupt our management or business. These transactions would entail numerous operational and financial risks, including exposure to unknown liabilities, disruption of our business and diversion of our management's time and attention in order to manage a collaboration or develop acquired products, product candidates or technologies, incurrence of substantial debt or dilutive issuances of equity securities to pay transaction consideration or costs, higher than expected collaboration, acquisition or integration costs, write-downs of assets or goodwill or impairment charges, increased amortization expenses, difficulty, and cost in facilitating the collaboration or combining the operations and personnel of any acquired business, impairment of relationships with key suppliers, manufacturers or customers of any acquired business due to changes in management and ownership, and the inability to retain key employees of any acquired business.

Accordingly, although there can be no assurance that we will undertake or successfully complete any transactions of the nature described above, any transactions that we do complete may be subject to the foregoing or other risks and would have a material and adverse effect on our business, financial condition, results of operations, and prospects. Conversely, any failure to enter any additional collaboration or other strategic transaction that would be beneficial to us could delay the development and potential commercialization of our product candidates and have a negative impact on the competitiveness of any product candidate that reaches market.

Risks Related to Our Business and Operations

The continued impact of the novel strain of coronavirus, SARS-CoV-2, which causes COVID-19 disease, could adversely impact our business, including our preclinical and clinical development activities.

Public health crises such as pandemics or similar outbreaks could adversely impact our business. The outbreak of a novel strain of coronavirus, which causes the disease called COVID-19, is a global pandemic. As a result of the COVID-19 pandemic, including the resurgence of cases relating to the spread of the Delta and Omicron variants, or similar pandemics, we may experience disruptions that could severely impact our business, manufacturing, preclinical development activities, preclinical studies and existing and planned clinical trial activities, including:

- delays or disruptions in preclinical development activities, including non-clinical experiments and investigational new drug application-enabling GLP standard toxicology studies due to unforeseen circumstances in supply chain;
- interruption or delays in the operations of the FDA and comparable foreign regulatory agencies, which may impact timelines for regulatory submission, trial initiation, and regulatory approval;
- interruption or delays in our CROs and collaborators meeting expected deadlines or complying with regulatory requirements related to preclinical development activities, preclinical studies, and clinical trial activities;
- interruptions of, or delays in receiving, supplies of our product candidates from our contract manufacturing organizations due to staffing shortages, productions slowdowns, limited availability of raw materials, or stoppages and disruptions in delivery systems;
- delays or difficulties in any planned clinical site initiation, including difficulties in obtaining IRB approvals, recruiting clinical site investigators and clinical site staff;
- delays or difficulties in enrolling patients in clinical trials;
- increased rates of patients withdrawing from any planned clinical trials following enrollment as a result of contracting COVID-19 or being forced to quarantine;
- diversion of healthcare resources away from the conduct of our preclinical development activities, preclinical studies and planned clinical trials, including the diversion of hospitals serving as clinical trial sites and potential clinical trial sites, and hospital staff supporting the conduct of clinical trial activities;
- interruption of planned key clinical trial activities, such as clinical trial site data monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others or interruption of clinical trial subject visits and study procedures (particularly any procedures that may be deemed non-essential), which may impact the integrity of subject data and planned clinical study endpoints;
- limitations on employee or collaborator resources that would otherwise be focused on the conduct of our preclinical development activities, preclinical studies and clinical trial activities, including because of sickness of employees or their families, the desire of employees to avoid contact with large groups of people, an increased reliance on working from home or mass transit disruptions; and
- reduced ability to engage with the medical and investor communities due to the cancellation of conferences scheduled throughout the year.

These and other factors arising from the COVID-19 pandemic could worsen in countries afflicted with COVID-19, or could return to countries where the pandemic has been partially contained, each of which could further adversely impact our ability to conduct preclinical development activities, preclinical studies and clinical trial activities and our business generally, and could have a material adverse impact on our operations and financial condition and results.

In addition, the trading prices for our common stock and other biopharmaceutical companies, as well as the broader equity and debt markets, have been highly volatile as a result of the COVID-19 pandemic and the resulting impact on economic activity. As a result, we may face difficulties raising capital when needed, and any such sales may be on unfavorable terms to us. Further, to the extent we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of existing stockholders will be diluted.

The extent to which the COVID-19 pandemic may impact our business, manufacturing, preclinical development activities, preclinical studies and clinical trial activities and will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of COVID-19, the duration of the pandemic, the potential for a second pandemic after it is contained, travel restrictions and actions to address the pandemic or treat its impact, such as social distancing and quarantines or lock-downs in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain and treat the disease.

We will need to grow our organization, and we may experience difficulties in managing our growth and expanding our operations, which could adversely affect our business.

As of December 31, 2021, we had approximately 91 full-time employees. As our development and commercialization plans and strategies develop, we expect to expand our employee base for managerial, operational, financial and other resources. In addition, we have limited experience in product development. As our product candidates enter and advance through preclinical studies and clinical trials, we will need to expand our development and regulatory capabilities and contract with other organizations to provide manufacturing and other capabilities for us. In the future, we expect to have to manage additional relationships with collaborators or partners, suppliers, and other organizations. Our ability to manage our operations and future growth will require us to continue to improve our operational, financial, and management controls, reporting systems, and procedures. We may not be able to implement improvements to our management information and control systems in an efficient or timely manner and may discover deficiencies in existing systems and controls. Our inability to successfully manage our growth and expand our operations could have a material and adverse effect on our business, financial condition, results of operations, and prospects.

Any inability to attract and retain qualified key management and technical personnel would impair our ability to implement our business plan.

Our success largely depends on the continued service of key management, advisors, and other specialized personnel. We currently do not maintain key person insurance on any of these individuals. The loss of one or more members of our management team or other key employees or advisors could delay our research and development programs and have a material and adverse effect on our business, financial condition, results of operations, and prospects. The relationships that our key managers have cultivated within our industry make us particularly dependent upon their continued employment with us. We are dependent on the continued service of our technical personnel because of the highly technical nature of our product candidates and technologies related to our Neoleukin platform, and the specialized nature of the regulatory approval process. Because our management team and key employees are not obligated to provide us with continued service, they could terminate their employment with us at any time without penalty.

Competition for skilled personnel in our market is intense and may limit our ability to hire and retain highly qualified personnel on acceptable terms or at all. We also face competition for personnel from other companies, universities, public and private research institutions, government entities and other organizations. Our future success will depend in large part on our continued ability to attract and retain other highly qualified scientific, technical and management personnel, as well as personnel with expertise in clinical testing, manufacturing, governmental regulation, and commercialization. If we are unable to continue to attract and retain high-quality personnel, the rate and success at which we can discover and develop product candidates will be limited which could have a material and adverse effect on our business, financial condition, results of operations and prospects.

Our relationships with healthcare professionals, principal investigators, consultants, customers (actual and potential) and third-party payors are and will be subject, directly and indirectly, to applicable anti-kickback, fraud and abuse, privacy, transparency and other healthcare laws and regulations, which could expose us to penalties, including without limitation, civil, criminal and administrative sanctions, civil penalties, damages, fines, disgorgement, individual imprisonment, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, integrity obligations, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings and the curtailment or restructuring of our operations.

As a biopharmaceutical company, even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are and will be applicable to our future arrangements with third-party payors and customers who are in a position to purchase, recommend and/or prescribe our product candidates for which we obtain marketing approval. These broadly applicable fraud and abuse and other healthcare laws and regulations may constrain our future business or financial arrangements and relationships with healthcare professionals, principal investigators, consultants, customers, and third-party payors and other entities, including our marketing practices, educational programs and pricing policies. Restrictions under applicable federal and state healthcare laws and regulations that may affect our ability to operate include, but are not limited to, the following:

- the federal Anti-Kickback Statute, which, among other things, prohibits persons from knowingly and willfully soliciting, offering, receiving or providing paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;
- federal civil and criminal false claims laws, including the federal civil False Claims Act, and civil monetary penalty laws impose criminal and civil penalties, including through civil whistleblower or qui tam actions, among other things, prohibits individuals or entities from knowingly presenting, or causing to be presented, to the federal government, including the Medicare and Medicaid programs, claims for payment or approval that are false or fraudulent or from knowingly making a false statement to improperly avoid, decrease or conceal an obligation to pay money to the federal government;
- HIPAA, which, among other things, imposes criminal liability for knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or to obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g. public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of or payment for healthcare benefits, items or services relating to healthcare matters;
- HIPAA, as amended by HITECH, and its implementing regulations, which also imposes certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without the appropriate authorization by entities subject to the law, such as health plans, healthcare clearinghouses and healthcare providers;

- the federal Physician Payments Sunshine Act and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to CMS, information related to "payments or other transfers of value" made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), physician assistants, certain types of advance practice nurses and teaching hospitals, and applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by physicians (as defined above) and their immediate family members and payments or other "transfers of value" to such physician owners and their immediate family members; and
- analogous local, state and foreign laws and regulations, including: state anti-kickback and false claims laws which may apply to our business practices, including, but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by state governmental and non-governmental third-party payors, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government; local, state and foreign laws that require drug manufacturers to track gifts and other remuneration and items of value provided to healthcare professionals and entities and file reports relating to pricing and marketing information and/or register their pharmaceutical sales representatives; and local, state and foreign laws that govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and often are not pre-empted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our internal operations and any business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Recent healthcare reform legislation has also strengthened these laws. For example, the Affordable Care Act, among other things, amends the intent requirement of the federal Anti-Kickback Statute, such that a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the Affordable Care Act codified case law that a claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations, agency guidance, or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental laws and regulations that may apply to us, we may be subject to penalties, including without limitation, significant civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, integrity obligations, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings, and the curtailment or restructuring of our operations. If any physicians or other healthcare providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. Moreover, we expect there will continue to be federal, state, local and foreign laws and regulations, proposed and implemented, that could impact our operations and business. The extent to which future legislation or regulations, if any, relating to healthcare fraud abuse laws or enforcement, may be enacted or what effect such legislation or regulation would have on our business remains uncertain.

We may form strategic alliances in the future, and we may not realize the benefits of such alliances.

We may form strategic alliances, create joint ventures or collaborations or enter into licensing arrangements with third parties that we believe will complement or augment our existing business. These relationships or those like them may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our stockholders or disrupt our management and business. In addition, we face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for any future drug candidates and programs because our research and development pipeline may be insufficient, our drug candidates and programs may be deemed to be at too early a stage of development for collaborative effort and third parties may not view our drug candidates and programs as having the requisite potential to demonstrate safety and efficacy. If we license products or businesses, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture. We cannot be certain that, following a strategic transaction or license, we will achieve the revenues or specific net income that justifies such transaction. Any delays in entering into new strategic partnership agreements related to our drug candidates could also delay the development and commercialization of our drug candidates and reduce their competitiveness even if they reach the market.

Our employees, independent contractors, principal investigators, CROs, consultants, vendors and collaboration partners may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of fraud or other misconduct by our employees, independent contractors, principal investigators, CROs, consultants, vendors and collaboration partners, including intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards we have established, comply with federal and state data privacy and security, fraud and abuse and other healthcare laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Specifically, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use or misrepresentation of information obtained in the course of clinical trials or creating fraudulent data in our pre-clinical studies or clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct for our directors, officers and employees, but it is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, results of operations, financial condition and cash flows from future prospects, including the imposition of significant fines or other sanctions.

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

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

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

We currently maintain product liability insurance coverage for our clinical trials, but the amount may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage for each new clinical trial we begin and if we successfully commercialize any product candidate. 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.

We may engage in future acquisitions that could disrupt our business, cause dilution to our stockholders and harm our business, results of operations, financial condition and cash flows and future prospects.

We may, in the future, make acquisitions of, or investments in, companies that we believe have products or capabilities that are a strategic or commercial fit with our future product candidates and business or otherwise offer opportunities for our company. In connection with these acquisitions or investments, we may:

- issue stock that would dilute our stockholders' percentage of ownership;
- incur debt and assume liabilities; and
- incur amortization expenses related to intangible assets or incur large and immediate write-offs.

We may not be able to complete acquisitions on favorable terms, if at all. If we do complete an acquisition, we cannot assure you that it will ultimately strengthen our competitive position or that it will be viewed positively by customers, financial markets or investors. Furthermore, future acquisitions could pose numerous additional risks to our operations, including:

- problems integrating the purchased business, products or technologies;
- increases to our expenses;
- the failure to discover undisclosed liabilities of the acquired asset or company;
- diversion of management's attention from their day-to-day responsibilities;
- harm to our operating results or financial condition;
- entrance into markets in which we have limited or no prior experience; and
- potential loss of key employees, particularly those of the acquired entity.

We may not be able to complete any acquisitions or effectively integrate the operations, products or personnel gained through any such acquisition.

Our ability to use our U.S. net operating losses to offset future taxable income will be subject to Section 382 limitations and may be limited by other factors.

As of December 31, 2021, we had U.S. net operating losses, or NOLs, of $108.2 million, for federal tax purposes, for which we have recorded a full valuation allowance, and R&D credit carryovers of $2.4 million, which may be offset by future taxable income. The R&D credit carryforwards and certain of our NOL carryforwards will expire in various years beginning in 2028, if not utilized. Unused losses incurred in taxable years beginning on or prior to December 31, 2017 will carry forward to offset future taxable income, if any, until such unused losses expire. Under the Tax Cuts and Jobs Act, as modified by the CARES Act, unused U.S. federal NOLs generated in tax years beginning after December 31, 2017, will not expire and may be carried forward indefinitely but the deductibility of such federal NOLs (particularly those generated in taxable years beginning after December 31, 2020) in taxable years beginning after December 31, 2020, is limited to 80% of current year taxable income. It is uncertain if and to what extent various states will conform to the Tax Cuts and Jobs Act or the CARES Act. Furthermore, utilization of certain of our NOLs and R&D credit carryforwards will be subject to annual limitations on their use as a result of ownership changes under the rules of Sections 382 and 383 of the Internal Revenue Code, or the Code that have historically occurred. Based on our Section 382 analysis to date, we underwent ownership changes in August 2015 and August 2019. As a result of these ownership changes, we believe that certain of our NOLs will be likely to expire before they are able to be utilized under Section 382. In addition, we may experience ownership changes in the future as a result of future changes in our stock ownership, some of which changes are outside of our control, and as a result, our ability to utilize NOL and R&D credit carryforwards could become further limited under Sections 382 and 383 and the tax benefits related to our NOLs and R&D credits may be diminished or lost. Any such disallowances may result in greater tax liabilities than we would incur in the absence of such a limitation and any increased liabilities could adversely affect our business, results of operations, financial condition, cash flow and future prospects. As a result, even if we attain profitability, we may be unable to use all or a material portion of our NOLs and other tax attributes, which could adversely affect our future cash flows.

Risks Related to Intellectual Property

If we are not able to obtain, maintain, and enforce patent protection and other intellectual property rights for our product candidates, our Neoleukin platform technology, or other proprietary technologies we may develop, development and commercialization of our product candidates may be adversely affected.

Our success depends in part on our ability to obtain and maintain patents and other forms of intellectual property rights, including in-licenses of intellectual property rights of others, for our product candidates, as well as our ability to preserve our trade secrets, to prevent third parties from infringing upon our proprietary rights and to operate without infringing upon the proprietary rights of others. Under our License Agreement with the University of Washington, dated July 8, 2019, as amended on October 29, 2020, effective July 24, 2020, and again on December 27, 2021, effective December 15, 2021 we have an exclusive license to develop and commercialize products covered by patent applications with claims covering the composition of matter of key molecule families as well as methods of using the computational algorithms that form the basis of the Neoleukin platform. However, we may not be able to apply for patents on certain aspects of our product candidates in a timely fashion or at all. Further, we may not be able to prosecute all necessary or desirable patent applications, or maintain, enforce, and license any patents that may issue from such patent applications, at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. We may not have the right to control the preparation, filing, and prosecution of all patent applications that we license from third parties, or to maintain the rights to patents licensed to third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. Patents we currently hold, or in the future may obtain, may not be sufficiently broad to prevent others from using our technology or from developing competing products and technology. There is no guarantee that any of our pending patent applications will result in issued or granted patents, that any of our future issued or granted patents will not later be found to be invalid or unenforceable or that any future issued or granted patents will include claims that are sufficiently broad to cover our product candidates or to provide meaningful protection from our competitors. Moreover, the patent position of biotechnology and biopharmaceutical companies can be highly uncertain because it involves complex legal and factual questions. We will be able to protect our proprietary rights from unauthorized use by third parties only to the extent that our current and future proprietary technology and product candidates are covered by valid and enforceable patents or are effectively maintained as trade secrets. If third parties disclose or misappropriate our proprietary rights, it may materially and adversely affect our position in the market.

Our pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications. Assuming the other requirements for patentability are met, currently, the first to file a patent application is generally entitled to the patent. However, prior to March 16, 2013, in the United States, the first to invent was entitled to the patent. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in our pending patent applications, or that we were the first to file for patent protection of such inventions.

The U.S. Patent and Trademark Office, or USPTO, and various foreign governmental patent agencies require compliance with a large number of procedural, documentary, fee payment and other provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case. The standards applied by the USPTO and foreign patent offices in granting patents are not always applied uniformly or predictably. For example, there is no uniform worldwide policy regarding patentable subject matter or the scope of claims allowable in biotechnology and biopharmaceutical patents. As such, we do not know the degree of future protection that we will have on our proprietary products and technology. The process of obtaining patents is time consuming, expensive and sometimes unpredictable.

Once granted, for a given period after allowance or grant patents may remain open to opposition, interference, re-examination, post-grant review, *inter partes* review, nullification, or derivation action in court or before patent offices or similar proceedings, during which time third parties can raise objections against such initial grant. Such proceedings may continue for a protracted period of time and an adverse determination in any such proceedings could reduce the scope of the allowed or granted claims thus attacked, or could result in our patents being invalidated in whole or in part, or being held unenforceable, which could allow third parties to commercialize our product candidates and compete directly with us without payment to us. In addition, there can be no assurance that:

- others will not or may not be able to make, use or sell compounds that are the same as or similar to our product candidates but that are not covered by the claims of the patents that we own or license;
- we or our licensors, or our future collaborators are the first to make the inventions covered by each of our issued patents and pending patent applications that we own or license;

- we or our licensors, or our future collaborators are the first to file patent applications covering certain aspects of our inventions;
- others will not independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- a third party may not challenge our patents and, if challenged, a court would hold that our patents are valid, enforceable and infringed;
- any issued patents that we own or have licensed or that we may license in the future will provide us with any competitive advantages, or will not be challenged by third parties;
- we may develop additional proprietary technologies that are patentable;
- the patents of others will not have a material or adverse effect on our business, financial condition, results of operations, and prospects; and
- our competitors do not conduct research and development activities in countries where we do not have enforceable patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets.

If we or our licensors or collaborators fail to maintain patent applications and later-issued patents covering our product candidates, our competitors might be able to enter the market, which could have a material and adverse effect on our business, financial condition, results of operations, and prospects. In addition, if the breadth or strength of protection provided by our patent applications and later-issued patents is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

We could be required to incur significant expenses to strengthen our intellectual property rights, and our intellectual property rights may be inadequate to protect our competitive position.

The patent prosecution process is expensive and time-consuming, and we or our future potential licensors may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we or our future potential licensors will fail to identify patentable aspects of inventions made in the course of our development and commercialization activities before it is too late to obtain patent protection on them. Further, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. We expect to seek extensions of patent terms in the United States and, if available, in other countries where we are prosecuting patents. In the United States, the Drug Price Competition and Patent Term Restoration Act of 1984 permits a patent term extension of up to five years beyond the expiration of the patent. However, the applicable authorities, including the FDA in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. The laws of foreign countries may not protect our rights to the same extent as the laws of the United States, and these foreign laws may also be subject to change. For example, methods of treatment and manufacturing processes may not be patentable in certain jurisdictions. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing or in some cases not at all. Therefore, we cannot be certain that we or our licensors were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we or our licensors were the first to file for patent protection of such inventions.

Our patent applications and the enforcement or defense of our issued patents may be impacted by the application of or changes in U.S. and foreign standards.

The standards that the USPTO and foreign patent offices use to grant patents are not always applied predictably or uniformly and can change. Consequently, our pending patent applications may not be allowed and, if allowed, may not contain the type and extent of patent claims that will be adequate to conduct our business as planned. Additionally, any issued patents we currently own or obtain in the future may have a shorter patent term than expected or may not contain claims that will permit us to stop competitors from using our technology or similar technology or from copying our product candidates. Similarly, the standards that courts use to interpret patents are not always applied predictably or uniformly and may evolve, particularly as new technologies develop. In addition, changes to patent laws in the United States or other countries may be applied retroactively to affect the validation enforceability, or term of our patent. For example, the U.S. Supreme Court has recently modified some legal standards applied by the USPTO in examination of U.S. patent applications, which may decrease the likelihood that we will be able to obtain patents and may increase the likelihood of challenges to patents we obtain or license. In addition, changes to the U.S. patent system have come into force under the Leahy-Smith America Invents Act, or the Leahy-Smith Act, which was signed into law in September 2011. The Leahy-Smith Act included a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. In particular, under the Leahy-Smith Act, the United States transitioned in March 2013 to a "first to file" system in which the first inventor to file a patent application will be entitled to the patent. Third parties are allowed to submit prior art before the issuance of a patent by the USPTO, and may become involved in opposition, derivation, reexamination, inter-partes review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, which could adversely affect our competitive position.

While we cannot predict with certainty the impact the Leahy-Smith Act or any potential future changes to the U.S. or foreign patent systems will have on the operation of our business, the Leahy-Smith Act and such future changes could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, results of operations, financial condition and cash flows and future prospects.

Obtaining and maintaining any patent protection we may receive will depend on compliance with various procedural, document submissions, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance and annuity fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or our future licensors fail to maintain the patents and patent applications covering our product candidates, our competitive position would be adversely affected.

We may be subject to claims by third parties claiming ownership of what we regard as our own intellectual property, which may prevent, delay or otherwise interfere with our product discovery and development efforts.

Many of our employees, including our senior management, were previously employed at universities or at other biotechnology or biopharmaceutical companies, including our competitors or potential competitors. Some of these employees, including members of our senior management, executed proprietary rights, non-disclosure and non-competition agreements, in connection with such previous employment. Although we try to ensure that our employees 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 these employees, have used or disclosed confidential information or intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. We are not aware of any threatened or pending claims related to these matters or concerning the agreements with our senior management, but in the future litigation may be necessary to defend against such claims. In addition, third parties may from time to time make claims over what we regard as our intellectual property, or we may get into disputes with licensors or licensees of our intellectual property rights over the interpretation of the license terms. If a third party claims that we infringe, misappropriate or otherwise violate their intellectual property rights, we may face a number of issues, including, but not limited to:

- infringement and other intellectual property claims that, regardless of merit, may be expensive and time-consuming to litigate and may divert our management's attention from our core business;

- substantial damages for infringement, which we may have to pay if a court decides that the product candidate or technology at issue infringes on or violates the third party's rights, and, if the court finds that the infringement was willful, we could be ordered to pay treble damages plus the patent owner's attorneys' fees;
- a court prohibiting us from developing, manufacturing, marketing or selling our product candidates, or from using our proprietary technologies, unless the third-party licenses its product rights or proprietary technology to us, which it is not required to do, on commercially reasonable terms or at all;
- if a license is available from a third party, we may have to pay substantial royalties, upfront fees and other amounts, and/or grant cross-licenses to intellectual property rights for our product candidates;
- the requirement that we redesign our product candidates or processes so they do not infringe, which may not be possible or may require substantial monetary expenditures and time; and
- there could be public announcements of the results of hearings, motions, or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

Our licensors may have the right to terminate their license agreements with us or pursue damages or other legal remedies. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel or sustain damages. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms or at all. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or could otherwise have a material adverse effect on our business, financial condition, results of operations and prospects.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time-consuming and unsuccessful and could result in a finding that such patents are unenforceable or invalid.

Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that one or more of our patents is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question.

In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. These types of mechanisms include re-examination, post-grant review, inter partes review, interference proceedings, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). These types of proceedings could result in revocation or amendment to our patents such that they no longer cover our product candidates. The outcome for any particular patent following legal assertions of invalidity and unenforceability is unpredictable. If a defendant were to prevail on a legal assertion of invalidity and/ or unenforceability, or if we are otherwise unable to adequately protect our rights, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Defense of these types of claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business.

Conversely, we may choose to challenge the patentability of claims in a third party's U.S. patent by requesting that the USPTO review the patent claims in re-examination, post-grant review, inter partes review, interference proceedings, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings), or we may choose to challenge a third party's patent in patent opposition proceedings in the Canadian Intellectual Property Office, or CIPO, the European Patent Office, or EPO, or another foreign patent office. Even if successful, the costs of these opposition proceedings could be substantial, and may consume our time or other resources. If we fail to obtain a favorable result at the USPTO, CIPO, EPO or other patent office then we may be exposed to litigation by a third party alleging that the patent may be infringed by our product candidates or proprietary technologies.

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

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

In addition to seeking patents for some of our technology and products, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturing organizations, consultants, advisors and other third parties. We also generally enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts both within and outside the United States may be less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position.

Although we expect 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 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 or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Additionally, 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, as part of its Transparency Initiative, is currently 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 currently clear how the FDA's disclosure policies may change in the future, if at all.

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

Filing, prosecuting and defending patents on our product candidates throughout the world would be prohibitively expensive. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we and our licensors or future collaborators may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and may export otherwise infringing products to territories where we have patent protection, but where enforcement is not as strong as that in the United States. These products may compete with our products in jurisdictions where we do not have any issued patents and our patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful.

The requirements for patentability may differ in certain countries, particularly developing countries. For example, unlike other countries, China has a heightened requirement for patentability, and specifically requires a detailed description of medical uses of a claimed drug. In India, unlike the United States, there is no link between regulatory approval of a drug and its patent status. Furthermore, generic or biosimilar drug manufacturers or other competitors may challenge the scope, validity or enforceability of our or our licensors' or collaborators' patents, requiring us or our licensors or collaborators to engage in complex, lengthy and costly litigation or other proceedings. Generic or biosimilar drug manufacturers may develop, seek approval for, and launch biosimilar versions of our products. In addition to India, certain countries in Europe and developing countries, including China, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In those countries, we and our licensors or collaborators may have limited remedies if patents are infringed or if we or our licensors or collaborators are compelled to grant a license to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. Accordingly, our and our licensors' or collaborators' efforts to enforce intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we own or license.

Intellectual property rights do not necessarily provide sufficient protection of our technology or address all potential threats to any competitive advantage we may have.

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 compounds that are the same as or similar to our future product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed.
- We or any of our licensors or strategic partners might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed.
- We or any of our licensors or strategic partners 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.
- It is possible that there are prior public disclosures that could invalidate our owned or exclusively licensed patents, as the case may be, or parts of our owned or exclusively licensed patents.
- It is possible that there are unpublished applications or patent applications maintained in secrecy that may later issue with claims covering our product candidates or technology similar to ours.
- It is possible that our owned or exclusively licensed patents or patent applications omit one or more individuals that should be listed as inventors or include one or more individuals that should not be listed as inventors, which may cause these patents or patents issuing from these patent applications to be held invalid or unenforceable or such omitted individuals may grant licenses to third parties.
- Issued patents that we own or have exclusively licensed may not provide us with any competitive advantages, or may be held invalid or unenforceable, as a result of legal challenges by our competitors.
- Our competitors might conduct research and development activities in the United States and other countries that provide a safe harbor from patent infringement claims for certain research and development activities, as well as 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 have engaged in scientific collaborations in the past and will continue to do so in the future and our collaborators may develop adjacent or competing products that are outside the scope of our patents.
- We may not develop additional proprietary technologies that are patentable.
- The patents of others may have an adverse effect on our business.

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

The growth of our business may depend in part on our ability to acquire, license or use third-party proprietary rights.

For example, our product candidates may require specific formulations to work effectively and efficiently, we may develop product candidates containing pre-existing pharmaceutical compounds, or we may be required by the FDA or comparable foreign regulatory authorities to provide a companion diagnostic test or tests with our product candidates, any of which could require us to obtain rights to use intellectual property held by third parties. In addition, with respect to any patents we may co-own with third parties, we may require licenses to such co-owners interest to such patents. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties we identify as necessary or important in our business operations. In addition, we may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. Were that to happen, we may need to cease use of the compositions or methods covered by those third-party intellectual property rights, and may need to seek to develop alternative approaches that do not infringe on those intellectual property rights, which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. Even if we are able to obtain a license, it may be nonexclusive, which means our competitors may also receive access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology.

We sometimes collaborate with academic institutions to accelerate our preclinical research or development under written agreements with these institutions. In certain cases, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Even if we hold such an option, we may be unable to negotiate a license from the institution within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to others, potentially blocking our ability to pursue our program.

The licensing and acquisition of third-party intellectual property rights is a competitive area, and companies that may be more established or have greater resources than we do may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. There can be no assurance that we will be able to successfully complete these types of negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to develop or market. If we are unable to successfully obtain rights to required third-party intellectual property or to maintain the existing intellectual property rights we have, we may have to abandon development of certain programs and our business financial condition, results of operations and prospects could suffer.

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

Inventions contained within some of our in-licensed patents and patent applications may have been made using U.S. government funding or other non-governmental funding. As a result, the U.S. government may have certain rights to intellectual property embodied in our current or future product candidates pursuant to the Bayh-Dole Act of 1980, or Bayh-Dole Act, and implementing regulations. We rely on our licensors to ensure compliance with applicable obligations arising from such funding, such as timely reporting, an obligation associated with in-licensed patents and patent applications. The failure of our licensors to meet their obligations may lead to a loss of rights or the unenforceability of relevant patents. For example, the government could have certain rights in such in-licensed patents, including a non-exclusive license authorizing the government to use the invention or to have others use the invention on its behalf for non-commercial purposes. In addition, our rights in such in-licensed government-funded inventions may be subject to certain requirements to manufacture products embodying such inventions in the United States. Any of the foregoing could harm our business, financial condition, results of operations and prospects significantly.

Risks Related to Ownership of Our Common Stock

Our stock price has been and will likely continue to be volatile and may decline regardless of our operating performance, resulting in substantial losses for investors.

The trading price of our common stock has been, and is likely to continue to be, volatile for the foreseeable future. The trading price of our common stock could be subject to wide fluctuations in response to various factors, some of which are beyond our control. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this report, these factors include:

- the success of competitive products or technologies;
- regulatory actions with respect to our products or our competitors' products;
- actual or anticipated changes in our growth rate relative to our competitors;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- results of clinical trials, including both safety and efficacy, of any of our current or future product candidates or those of our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our future product candidates or clinical development programs;
- the results of our efforts to in-license or acquire additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- share price and volume fluctuations attributable to inconsistent trading volume levels of our shares;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or our other stockholders;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors; and
- general economic, industry and market conditions, including market volatility and economic uncertainty related to the COVID-19 pandemic.

In addition, the stock market in general, and pharmaceutical and biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. The realization of any of these risks or any of a broad range of other risks, including those described in this "Risk Factors" section and elsewhere in this report, could have a dramatic and material adverse impact on the market price of our common stock.

Some provisions of our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our amended and restated certificate of incorporation, or certificate of incorporation, and amended and restated bylaws, or bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders, or remove our current management. These include provisions that:

- permit our board of directors to issue up to 5,000,000 shares of preferred stock, with any rights, preferences and privileges as they may designate;
- provide that all vacancies on our board of directors, including as a result of newly created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- require that any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and not be taken by written consent;
- provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide advance notice in writing, and also specify requirements as to the form and content of a stockholder's notice;
- not provide for cumulative voting rights, thereby allowing the holders of a majority of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election; and
- provide that special meetings of our stockholders may be called only by the board of directors or by such person or persons requested by a majority of the board of directors to call such meetings.

These provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, who are responsible for appointing the members of our management. Because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which may discourage, delay or prevent someone from acquiring us or merging with us whether or not it is desired by or beneficial to our stockholders. Under Delaware law, a corporation may not, in general, engage in a business combination with any holder of 15% or more of its capital stock unless the holder has held the stock for three years or, among other things, the board of directors has approved the transaction. Any provision of our certificate of incorporation or bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

The exclusive forum provisions in our certificate of incorporation and bylaws may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or any of our directors, officers, or other employees, which may discourage lawsuits with respect to such claims.

Our certificate of incorporation, to the fullest extent permitted by law, provides that the Court of Chancery of the State of Delaware will be the exclusive forum for: 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 pursuant to the Delaware General Corporation Law, or the DGCL, our certificate of incorporation, or our bylaws; or any action asserting a claim against us that is governed by the internal affairs doctrine. This exclusive forum provision does not apply to suits brought to enforce a duty or liability created by the Securities Exchange Act of 1934, as amended, or the Exchange Act. It could apply, however, to a suit that falls within one or more of the categories enumerated in the exclusive forum provision and asserts claims under the Securities Act of 1933, as amended, or the Securities Act, inasmuch as Section 22 of the Securities Act, creates concurrent jurisdiction for federal and state courts over all suits brought to enforce any duty or liability created by the Securities Act or the rule and regulations thereunder. There is uncertainty as to whether a court would enforce such provision with respect to claims under the Securities Act, and our stockholders will not be deemed to have waived our compliance with the federal securities laws and the rules and regulations thereunder.

In April 2020, we amended and restated our bylaws to provide that the federal district courts of the United States of America will, to the fullest extent permitted by law, be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, or a Federal Forum Provision. Our decision to adopt a Federal Forum Provision followed a decision by the Supreme Court of the State of Delaware holding that such provisions are facially valid under Delaware law.

While there can be no assurance that federal or state courts will follow the holding of the Delaware Supreme Court or determine that the Federal Forum Provision should be enforced in a particular case, application of the Federal Forum Provision means that suits brought by our stockholders to enforce any duty or liability created by the Securities Act must be brought in federal court and cannot be brought in state court.

These choice of 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 any of our directors, officers, or other employees, which may discourage lawsuits with respect to such claims. Alternatively, if a court were to find the choice of forum provisions contained in our restated certificate of incorporation or amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could harm our business, results of operations and financial condition.

We are no longer an "emerging growth company," however, we are still a "smaller reporting company," and the reduced disclosure requirements applicable to smaller reporting companies may make our common stock less attractive to investors.

Although we ceased to be an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or JOBS Act, on December 31, 2019, we are a "smaller reporting company," meaning that the market value of our stock held by non-affiliates is less than $700.0 million and our annual revenue is less than $100.0 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 stock held by non-affiliates is less than $250.0 million or (ii) our annual revenue is less than $100.0 million during the most recently completed fiscal year and the market value of our stock held by non-affiliates is less than $700.0 million. As a smaller reporting company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies. Specifically, 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. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

We may become a "large accelerated filer" and have to comply with more rigorous disclosure and reporting requirements and regulations.

If we cease to be a "smaller reporting company" or a "non-accelerated filer" in the future, we may be subject to certain disclosure requirements that are applicable to other public companies that had not been applicable to us previously. These requirements include:

- compliance with the auditor attestation requirements in the assessment of our internal control over financial reporting once we are an accelerated filer or large accelerated filer;
- compliance with any requirement that may be adopted by the PCAOB regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements; and
- full disclosure and analysis obligations regarding executive compensation.

There can be no assurance that we will be able to comply with the applicable regulations in a timely manner, if at all. Inability to comply with these regulations could impact our ability to raise additional capital.

General Risk Factors

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

The trading price of our common stock has been and will continue to be volatile. In the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

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

Our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates together beneficially own a majority of our outstanding voting stock. These stockholders are able to determine the outcome of all matters requiring stockholder approval. For example, these stockholders are able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders. The interests of this group of stockholders may not always coincide with your interests or the interests of other stockholders and they may act in a manner that advances their best interests and not necessarily those of other stockholders, including seeking a premium value for their common stock, and might affect the prevailing market price for our common stock.

If we fail to maintain an effective system of internal control over financial reporting in the future, we may not be able to accurately report our business, results of operations, financial condition and cash flows and future prospects, which may adversely affect investor confidence in us and, as a result, the value of our common stock.

The Sarbanes-Oxley Act requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures and that we furnish a report by management on, among other things, the effectiveness of our internal control over financial reporting. This assessment needs to include disclosure of any material weaknesses identified by our management in our internal control over financial reporting. A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting that results in more than a reasonable possibility that a material misstatement of annual or interim financial statements will not be prevented or detected on a timely basis. Section 404 of the Sarbanes-Oxley Act also generally requires an attestation from our independent registered public accounting firm on the effectiveness of our internal control over financial reporting. However, for as long as we are not an accelerated filer or large accelerated filer, we intend to take advantage of the exemption permitting us not to comply with the independent registered public accounting firm attestation requirement.

Our compliance with Section 404 will require that we incur substantial accounting expense and expend significant management efforts. We currently do not have an internal audit group, and we will need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge and compile the system and process documentation necessary to perform the evaluation needed to comply with Section 404. We may not be able to complete our evaluation, testing and any required remediation in a timely fashion. During the evaluation and testing process, if we fail to identify and to remediate any significant deficiencies or material weaknesses that may be identified, or encounter problems or delays in the implementation of internal control over financial reporting, we will be unable to assert that our internal control over financial reporting is effective. We cannot assure you that there will not be material weaknesses or significant deficiencies in our internal control over financial reporting in the future. Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations or cash flows. If we are unable to conclude that our internal control over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness or significant deficiency in our internal control over financial reporting, we could lose investor confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by the Nasdaq Stock Market, or Nasdaq, the SEC or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets.

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

We are subject to the periodic reporting requirements of the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

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

Our internal computer and information systems, or those used by our CROs, or other contractors or consultants, may fail or suffer security incidents (e.g., cyber-attacks) or other technical failures, which could result in a material disruption of our development programs and may result in extensive and costly legal compliance requirements.

Our de novo protein technology depends on sophisticated computational facilities and storage of vast amounts of data which could be lost or stolen. In the ordinary course of our business, we collect, store, and transmit confidential information, including intellectual property, proprietary business information and personal information. Despite the implementation of appropriate security measures, our internal computer and information systems and those of our current and any future CROs, and other contractors or consultants may become vulnerable to damage from security incidents (such as data breaches, viruses or other malicious code, coordinated attacks, data loss, phishing attacks, ransomware, denial of service attacks, or other security or information technology incidents caused by threat actors, technological vulnerabilities or human error), natural disasters, terrorism, war, and telecommunication/electrical failures.

While we have not experienced any such material system failure or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations. For example, the loss of data from completed or future preclinical studies and clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third parties for the manufacture of our product candidates and to conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed, and the further development and commercialization of our product candidates could be significantly delayed.

Our internal and outsourced information technology systems and infrastructure are also vulnerable to damage from natural disasters, terrorism, war, telecommunication and electrical failures. System failures or outages, including any potential disruptions due to significantly increased global demand on certain cloud-based systems during the COVID-19 pandemic, could compromise our ability to perform our day-to-day operations, which could harm our ability to conduct business or delay our financial reporting. Such failures could materially adversely affect our operating results and financial condition.

Although we devote resources to protect our information systems, we realize that cyberattacks resulting in a security incident are a threat, and there can be no assurance of our efforts will prevent information security breaches that would result in business, legal, financial, or reputational harm to the Company, or would have a material adverse effect on our results of operations and financial condition. A successful cyberattack could cause serious negative consequences for us, including, without limitation, the disruption of operations, the misappropriation of confidential business information, including financial information, trade secrets, financial loss and the disclosure of corporate strategic plans. The COVID-19 pandemic is generally increasing the attack surface available to criminals, as more companies and individuals work online and work remotely, and as such, the risk of a cybersecurity incident potentially occurring, and our investment in risk mitigations against such an incident, is increasing.

Federal, state, and foreign government requirements include obligations of companies to notify regulators and/or individuals of security breaches involving personally identifiable information, which could result from breaches experienced by us or by our vendors, contractors, or organizations with which we have formed strategic relationships. Even though we may have contractual protections with such vendors, contractors, or other organizations, notifications and follow-up actions related to a security breach could impact our reputation and cause us to incur significant costs. Any failure to prevent or mitigate security breaches or improper access to, use, disclosure or other misappropriation of our data or consumers' personal data could result in significant legal liability, such as under state breach notification laws, federal law (including HIPAA/HITECH), and international law (e.g., GDPR). 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 and possible government oversight. Our failure to comply with such laws or to adequately secure the information we hold could result in significant liability or reputational harm and, in turn, a material adverse effect on our client base, member base and revenue. Further, if we are unable to generate or maintain access to essential patient samples or data for our research and development and manufacturing activities for our programs, our business could be materially adversely affected.

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

Our operations could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics such as the COVID-19 pandemic and other natural or manmade disasters or business interruptions, for which we are predominantly self-insured. We do not carry insurance for all categories of risk that our business may encounter. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses. We rely on third-party manufacturers to produce our product candidates. Our ability to obtain clinical supplies of product candidates could be disrupted, if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption. The ultimate impact on us, our significant suppliers and our general infrastructure of being consolidated in certain geographical areas is unknown, but our operations and financial condition could suffer in the event of a major earthquake, fire or other natural disaster. In addition, the long-term effects of climate change on general economic conditions and the pharmaceutical industry in particular are unclear, and may heighten or intensify existing risk of natural disasters. Further, any significant uninsured liability may require us to pay substantial amounts, which would adversely affect our business, results of operations, financial condition and cash flows from future prospects.

We have incurred and will incur increased costs as a result of operating as a public company, and our management is required to devote substantial time to new compliance initiatives.

As a public company, we have incurred and will incur significant legal, accounting and other expenses that we did not incur as a private company, and these expenses will likely increase even more given we are no longer an "emerging growth company." We are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Protection Act, as well as rules adopted, and to be adopted, by the SEC and Nasdaq. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have substantially increased our legal and financial compliance costs and made some activities more time-consuming and costly. The increased costs will increase our consolidated net loss. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements.

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

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

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

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock.

We have in the past and may in the future grant rights to some of our stockholders that require us to register the resale of our common stock or other securities on behalf of these stockholders and/or facilitate public offerings of our securities held by these stockholders, including in connection with potential future acquisition or capital-raising transactions. For example, in connection with our public offering of common stock on September 19, 2016, we entered into a registration rights agreement with the Baker Entities that together, based on information available to us, collectively beneficially owned approximately 45.1% of our common stock as of September 19, 2016. Under the registration rights agreement, we agree that, if at any time and from time to time after December 19, 2016, the Baker Entities demand that we register their shares of our common stock for resale under the Securities Act, we would be obligated to effect such registration. On January 6, 2017, pursuant to the registration rights agreement, we registered for resale, from time to time, up to 10,536,092 shares of our common stock held by the Baker Entities. Our registration obligations under this registration rights agreement cover all shares now held or hereafter acquired by the Baker Entities, would be in effect for up to ten years, and would include our obligation to facilitate certain underwritten public offerings of our common stock by the Baker Entities in the future. If the Baker Entities or any other holders of registration rights with respect to our common stock, by exercising their registration and/or underwriting rights or otherwise, sell a large number of our shares, or the market perceives that the Baker Entities or such holders intend to sell a large number of our shares, this could adversely affect the market price of our common stock. We have registered all currently reserved shares of common stock that we may issue under our equity compensation plans and intend to register in the future any additional reserved or issued shares of common stock. These registered shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates. We have also filed a shelf registration statement covering the sale of up to $400.0 million of any combination of our common stock, preferred stock, debt securities, or warrants and may conduct one or more sales of securities pursuant to such registration statement, from time to time. In November 2021, we entered into an ATM "at-the-market" Equity Offering Sales Agreement, or Sales Agreement, with BofA Securities, Inc., or BofA, pursuant to which, from time to time, we may offer and sell through BofA up to $40.0 million of the common stock registered under the shelf registration statement pursuant to one or more "at the market" offerings. Sales of our common stock under the Sales Agreement with BofA could be subject to business, economic or competitive uncertainties and contingencies, many of which may be beyond our control, and which could cause actual results from the sale of our common stock to differ materially from expectations.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

We expect that significant additional capital will be needed in the future to continue our planned operations. To raise capital, we may sell substantial amounts of common stock or securities convertible into or exchangeable for common stock. These future issuances of common stock or common stock-related securities, including the exercise of outstanding options and any additional shares issued in connection with acquisitions, if any, may result in material dilution to our stockholders. New investors could also gain rights, preferences, and privileges senior to those of holders of our common stock.

Pursuant to our 2014 Equity Incentive Plan, as amended, or 2014 Plan, our compensation committee is authorized to grant equity-based incentive awards to our directors, executive officers, and other employees and service providers, including officers, employees and service providers of our subsidiaries and affiliates. Future option grants and issuances of common stock under our 2014 Plan may have an adverse effect on the market price of our common stock.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our stock price and trading volume could decline.

The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us, or our business. If one or more of the securities or industry analysts who cover us downgrade our stock or publish inaccurate or unfavorable research about our business, our stock price would likely decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our corporate headquarters are located at 188 East Blaine Street, Suite 450, Seattle, Washington 98102 where we lease 33,300 square feet of office space that we use for laboratory, discovery, research and development and general and administrative purposes.

We also lease approximately 6,272 square feet of office space at 360-1616 Eastlake Avenue East, Seattle, Washington 98102.

We believe that our existing facilities are adequate for our near-term needs. We believe that suitable additional or alternative space would be available if required in the future on commercially reasonable terms.

Item 3. Legal Proceedings.

We are not currently subject to any material legal proceedings.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Price Range of Our Common Stock

Our common stock is traded on The Nasdaq Global Market under the symbol "NLTX."

Stockholders

As of February 28, 2022, there were 42,493,971 shares of our common stock outstanding, which were held by 5 holders of record of our common stock, including The Depository Trust Company, which holds shares of our common stock on behalf of an indeterminate number of beneficial owners.

Dividend Policy

We have not paid any cash dividends on our common stock since our inception. We do not intend to pay any cash dividends in the foreseeable future, but intend to retain all earnings, if any, for use in our business operations.

Securities Authorized for Issuance under Equity Compensation Plans

The information required by this item will be included in an amendment to this Annual Report on Form 10-K or incorporated by reference from our definitive proxy statement to be filed pursuant to Regulation 14A.

Stock Performance Graph

As a "smaller reporting company," as defined by Rule 12b-2 of the Exchange Act, and pursuant to Instruction 6 to Item 201(e) of Regulation S-K we are not required to provide the stock performance graph.

Item 6. [Reserved].

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

Forward-Looking Statements

The following discussion of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. This discussion contains forward-looking statements that reflect our plans, estimates and beliefs, and involve risks and uncertainties. Actual events or results may differ materially. Our forward-looking statements can be affected by inaccurate assumptions we might make or by known or unknown risks, uncertainties and other factors. We discuss many of these risks, uncertainties and other factors in this Annual Report on Form 10-K in greater detail under the heading "Item 1A—Risk Factors." We caution investors that our business and financial performance are subject to substantial risks and uncertainties.

Overview

We are a biopharmaceutical company creating next generation immunotherapies for cancer, inflammation, and autoimmunity using *de novo* protein design technology. We use sophisticated computational methods to design proteins that demonstrate specific pharmaceutical properties that provide potentially superior therapeutic benefit over native proteins. Our lead product candidate, NL-201, is a combined IL-2 and IL-15 agonist designed to eliminate alpha receptor binding.

Results of Operations

Operating Loss

The following table summarizes our operating expenses for the years ended December 31, 2021 and 2020 (in thousands):

	Years Ended December 31,			
	2021	2020	$ Change	% Change
Research and development	$ 39,162	$ 24,344	$ 14,818	61 %
General and administrative	21,536	17,210	4,326	25 %
Gain on sale of Aquinox Canada	—	(7,826)	7,826	(100)%
Total operating loss	$ 60,698	$ 33,728	$ 26,970	80 %

Research and Development Expenses

Research and development expenses consists primarily of costs incurred under arrangements with third parties, such as CROs, manufacturing organizations, and consultants, personnel related costs (including stock-based compensation and travel expenses), facility-related costs, and lab supplies.

Research and development expenses for the year ended December 31, 2021 were $39.2 million compared to $24.3 million for the year ended December 31, 2020. The increase in research and development expenses during the year ended December 31, 2021 was primarily due to increased expenses incurred from clinical trial activities related to our lead product candidate, NL-201, personnel-related costs, and in connection with the advancement of other Neoleukin technologies. The increase was also due to facility-related costs associated with the build-out of our new headquarters and laboratory in Seattle, Washington.

General and Administrative Expenses

General and administrative expenses consist primarily of personnel related costs (including stock-based compensation and travel expenses), facility-related costs, insurance, and professional fees for consulting, legal, and accounting services.

For the year ended December 31, 2021, general and administrative expenses were $21.5 million compared to $17.2 million for the year ended December 31, 2020. The increase in general and administrative expenses during the year ended December 31, 2021 as compared to the year ended December 31, 2020 was primarily due to increases in personnel-related costs.

Gain on sale of Aquinox Canada

The gain relates to the sale of Aquinox Canada in July 2020. The gain of $7.8 million recognized is the total consideration of $8.2 million, less transaction costs of $0.4 million.

Other income, net (in thousands)

	Years Ended December 31,			
	2021	2020	$ Change	% Change
Interest income	$ 19	$ 490	$ (471)	(96)%
Foreign exchange losses	(1)	5	(6)	(120)%
Other expenses	(12)	(44)	32	(73)%
Total other income, net	$ 6	$ 451	$ (445)	(99)%

Interest income during the year ended December 31, 2021 decreased compared to the year ended December 31, 2020 due to a decrease in interest rates, partially offset by higher money market fund balances for the year ended December 31, 2021.

Liquidity and Capital Resources

Since our inception, we have incurred net losses and negative cash flows from our operations and relied upon sales of common and preferred stock to fund our operations. Our operating activities used $47.6 million and $24.6 million of cash during the years ended December 31, 2021 and 2020, respectively. As of December 31, 2021, we had an accumulated deficit of $393.5 million, working capital of $135.4 million, and cash and cash equivalents of $142.5 million. We believe that our existing capital resources will be sufficient to fund our operations into the second half of 2023.

On November 4, 2021, we entered into an ATM "at-the-market" Equity Offering Sales Agreement, or the Sales Agreement, with BofA Securities, Inc.,or BofA, pursuant to which we may, but are not obligated to, offer and sell, from time to time, shares of our common stock with an aggregate offering price up to $40.0 million through BofA, as sales agent. No sales of common stock have been made pursuant to this Sales Agreement to date.

Cash Flows

The following table summarizes our cash flows for the years ended December 31, 2021 and 2020 (in thousands):

	Years Ended December 31,	
	2021	2020
Net cash (used in) provided by:		
Operating activities	$ (47,558)	$ (24,575)
Investing activities	(3,263)	(2,219)
Financing activities	732	77,135
Net change in cash, cash equivalents and restricted cash	$ (50,089)	$ 50,341

Net cash used in operating activities

Net cash used in operating activities was $47.6 million for the year ended December 31, 2021 compared to $24.6 million for the year ended December 31, 2020. Net cash used in operating activities for the year ended December 31, 2021 increased compared to the year ended December 31, 2020 due to an increase in operating expenses resulting primarily from expenses incurred in developing our lead product candidate, NL-201, and in connection with the advancement of other Neoleukin technologies. The increase is also due to personnel-related costs and facility-related costs associated with the build-out of our new headquarters in Seattle, Washington.

Net cash used in investing activities

Net cash used in investing activities was $3.3 million for the year ended December 31, 2021 and consisted primarily of acquiring laboratory equipment and office furnishings. Net cash used in investing activities of $2.2 million in the year ended December 31, 2020 consisted primarily of purchases of laboratory and IT equipment.

Net cash provided by financing activities

Net cash provided by financing activities was $0.7 million for the year ended December 31, 2021 compared to $77.1 million in the year ended December 31, 2020. For the year ended December 31, 2021, net cash provided by financing activities consisted primarily of proceeds from stock option exercises and our Employee Stock Purchase Plan. For the year December 31, 2020, net cash provided by financing activities consisted primarily of net proceeds received in our offering of common stock and pre-funded warrants of $71.3 million, net of underwriting discounts and commissions and offering costs.

Operating and Capital Expenditure Requirements

We have not generated product revenue or achieved profitability since our inception and we expect to continue to incur net losses for the foreseeable future. As of December 31, 2021, we had approximately $142.5 million in cash and cash equivalents. Based on our current business plans, we believe that our existing cash and cash equivalents will be sufficient to fund our planned operations into the second half of 2023. However, our future capital requirements and the period for which we expect our existing resources to support our operations, fund expansion, develop new or enhanced products, or otherwise respond to competitive pressures, may vary significantly from our expectation and we may need to seek additional funds sooner than planned. Unless and until we generate sufficient revenue to be profitable, we will seek to fund our operations through public or private equity or debt financings or other sources. If we raise additional funds through the issuance of convertible debt securities, these securities could have rights senior to those of our common stock and could contain covenants that restrict our operations. There can be no assurance that we will be able to obtain additional equity or debt financing on terms acceptable to us, if at all. Our failure to obtain sufficient funds on acceptable terms when needed could have a negative impact on our business, results of operations, financial condition, cash flows and future prospects. Our future capital requirements will depend on many factors, including:

- the number and characteristics of any future product candidates we develop or may acquire;
- the scope, progress, results and costs of researching and developing our product candidates or any future product candidates, and conducting preclinical studies and clinical trials;
- the timing of, and the costs involved in, obtaining regulatory approvals for any future product candidates;
- the cost of manufacturing our future product candidates and any products that may achieve regulatory approval;
- the cost of commercialization activities if any future product candidates are approved for sale, including marketing, sales and distribution costs;
- the timing, receipt and amount of sales of, or royalties on, future approved products, if any;
- our ability to establish and maintain strategic collaborations, licensing or other arrangements and the financial terms of such agreements;
- any product liability or other lawsuits related to our products;
- the potential delays in our preclinical studies, our development programs and our existing and planned clinical trials due to the effects of the COVID-19 pandemic, including the resurgence of cases relating to the spread of the Delta and Omicron variants;
- the expenses needed to attract and retain skilled personnel; and
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims, including litigation costs and the outcome of such litigation.

Please see Item 1A of this Annual Report on Form 10-K titled “Risk Factors” for additional risks associated with our substantial capital requirements.

Contractual Obligations and Commitments

The following is a summary of our long-term contractual cash obligations as of December 31, 2021 (in thousands):

	TOTAL	2022	2023	2024	2025	2026	Thereafter
Operating lease obligations (1)	$ 19,198	$ 2,657	$ 2,718	$ 2,781	$ 2,845	$ 2,806	$ 5,391
Finance lease obligations	137	64	64	4	4	1	—
	$ 19,335	$ 2,721	$ 2,782	$ 2,785	$ 2,849	$ 2,807	$ 5,391

1. Operating lease obligations reflect remaining minimum commitments for our office and laboratory spaces in Seattle, Washington. Please see Note 6, *Leases* in the Notes to Consolidated Financial Statements included in Part II Item 8 of this Annual Report on Form 10-K for additional information pertaining to operating lease commitments.

We enter into contracts in the normal course of business with CROs for clinical and preclinical research studies, external manufacturers for product for use in our clinical trials, and other research supplies and other services as part of our operations. These contracts generally provide for termination on notice, and therefore are cancelable contracts and not included in the table of contractual obligations and commitments.

Milestone, Royalty-Based, and Other Commitments

We have an exclusive license agreement with UW, under which UW (on behalf of itself and Stanford University) granted us an exclusive worldwide license under certain patent rights, to make, have made, use, offer to sell, sell, offer to lease or lease, import, export or otherwise offer to dispose of licensed products in all fields of use, and a nonexclusive worldwide license to use certain know-how. The foregoing licenses are sublicensable without UW's consent, subject to certain limited conditions.

As consideration for the licensed rights, we issued shares of common stock to UW, which upon the Merger were exchanged for 188,974 shares of our common stock and 4,197 shares of our non-voting convertible preferred stock. Such convertible preferred shares were subsequently converted into 419,700 shares of our common stock in November 2019.

Furthermore, we are required to pay; (i) an annual maintenance fee starting in January 2022 (but excluding any year in which minimum annual royalties are paid); (ii) up to $0.9 million in combined development and regulatory milestone payments with respect to each distinct class of licensed product; (iii) up to $10.0 million in combined commercial milestone payments based on cumulative net sales of licensed products within each distinct class of licensed products, beginning when cumulative net sales of the class of licensed products equals or exceeds $100.0 million, with the majority payable when cumulative net sales of the class of licensed products equals or exceeds $1.0 billion; (iv) a low single-digit royalty on net sales of licensed products sold by us and our sublicensees, which may be subject to reductions, and subject to minimum annual royalty payments following the first commercial sale of a licensed product; (v) a certain percentage of any sublicense consideration (other than royalties) we receive from sublicensees, based on the stage of development at the time the sublicense is executed; and (vi) a certain percentage of consideration we receive from an acquisition of us or our assets based on the stage of development at the relevant time. We are obligated to pay royalties on a country-by-country basis until the expiration of the last valid claim within the licensed patent rights in such country.

Critical Accounting Policies and Significant Judgments and Estimates

The preparation of these consolidated financial statements in accordance with U.S. GAAP requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenue and expenses and the disclosure of contingent assets and liabilities. We evaluate those estimates and judgments on an ongoing basis. We base our estimates on historical experience, known trends and events and various other factors that we believe to be 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. Actual results may differ from these estimates under different assumptions or conditions.

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

Research and Development Expenses

Research and development costs are charged to expense as incurred and include, but are not limited to, employee-related expenses, including salaries, benefits, and stock-based compensation, expenses incurred under agreements with CROs that conduct clinical trials and preclinical studies, the cost of acquiring, developing and manufacturing clinical trial materials, costs incurred in relation to purchase of technology licenses and patent rights, facilities and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, and other supplies and costs associated with clinical trials, preclinical activities, and regulatory operations.

Development costs are expensed in the period incurred unless we believe a development project meets generally accepted accounting criteria for deferral and amortization. No product development expenditures have been deferred to date. We record costs for certain development activities based on our evaluation of the progress to completion of specific tasks or information provided to us by our vendors on their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the consolidated financial statements as prepaid or accrued liabilities.

Stock-Based Compensation

We measure the cost of services received in exchange for an award of equity instruments based on the grant-date fair value of the award. The cost of such award will be recognized over the period during which services are provided in exchange for the award, generally the vesting period. Share-based payments vest either upon service or performance conditions. We account for forfeitures as they occur. All share-based payments to employees are recognized in the consolidated financial statements based upon their respective grant-date fair values.

We estimate the fair value of options granted using the Black-Scholes option pricing model. This approximation uses assumptions regarding a number of inputs that required us to make significant estimates and judgments, including the expected term of the options. We also make decisions regarding the method of calculating the expected stock price volatility and the risk-free interest rate used in the model. The expected volatility assumption is based on industry peer information and we expect to continue to do so until it has adequate and relevant historical volatility of its common stock. Additionally, because we have no significant history to calculate the expected term, the simplified method calculation is used.

There is inherent uncertainty in our forecasts and projections and, if we had made different assumptions and estimates than those described previously, the amount of our stock-based compensation expense, net loss and net loss per common stock amounts could have been materially different.

Recent Accounting Pronouncements

See Note 2(n), *Recently issued and recently adopted accounting standards* in the Notes to Consolidated Financial Statements included in Part II Item 8 of this Annual Report on Form 10-K.

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

As a "smaller reporting company," as defined by Rule 12b-2 of the Exchange Act, and pursuant to Item 305 of Regulation S-K we are not required to provide quantitative and qualitative disclosures about market risk.

Item 8. Financial Statements and Supplementary Data.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

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

Opinion on the Financial Statements

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

Basis for Opinion

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

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

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

Critical Audit Matters

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

/s/ Deloitte & Touche LLP

Seattle, Washington
March 1, 2022

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

NEOLEUKIN THERAPEUTICS, INC.
Consolidated Balance Sheets
(in thousands, except share and per share amounts)

	December 31,	
	2021	**2020**
Assets		
Current assets		
Cash and cash equivalents	$ 142,467	$ 192,556
Other current assets	1,522	1,966
Total current assets	143,989	194,522
Property and equipment, net	6,452	3,570
Operating lease right-of-use asset	10,766	10,154
Intangible asset, net	128	347
Other non-current assets	1,928	1,926
Total assets	$ 163,263	$ 210,519
Liabilities		
Current liabilities		
Accounts payable and other liabilities	$ 7,415	$ 7,181
Operating lease liability	1,166	659
Finance lease liability	55	49
Total current liabilities	8,636	7,889
Non-current operating lease liability	11,696	11,306
Non-current finance lease liability	67	108
Total liabilities	20,399	19,303
Stockholders' equity		
Common stock, $0.000001 par value - authorized, 100,000,000 as of December 31, 2021 and December 31, 2020; issued and outstanding, 42,457,471 as of December 31, 2021 and 42,196,296 as of December 31, 2020.	—	—
Preferred stock, $0.000001 par value - authorized, 5,000,000 as of December 31, 2021 and December 31, 2020; issued and outstanding, 0 as of December 31, 2021 and December 31, 2020	—	—
Additional paid-in capital	536,362	524,022
Accumulated deficit	(393,498)	(332,806)
Total stockholders' equity	142,864	191,216
Total liabilities and stockholders' equity	$ 163,263	$ 210,519

The accompanying notes form an integral part of these consolidated financial statements

NEOLEUKIN THERAPEUTICS, INC.
Consolidated Statements of Operations
(in thousands, except share and per share amounts)

	Years Ended December 31,	
	2021	**2020**
Operating loss		
Research and development	$ 39,162	$ 24,344
General and administrative	21,536	17,210
Gain on sale of Aquinox Canada	—	(7,826)
Total operating loss	60,698	33,728
Other income, net	6	451
Net loss	$ (60,692)	$ (33,277)
Net loss per common stock - basic and diluted	$ (1.10)	$ (0.64)
Basic and diluted weighted average number of common stock outstanding	55,041,662	51,825,022

The accompanying notes form an integral part of these consolidated financial statements

NEOLEUKIN THERAPEUTICS, INC.
Consolidated Statements of Cash Flows
(in thousands)

	Years Ended December 31,	
	2021	**2020**
Operating activities		
Net loss	$ (60,692)	$ (33,277)
Adjustments to reconcile net loss used in operating activities:		
Stock-based compensation	11,557	5,622
Depreciation and amortization	1,306	785
Amortization of right-of-use asset	971	1,036
Loss on disposal of property and equipment	—	180
Write-off of right-of-use asset upon lease termination	—	113
Changes in operating assets and liabilities:		
Other current assets and non-current assets	129	(2,481)
Accounts payable and accrued liabilities	(142)	3,018
Operating lease right-of-use assets	—	(169)
Operating lease liabilities	(687)	598
Net cash used in operating activities	(47,558)	(24,575)
Investing activities		
Purchases of property and equipment	(3,263)	(2,219)
Net cash used in investing activities	(3,263)	(2,219)
Financing activities		
Proceeds from issuance of common stock and pre-funded warrants, net of commissions of $4.6 million	—	71,675
Payment of offering costs	—	(355)
Proceeds from exercise of stock options	411	5,665
Proceeds from issuance of common stock under Employee Stock Purchase Plan	372	199
Payment on finance lease obligations	(51)	(49)
Net cash provided by financing activities	732	77,135
Net change in cash, cash equivalents, and restricted cash during the year	(50,089)	50,341
Cash, cash equivalents, and restricted cash at beginning of year	193,434	143,093
Cash, cash equivalents, and restricted cash at end of year	$ 143,345	$ 193,434
Supplemental disclosure of non-cash investing and financing activities:		
Operating lease liabilities arising from obtaining right-of-use asset	$ 1,584	$ 10,364
Purchase of property and equipment unpaid at period end	$ 412	$ 36

The accompanying notes form an integral part of these consolidated financial statements

NEOLEUKIN THERAPEUTICS, INC.
Consolidated Statements of Stockholders' Equity
(in thousands, except share amounts)

	Common Stock		Additional Paid-In Capital	Accumulated Deficit	Other Comprehensive Loss	Total Stockholders' Equity
	Number	Amount	Amount	Amount	Amount	Amount
Balances, December 31, 2019	37,996,849	$ —	$ 441,216	$ (299,529)	$ —	$ 141,687
Issuance of common stock and pre-funded warrants, net of commissions and offering expenses of $4,930	3,262,471	—	71,320	—	—	71,320
Common stock issued upon exercises of stock options	882,624	—	5,665	—	—	5,665
Common stock issued upon vesting of restricted stock units	36,000	—	—	—	—	—
Issuance of common stock under Employee Stock Purchase Plan	18,352	—	199	—	—	199
Stock-based compensation	—	—	5,622	—	—	5,622
Net loss	—	—	—	(33,277)	—	(33,277)
Balances, December 31, 2020	42,196,296	$ —	$ 524,022	$ (332,806)	$ —	$ 191,216
Common stock issued upon exercises of stock options	124,928	—	411	—	—	411
Common stock issued upon vesting of restricted stock units	84,500	—	—	—	—	—
Issuance of common stock under Employee Stock Purchase Plan	51,747	—	372	—	—	372
Stock-based compensation	—	—	11,557	—	—	11,557
Net loss	—	—	—	(60,692)	—	(60,692)
Balances, December 31, 2021	42,457,471	$ —	$ 536,362	$ (393,498)	$ —	$ 142,864

The accompanying notes form an integral part of these consolidated financial statements

1. Nature of operations

Neoleukin Therapeutics, Inc. ("Neoleukin" or the "Company") is a biopharmaceutical company creating next generation immunotherapies for cancer, inflammation, and autoimmunity using *de novo* protein design technology. Neoleukin uses sophisticated computational methods to design proteins that demonstrate specific pharmaceutical properties that provide potentially superior therapeutic benefit over native proteins. The Company's lead product candidate, NL-201, is a combined IL-2 and IL-15 agonist designed to eliminate alpha receptor binding.

2. Basis of presentation and summary of significant accounting policies

(a) Basis of presentation

The accompanying consolidated financial statements are presented in United States ("U.S.") dollars and have been prepared in accordance with accounting principles generally accepted in the United States of America ("U.S. GAAP"). The financial results are presented on a consolidated basis. All intercompany transactions are eliminated on consolidation.

In July 2020, the Company sold all of the issued and outstanding capital stock of Aquinox Pharmaceuticals (Canada) ("Aquinox Canada") to an unrelated third party, as further described in Note 13, *Sale of Aquinox Canada*. On December 31, 2020, Neoleukin Corporation, the Company's wholly owned subsidiary, was merged into the Company. As a result, the Company has consisted of a single operating company without any subsidiaries since December 31, 2020.

(b) Use of estimates and assumptions

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 the 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 areas requiring estimates include valuation and recognition of stock-based compensation, the incremental borrowing rate utilized in the measurement of operating and finance lease liabilities, estimated useful lives utilized in the amortization and depreciation of property, plant and equipment and intangible assets, and pre-clinical, clinical, and other accruals. Actual results could differ from those estimates.

(c) Leases

At contract inception, the Company determines if the contract is or contains a lease. Lease liabilities are recognized on the lease commencement date based on the estimated present value of lease payments over the lease term. To determine the present value of the lease payments, the Company utilizes its estimated incremental borrowing rate based on information available at the lease commencement date as the interest rate implicit in the lease is typically not readily determinable. The related right-of-use assets are recorded net of any lease incentives received. Variable lease cost primarily includes building operating expenses as charged to the Company by its landlords and payments for lessor-owned assets that are not covered by a tenant improvement allowance.

The Company includes options to extend the lease in its lease liability and right-of-use asset when it is reasonably certain that it will exercise that option. None of the Company's options to extend the rental term of any of its existing leases were considered reasonably certain as of December 31, 2021.

For leases of office space, the Company has elected to not separate the lease components from the non-lease components.

For leases of office space with a lease term of 12 months or less and which do not include an option to purchase the underlying asset, the Company has elected to recognize the lease payments in the statement of operations on a straight-line basis over the lease term.

(d) Cash, cash equivalents, and restricted cash

All highly liquid investments with maturities of three months or less at the date of acquisition are considered to be cash equivalents.

Restricted cash, included in Other non-current assets in the consolidated balance sheets, includes cash deposits the Company maintains with its bank as collateral for the irrevocable letters of credits related to its lease obligations.

The following table provides a reconciliation of cash, cash equivalents, and restricted cash reported within the consolidated balance sheets that sum to the total of the same such amounts shown in the consolidated statements of cash flows (in thousands):

	December 31,	
	2021	2020
Cash and cash equivalents	$ 142,467	$ 192,556
Restricted cash	878	878
Total cash, cash equivalents, and restricted cash	$ 143,345	$ 193,434

(e) Property and equipment

Property and equipment are recorded at cost and are amortized using the straight-line basis over a range of three to seven years. Expenditures for maintenance and repairs are expensed as incurred.

The Company reviews the carrying value of property and equipment for impairment whenever events and circumstances indicate that the carrying value of an asset may not be recoverable from the estimated future cash flows expected to result from its use and eventual disposition. In cases where undiscounted expected future cash flows are less than the carrying value, an impairment loss is recognized equal to an amount by which the carrying value exceeds the fair value of assets. The factors considered by management in performing this assessment include current operating results, trends and prospects, the manner in which the property is used, and the effects of obsolescence, demand, competition, and other economic factors. Based on management's assessment there were no indicators of impairment of property and equipment as of December 31, 2021 and 2020.

(f) Earnings (loss) per share

Basic net loss per share is calculated by dividing the net loss by the weighted average number of shares of common stock outstanding for the period, without consideration for common stock equivalents. Common stock equivalents are included in the calculation of diluted earnings per share only in periods of net income. Such common stock equivalents are excluded in the calculation of diluted net loss per share in periods of net loss as inclusion of such amounts would be anti-dilutive. Outstanding pre-funded warrants as of December 31, 2021 and 2020 of 12,663,010 are considered outstanding as of their issuance date and are included in the basic and diluted net loss per share calculation because they are fully vested and exercisable at any time for a nominal cash consideration.

(g) Intangible assets subject to amortization

Long-lived intangible assets are recorded at the acquired cost and amortized using the straight-line method over their estimated useful life.

The intangible asset is tested for impairment when events or changes in circumstances indicate that the carrying value of the asset may not be recoverable. The Company recognizes an impairment loss when carrying amount is not recoverable and the estimated fair value of the intangible asset is less than its carrying value. Based on management's assessment there were no indicators of impairment of intangible assets as of December 31, 2021 and 2020.

(h) Income taxes

The Company accounts for income taxes using an asset and liability approach that requires the recognition of deferred tax assets and liabilities for the differences between events that have been recognized in the Company's consolidated financial statements and the tax bases of assets and liabilities and tax carryforwards recognized at enacted tax rates. The measurement of deferred tax assets is reduced, if necessary, to the amount more likely than not to be realized by a valuation allowance.

Investment tax credits relating to scientific research and experimental development are accounted for as a reduction in operating expenses. They are recorded in the period when there is reasonable assurance the credits will be realized. If investment tax credit amounts subsequently received are less or more than originally recorded, the difference is treated as a change in estimate.

(i) Research and development costs

Research and development costs are charged to expense as incurred and include items such as: employee related expenses, including salaries, stock-based compensation, and benefits, expenses incurred under agreements with contract research organizations that conduct clinical trials and preclinical studies, the cost of acquiring, developing, and manufacturing clinical trial materials, facilities, and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, and other supplies and costs associated with clinical trials, preclinical activities, and regulatory operations.

Development costs are expensed in the period incurred unless management believes a development project meets generally accepted accounting criteria for deferral and amortization. No product development expenditures have been deferred to date. The Company records costs for certain development activities based on management's evaluation of the progress to completion of specific tasks or information provided to the Company by vendors on their actual costs incurred. Payments for these activities are based on the terms of the individual arrangements, which may differ from the pattern of costs incurred, and are reflected in the consolidated financial statements as prepaid or accrued expense.

(j) Accounting for stock-based compensation

The Company has issued stock options and restricted stock units ("RSUs"). The Company measures the cost of services received in exchange for an award of equity instruments based on the grant-date fair value of the award. The cost of such award is recognized on a straight-line basis over the requisite service period, which is generally the vesting period. Awards subject to performance-based vesting requirements are expensed utilizing a graded vesting model if achievement of the performance criteria is determined to be probable. The Company accounts for forfeitures as they occur. The Company utilizes newly issued shares to satisfy option exercises, the vesting of RSUs, and Employee Stock Purchase Plan purchases.

The Company estimates the fair value of options using the Black-Scholes option pricing model on the grant date. This approximation uses assumptions regarding a number of inputs that requires management to make significant estimates and judgments. The expected term represents the period that the Company's stock-based awards are expected to be outstanding. As the Company does not have sufficient historical experience for determining the expected term of the stock option awards granted, the Company has based its expected term for awards issued to employees on the simplified method, which represents the average period from vesting to the expiration of the stock option. In addition, the Company does not have sufficient trading history for the Company's common stock, and therefore, the expected stock price volatility for the Company's common stock was estimated by taking the average historical price volatility for industry peers. The Company has never declared or paid any cash dividends to common stockholders and does not presently plan to pay cash dividends in the foreseeable future. Consequently, the Company used an expected dividend yield of zero. The risk-free interest rate was based on the yields of treasury securities with maturities similar to the expected term of the options for each option group.

The fair value of each RSU is measured using the closing price of the Company's common stock on the date of grant.

(k) Segment reporting

The Company operates in one segment, the research and development of *de novo* protein therapeutics using sophisticated computational algorithms and methods to address unmet medical needs. The Company's primary areas of focus are in oncology, inflammation, and autoimmunity. The Company's operations and its assets are held in the United States.

(l) Fair value of financial instruments

The carrying amounts of certain of the Company's financial instruments, including cash and cash equivalents, restricted cash, receivables, accounts payable, and other liabilities, approximate their fair values because of their nature and/or short maturities.

At December 31, 2021, and December 31, 2020, the Company had $140.9 million and $108.3 million in money market funds, respectively. Money market funds are level one financial instruments as they are valued at the closing price reported by the fund sponsor from an actively traded exchange.

(m) Concentration of credit risk

Financial instruments, which potentially subject the Company to significant concentrations of credit risk, consist primarily of cash and cash equivalents. Cash and cash equivalents are invested in accordance with the Company's investment policy. The primary objective for the Company's investment portfolio is the preservation of capital and maintenance of liquidity and includes guidelines on the quality of financial instruments and defines allowable investments that the Company believes minimizes the exposure to concentration of credit risk.

(n) Recently issued and recently adopted accounting standards

In December 2019, the FASB issued ASU 2019-12 "*Simplifying the Accounting for Income Taxes*". The objective of the standard is to improve areas of GAAP by removing certain exceptions permitted by ASC Topic 740-- *Income Taxes* and clarifying existing guidance to facilitate consistent application. ASU 2019-12 is effective for fiscal years and interim periods beginning after December 15, 2020. The Company adopted this standard on January 1, 2021 on a prospective basis. The adoption of ASU 2019-12 did not have a material impact on the Company's financial condition, results of operations, cash flows, and financial statement disclosures.

3. Property and equipment, net

Property and equipment, net consist of the following (in thousands):

	December 31, 2021		
	Cost	Accumulated Amortization	Net Book Value
Laboratory equipment	$ 6,237	$ 1,006	$ 5,231
Furniture, fixtures, and IT equipment	1,850	629	1,221
	$ 8,087	$ 1,635	$ 6,452

	December 31, 2020		
	Cost	Accumulated Amortization	Net Book Value
Laboratory equipment	$ 3,402	$ 426	$ 2,976
Furniture, fixtures, and IT equipment	753	159	594
	$ 4,155	$ 585	$ 3,570

Depreciation expense on property and equipment totaled $1.1 million and $0.6 million for the years ended December 31, 2021 and 2020, respectively.

4. Intangible asset, net

The following table summarizes intangible asset (in thousands):

	December 31,	
	2021	2020
Cost	$ 659	$ 659
Accumulated amortization	(531)	(312)
Net intangible asset	$ 128	$ 347

Intangible asset, net includes an assembled workforce that was acquired in 2019 and is being amortized over its expected life. Amortization expense was $0.2 million for each of the years ended December 31, 2021 and 2020. The amortization period has been established as 3 years based on management's judgement. The Company will recognize $0.1 million of amortization expense in fiscal year 2022.

5. Accounts payable and other liabilities

Accrued liabilities consist of the following (in thousands):

	December 31,	
	2021	2020
Trade accounts payable	$ 526	$ 1,323
Accrued clinical and preclinical expenses	2,399	1,687
Accrued compensation and vacation	3,263	3,244
Other accrued liabilities	1,227	927
	$ 7,415	$ 7,181

6. Leases

The Company enters into lease arrangements for its facilities as well as certain equipment, classified either as operating or finance leases.

The Company has an operating lease agreement, as amended by the execution of two subsequent amendments, for approximately 33,300 square feet of office space in Seattle, Washington for the Company's principal executive offices, a laboratory for research and development, and related uses. In January 2020, the Company issued an irrevocable letter of credit in the amount of $0.5 million for the security deposit in accordance with the terms of the lease. The lease term commenced on January 15, 2020 and payments of rent obligations began on February 1, 2021. The lease is scheduled to expire on February 1, 2029, with the option to extend the lease for two five-year terms. The lease provides for a tenant improvement allowance of up to $9.5 million, which is included in the base rent, and has been fully utilized as of December 31, 2021. The Company will also be responsible for the payment of additional rent to cover the Company's share of the annual operating, tax expenses, and utilities costs for the building.

The Company has an operating lease agreement for approximately 6,272 square feet of laboratory and office space in Seattle, Washington, for research and development and related uses. In March 2021, the Company executed an amendment to this lease pursuant to which the contractual lease term was extended through September 30, 2026, unless terminated earlier, with the option to extend the lease for an additional 28-month term. The execution of this amendment was accounted for as a modification to the lease due to the extension of the lease term and an increase in lease payments, and the Company recorded an increase in the lease liability and related right-of-use asset of $1.6 million.

On June 30, 2020, the Company terminated its lease agreement for 10,946 square feet of office space in Vancouver, Canada. The lease termination resulted in an extinguishment of the lease liability and the write-off of the related right-of-use asset. After incurring additional expenses included in the termination fee of $0.5 million, the Company recognized a loss of $0.3 million on the termination of the lease, which was recorded in general and administrative expenses in June 2020. In addition, the Company wrote-off leasehold improvements and other property and equipment associated with the lease and incurred a loss on disposal of $0.2 million in June 2020.

As of December 31, 2021, and December 31, 2020, the Company's operating lease right-of-use assets were $10.8 million and $10.2 million, respectively. As of December 31, 2021, and December 31, 2020, the Company's finance lease right-of use-assets, included within property and equipment on the consolidated balance sheet, were $0.2 million and $0.3 million, respectively.

The components of the lease expense were as follows (in thousands):

	December 31,	
	2021	2020
Finance lease cost		
Amortization of right-of-use asset	$ 49	$ 46
Interest on lease liabilities	12	14
Operating lease cost	2,535	2,368
Short term lease cost	40	348
Variable lease cost	2,161	321
Total net lease cost	$ 4,797	$ 3,097

Supplemental balance sheet information related to leases is as follows:

	December 31,	
	2021	2020
Weighted average remaining lease term—finance leases	2.70 years	2.45 years
Weighted average remaining lease term—operating leases	6.86 years	7.97 years
Weighted average discount rate—finance leases	6.98%	7.11%
Weighted average discount rate—operating leases	12.42%	12.88%

Supplemental cash flow information related to leases was as follows (in thousands):

	December 31,	
	2021	2020
Cash paid for amounts included in the measurement of operating lease liabilities	$ 2,249	$ 460
Cash paid for amounts included in the measurement of finance lease liabilities	$ 63	$ 60

The calculation of the present value of the operating lease payments for the Blaine lease did not include the option to extend the lease for two five-year terms.

At December 31, 2021, the future payments under the Company's operating and finance lease liabilities were as follows (in thousands):

	Finance Lease	Operating Lease
2022	$ 64	$ 2,657
2023	64	2,718
2024	4	2,781
2025	4	2,845
2026	1	2,806
Thereafter	—	5,391
Total undiscounted lease payments	137	19,198
Less: imputed interest	(15)	(6,336)
Total lease liabilities	122	12,862
Less: current portion	(55)	(1,166)
Non-current lease liabilities—December 31, 2021	$ 67	$ 11,696

7. Stockholders' equity

(a) Common stock and pre-funded warrants

The Company is authorized to issue 100,000,000 shares of common stock with a par value of $0.000001 per share as of December 31, 2021. As of December 31, 2021, and 2020, the total number of shares of common stock issued and outstanding was 42,457,471, and 42,196,296, respectively.

The Company had pre-funded warrants outstanding to purchase an aggregate of 12,663,010 shares of common stock as of December 31, 2021. The pre-funded warrants are exercisable at any time, with 61 days' notice, for an exercise price of $0.000001, except that the pre-funded warrants cannot be exercised by the holders if, after giving effect thereto, the holders would beneficially own more than 9.99% of the outstanding common stock, subject to certain exceptions. The holders of the pre-funded warrants will not have the right to vote on any matter except to the extent required by Delaware law.

On November 4, 2021, the Company entered into an ATM "at-the-market" Equity Offering Sales Agreement (the "Sales Agreement") with BofA Securities, Inc., as agent ("BofA"), pursuant to which the Company may offer and sell, from time to time through BofA, shares of the Company's common stock, having an aggregate offering price of up to $40.0 million. The offer and sale of the shares will be made pursuant to a shelf registration statement on Form S-3 and the related prospectus filed on December 11, 2020, and declared effective by the SEC on December 21, 2020, as supplemented by a prospectus supplement dated November 4, 2021. The Company has no obligation to sell any such shares under the Sales Agreement. As of December 31, 2021, no sales of common stock had been made pursuant to the Sales Agreement.

On July 7, 2020, the Company completed an underwritten public offering of 3,262,471 shares of its common stock at a price of $15.25 per share and pre-funded warrants to purchase 1,737,529 shares of its common stock at a price of $15.249999 per prefunded warrant. The pre-funded warrants can be exercised at any time after issuance for an exercise price of $0.000001 per share. The aggregate net proceeds received by the Company from the offering were $71.3 million, net of underwriting discounts, commissions, and offering costs of approximately $4.9 million.

(b) Preferred stock

The Company is authorized to issue 5,000,000 shares of preferred stock with a par value of $0.000001 per share. As of December 31, 2021 and 2020, 0 shares of preferred stock were issued or outstanding.

(c) Stock option plan

The 2014 Equity Incentive Plan ("2014 Plan"), as amended and restated on May 13, 2021, became effective in March 2014 and is the successor to and continuation of the Joint Canadian Stock Option Plan (the "2006 Plan"). No further grants will be made under the 2006 Plan. The 2014 Plan provides for the grant of stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards, performance stock awards, performance cash awards, and other forms of equity awards to employees, directors, and consultants.

As of December 31, 2021, the maximum number of shares of common stock that may be issued under the 2014 Plan was 11,264,787. The number of shares of common stock reserved for issuance under the 2014 Plan will be increased by the number of shares subject to stock options granted under the 2006 Plan that would have otherwise returned to the 2006 Plan, such as upon the expiration or termination of a stock award prior to vesting. As of December 31, 2021, there were 23,958 shares subject to stock options granted under the 2006 Plan. Additionally, the number of shares of common stock reserved for issuance under the 2014 Plan will automatically increase on January 1 of each year, beginning on January 1, 2022 and ending on and including January 1, 2030, by 4.00% of the sum of (A) the total number of shares of capital stock and (B) the total number of shares of common stock subject to pre-funded warrants, in each case outstanding on December 31 of the preceding calendar year, or a lesser number of shares determined by the board of directors. On January 1, 2022, the number of shares of common stock reserved under the 2014 Plan was increased by 2,204,819 shares. All stock options granted pursuant to the 2014 Plan have a contractual term of ten years. All awards granted to date are equity classified and subject to either service or performance based vesting, typically over a period of one to four years.

The number of shares available to be granted under the 2014 Plan was 5,040,300 and 6,037,532 as of December 31, 2021 and 2020, respectively.

Stock options

A summary of the Company's stock option activity and related information for the year ended December 31, 2021 is as follows:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life (In Years)	Aggregate Intrinsic Value (In Thousands)
Outstanding at December 31, 2020	6,846,289	$ 6.42	8.71	$ 53,127
Options granted	3,346,049	$ 8.70		
Options exercised	(124,928)	$ 3.28		
Options cancelled/forfeited	(1,103,465)	$ 7.31		
Outstanding at December 31, 2021	8,963,945	$ 7.20	8.32	$ 6,912
Exercisable as of December 31, 2021	3,665,224	$ 5.99	7.45	$ 4,729

During the year ended December 31, 2021, 124,928 shares of common stock were issued upon exercise of options with an aggregate intrinsic value of $1.3 million. During the year ended December 31, 2020, 882,624 shares of common stock were issued upon exercise of options with an aggregate intrinsic value of $6.0 million. The weighted-average grant date fair value of options granted during the years ended December 31, 2021 and 2020 was $6.37 and $8.70 per share, respectively.

The fair value of stock options granted is estimated using the Black-Scholes option pricing model with the following weighted average assumptions:

	December 31,	
	2021	2020
Expected volatility	89 %	93 %
Expected dividends	0 %	0 %
Expected terms (years)	6.03	6.02
Risk free rate	0.93 %	0.42 %

Restricted stock units

A summary of the Company's restricted stock unit activity and related information for the year ended December 31, 2021 is as follows:

	Number of Shares		Weighted Average Grant Date Fair Value
Non-vested at December 31, 2020	186,500	$	8.19
Restricted stock units granted	70,000	$	12.94
Restricted stock units vested	(84,500)	$	7.20
Restricted stock units forfeited	(40,000)	$	12.70
Non-vested at December 31, 2021	132,000	$	9.97

During the year ended December 31, 2021, the Company granted 50,000 RSUs, which vest based on certain performance conditions in two equal tranches. Twenty-five thousand of such performance-based RSUs vested during the year ended December 31, 2021 as the related performance condition was met. Related stock-based compensation expense recognized was $0.3 million. The remaining 25,000 RSUs were forfeited prior to December 31, 2021. Each vested RSU entitles the holder to receive one share of the Company's common stock.

(d) Stock-based compensation

Stock-based compensation expense is classified in the consolidated statements of operations as follows (in thousands):

	December 31,			
	2021		2020	
Research and development expenses	$	5,095	$	1,999
General and administrative expenses		6,462		3,623
Total stock-based compensation expense	$	11,557	$	5,622

Total unrecognized compensation for all stock-based compensation was $29.6 million as of December 31, 2021, which is expected to be recognized over a weighted-average period of 2.84 years.

(e) Employee stock purchase plan

The Company’s 2020 Employee Stock Purchase Plan (“2020 ESPP”) was adopted by the Company’s board of directors in March 2020 and approved by the Company’s stockholders in May 2020. A total of 759,936 shares of common stock have been reserved for issuance under the 2020 ESPP.

Subject to share and dollar limits as described in the plan, the 2020 ESPP allows eligible employees to contribute, through payroll deductions, up to 15% of their earnings for the purchase of the Company’s shares of common stock at the lower of 85% of the closing price of the Company’s common stock on the first trading day of the offering period or 85% of the closing price of the Company’s common stock on the last trading day of the offering period. There are two six-month offering periods during each fiscal year, ending on May 15 and November 15.

During the year ended December 31, 2021, the Company issued 22,972 shares of common stock at a price per share of $9.53 and 28,775 of shares of common stock at a price per share of $5.33, respectively, under the 2020 ESPP. During the year ended December 31, 2020, the Company issued 18,352 shares of common stock at a price per share of $10.84. Cash received from the purchases under the 2020 ESPP for the years ended December 31, 2021 and 2020 was $0.4 million and $0.2 million, respectively. As of December 31, 2021 and 2020, employee contributions included in accounts payable and accrued liabilities in the accompanying consolidated balance sheet were immaterial.

8. Other income, net

Other income is presented for all periods (in thousands):

	December 31	
	2021	2020
Interest income	$ 19	$ 490
Foreign exchange gains (losses)	(1)	5
Other expenses	(12)	(44)
	$ 6	$ 451

9. Net loss per common stock

The Company excluded the following potentially dilutive shares from diluted net loss per share as the effect would have been anti-dilutive for all periods presented:

	December 31,	
	2021	2020
Outstanding stock options	8,963,945	6,848,289
Restricted stock units	132,000	186,500
Shares issuable under 2020 ESPP	53,446	22,521
	9,149,391	7,057,310

10. Income taxes

Income tax recovery varies from the amounts that would be computed by applying the expected U.S. federal income tax rate (21%) as shown in the following table:

	December 31,	
	2021	2020
Statutory federal income tax rate	(21.0)%	(21.0)%
Foreign rate differential	—	(0.1)
Stock-based compensation	2.0	1.8
Disposal of Aquinox Canada	—	(5.2)
Change in valuation allowance	21.2	26.5
Expiration of NOLs (section 382)	—	0.5
Tax credits	(2.2)	(2.5)
Income tax recovery	— %	— %

Net loss before taxes (in thousands):	Years Ended December 31,	
	2021	2020
Canada	$ —	$ (522)
U.S.	(60,692)	(32,755)
Total	$ (60,692)	$ (33,277)

Deferred income tax assets and liabilities result from the temporary differences between the amount of assets and liabilities recognized for financial statement and income tax purposes. The significant components of the deferred income tax assets are as follows (in thousands):

	December 31,	
	2021	2020
Deferred tax assets:		
U.S. net operating losses	$ 22,863	$ 12,328
Research and development deductions and credits	2,414	1,040
Intangibles	457	422
Lease liability	2,701	2,513
Stock-based compensation	1,695	717
Other	186	162
Total deferred tax assets:	30,316	17,182
Deferred income tax liabilities		
Right-of-use assets	2,261	2,132
Other	287	157
Total deferred tax liabilities	2,548	2,289
Net deferred income tax assets	27,768	14,893
Less: valuation allowance	(27,768)	(14,893)
Deferred tax assets, net of valuation allowance	$ —	$ —

On July 31, 2020, the Company sold all issued and outstanding capital stock of its Canadian subsidiary, Aquinox Canada, to an unrelated third party for cash consideration. As of the date of sale, Aquinox Canada's remaining assets included intellectual property and other assets developed through past research and development activities, all of which had no book value. The transaction resulted in a net gain on sale of $7.8 million. The sale of Aquinox Canada triggered a significant capital loss carryforward for tax purposes. However, most of the capital loss carryforward is limited by the prior ownership change under Section 382. The remaining unlimited portion of the capital loss carryforward will be subject to a full valuation allowance as the Company has determined that it is more likely than not that the benefit of the loss will not be realized. After the sale, Aquinox Canada's tax attributes of $51.7 million including the net operating losses, scientific research and experimental development expenditures and investment tax credits are no longer reflected in the deferred tax assets and valuation allowance.

At December 31, 2021 and December 31, 2020, the Company had U.S. federal net operating losses ("NOL") carryforwards for tax purposes of approximately $108.2 million and $58.1 million, respectively, which were available to reduce taxable income. Of the $108.2 million of federal NOL carryforwards, $1.7 million will expire between the years 2028 and 2037 and the remaining $106.5 million are indefinite. The Company also has U.S. federal research & development tax credits of $2.4 million and $1.0 million as of December 31, 2021 and December 31, 2020, respectively, that begin to expire in 2039. The Company completed a formal study under IRC Section 382 through 2019 to determine the U.S. tax attributes available for use. The U.S. attributes disclosed reflect the conclusion of that study. However, subsequent ownership changes may further affect the limitation in future years.

The Company maintains a full valuation allowance on its net U.S. deferred tax assets. The assessment regarding whether a valuation allowance is required considers both positive and negative evidence when determining whether it is more likely than not that deferred tax assets are recoverable. In making this assessment, significant weight is given to evidence that can be objectively verified. In its evaluation, the Company considered its cumulative losses and its forecasted losses in the near-term as significant negative evidence. Therefore, the Company determined that the negative evidence outweighed the positive evidence and a full valuation allowance on its assets will be maintained. The Company will continue to assess the realizability of its assets going forward and will adjust the valuation allowance as needed. The valuation allowance increased by $12.9 million for the year ended December 31, 2021. The increase is primarily due to an increase in U.S. net operating losses and research and development tax credits. The valuation allowance decreased by $42.9 million for the year ended December 31, 2020. The decrease is primarily due to the sale of Aquinox Canada and the write-off of the related tax attributes, and partially offset by an increase in U.S. net operating losses and research and development tax credits.

The Company applies judgment in the determination of the financial statement recognition and measurement of tax positions taken or expected to be taken in a tax return. As of December 31, 2021, the Company had no uncertain tax positions.

The Company currently files income tax returns in the United States, the jurisdictions in which the Company believes that it is subject to tax. Further, while the statute of limitations in each jurisdiction where an income tax return has been filed generally limits the examination period, as a result of loss carryforwards, the limitation period for examination generally does not expire until several years after the loss carryforwards are utilized. Other than routine audits by tax authorities for tax credits and tax refunds that the Company has claimed, the Company is not aware of any other material income tax examination currently in progress by any taxing jurisdiction.

11. License and patent agreements

On July 8, 2019, Neoleukin Therapeutics, Inc., or Former Neoleukin, entered into an exclusive license agreement with the University of Washington ("UW"), under which UW (on behalf of itself and Stanford University) granted the Company an exclusive worldwide license under certain patent rights, to make, have made, use, offer to sell, sell, offer to lease or lease, import, export or otherwise offer to dispose of licensed products in all fields of use, and a nonexclusive worldwide license to use certain know-how. The foregoing licenses are sublicensable by the Company without UW's consent, subject to certain limited conditions. The Exclusive License Agreement was amended effective as of July 24, 2020 to, among other things, (i) add a jointly owned *de novo* cytokine antagonist to the agreement, (ii) specify royalties, milestone payments and sublicense consideration payments payable by Neoleukin for certain jointly licensed products, (iii) specify the term for achievement of performance milestones for certainly jointly licensed products, and (iv) terminate UW's right to participate in equity financings. The Exclusive License Agreement was amended a second time, effective as of December 15, 2021 to, among other things, add a second jointly owned patent application family directed to *de novo* cytokine antagonists to the agreement subject to the same terms of the first jointly owned patent application family.

As consideration for the licensed rights, Former Neoleukin issued 536,813 shares of common stock to UW. These shares were exchanged for 188,974 shares of common stock of the Company and 4,197 shares of non-voting convertible preferred stock on the completion of the merger of Former Neoleukin into the Company in August 2019. Such convertible preferred shares were subsequently converted into 419,700 shares of common stock in November 2019.

Furthermore, the Company is required to pay; (i) an annual maintenance fee starting in January 2022 (but excluding any year in which minimum annual royalties are paid); (ii) up to $0.9 million in combined development and regulatory milestone payments with respect to each distinct class of licensed product; (iii) up to $10.0 million in combined commercial milestone payments based on cumulative net sales of licensed products within each distinct class of licensed products, beginning when cumulative net sales of the class of licensed products equals or exceeds $100.0 million, with the majority payable when cumulative net sales of the class of licensed products equals or exceeds $1.0 billion; (iv) a low single-digit royalty on net sales of licensed products sold by the Company and its sublicensees, which may be subject to reductions, and subject to minimum annual royalty payments following the first commercial sale of a licensed product; (v) a certain percentage of any sublicense consideration (other than royalties) the Company receives from sublicensees, based on the stage of development at the time the sublicense is executed; and (vi) a certain percentage of consideration the Company receives from an acquisition of the Company or its assets based on the stage of development at the relevant time. The Company is obligated to pay royalties on a country-by-country basis until the expiration of the last valid claim within the licensed patent rights in such country.

The agreement will expire upon the expiration of the last valid claim within the licensed patent rights. The Company may terminate the agreement upon prior written notice to UW. UW may terminate the agreement by a specified number of days' notice if the Company permanently ceases operations, becomes insolvent or similar, or if the Company challenges the validity of the licensed patent rights. In addition, UW may terminate the agreement for material breach that is not cured within a specified number of days, which cure period is to be at least doubled if the Company is proceeding diligently to cure the default.

12. 401(k) plan

In May 2020, the Company established a 401(k) plan that allows full-time employees to contribute a portion of their salary, subject to statutory limits. The Company makes matching cash contributions up to a pre-defined annual maximum contribution per employee per year. During the years ended December 31, 2021 and December 31, 2020, the Company's total expense for the matching contributions was immaterial.

13. Sale of Aquinox Canada

On July 31, 2020, the Company sold all issued and outstanding capital stock of its Canadian subsidiary, Aquinox Canada, to an unrelated third party for cash consideration of $8.2 million. The Company concluded that the sale did not meet the criteria for discontinued operations reporting as it did not represent a strategic shift that had a major effect on the Company's operations and financial results. As of the date of sale, Aquinox Canada's remaining assets included intellectual property and other assets developed through past research and development activities, all of which had no book value. The transaction resulted in a net gain on sale of $7.8 million, after deducting $0.4 million in transaction costs, which is recorded as a reduction of operating loss in the Company's consolidated statement of operations. The sale of Aquinox Canada triggered a significant capital loss carryforward for tax purposes. However, the deferred tax asset related to the capital loss carryforward will be subject to a full valuation allowance as the Company has determined that it is more likely than not that the benefit of the loss will not be realized. Refer to Note 10, *Income taxes* for further information.

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

None.

Item 9A. Controls and Procedures.

Evaluation of disclosure controls and procedures. Our Chief Executive Officer (our principal executive officer) and our Chief Financial Officer (our principal accounting officer) have evaluated our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended) prior to the filing of this annual report on Form 10-K. Based on that evaluation, they have concluded that, as of the end of the period covered by this annual report on Form 10-K, our disclosure controls and procedures were, in design and operation, effective at a reasonable assurance level.

Management's Report on Internal Control Over Financial Reporting. Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rule 13a-15(f) under the Securities Exchange Act of 1934, as amended. Our management conducted an evaluation of the effectiveness of our internal control over financial reporting based on the 2013 framework in *Internal Control—Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on its evaluation under the framework in *Internal Control—Integrated Framework,* our management concluded that our internal control over financial reporting was effective as of December 31, 2021.

Changes in internal control over financial reporting. There have not been any changes in our internal control over financial reporting during the quarter ended December 31, 2021 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Inherent limitation on the effectiveness of internal control. The effectiveness of any system of internal control over financial reporting, including ours, is subject to inherent limitations, including the exercise of judgment in designing, implementing, operating, and evaluating the controls and procedures, and the inability to eliminate misconduct completely. Accordingly, any system of internal control over financial reporting, including ours, no matter how well designed and operated, can only provide reasonable, not absolute assurances. In addition, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate. We intend to continue to monitor and upgrade our internal controls as necessary or appropriate for our business, but cannot assure you that such improvements will be sufficient to provide us with effective internal control over financial reporting

This Annual Report on Form 10-K does not include an attestation report of the Company's independent registered public accounting firm regarding internal control over financial reporting. Management's report was not subject to attestation by the Company's independent registered public accounting firm pursuant to rules of the Securities and Exchange Commission that permit the Company to provide only management's report in this Annual Report on Form 10-K.

Item 9B. Other Information.

None.

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

None.

PART III

The information required by Part III is omitted from this report because we will file a definitive proxy statement within 120 days after the end of our 2021 fiscal year pursuant to Regulation 14A for our 2022 Annual Meeting of Stockholders, or the 2022 Proxy Statement, and the information to be included in the 2022 Proxy Statement is incorporated herein by reference.

Item 10. Directors, Executive Officers and Corporate Governance.

(1) The information required by this Item concerning our executive officers and our directors and nominees for director, including information with respect to our audit committee and audit committee financial expert, may be found under the section entitled "Proposal No. 1 Election of Directors," "Information Regarding the Board of Directors and Corporate Governance," and "Information About Our Executive Officers" appearing in the 2022 Proxy Statement. Such information is incorporated herein by reference.

(2) The information required by this Item concerning our code of ethics may be found under the section entitled "Information Regarding the Board of Directors and Corporate Governance" appearing in the 2022 Proxy Statement. Such information is incorporated herein by reference.

(3) The information required by this Item concerning compliance with Section 16(a) of the Securities Exchange Act of 1934 may be found in the section entitled "Delinquent Section 16(a) Reports" appearing in the 2022 Proxy Statement. Such information is incorporated herein by reference.

Item 11. Executive Compensation.

The information required by this Item may be found under the sections entitled "Director Compensation," "Executive Compensation" and "Equity Compensation Plan Information" appearing in the 2022 Proxy Statement. Such information is incorporated herein by reference.

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

(1) The information required by this Item with respect to security ownership of certain beneficial owners and management may be found under the section entitled "Security Ownership of Certain Beneficial Owners and Management" appearing in the 2022 Proxy Statement. Such information is incorporated herein by reference.

(2) The information required by this Item with respect to securities authorized for issuance under our equity compensation plans may be found under the sections entitled "Equity Compensation Plan Information" appearing in the 2022 Proxy Statement. Such information is incorporated herein by reference.

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

(1) The information required by this Item concerning related party transactions may be found under the section entitled "Transactions with Related Persons" appearing in the 2022 Proxy Statement. Such information is incorporated herein by reference.

(2) The information required by this Item concerning director independence may be found under the sections entitled "Information Regarding the Board of Directors and Corporate Governance—Independence of the Board of Directors" and "Information Regarding the Board of Directors and Corporate Governance—Information Regarding Committees of the Board of Directors" appearing in the 2022 Proxy Statement. Such information is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

The information required by this Item may be found under the section entitled "Proposal No. 2 Ratification of Appointment of Independent Registered Public Accounting Firm" appearing in the 2022 Proxy Statement. Such information is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a) The following documents are filed as part of this report:

(1) Financial Statements and Report of Independent Registered Public Accounting Firm

(2) Financial Statement Schedules

Financial Statement Schedules have been omitted because the information required to be set forth therein is not applicable or is shown in the financial statements or notes thereto.

(3) Exhibits are incorporated herein by reference or are filed with this report as indicated below (numbered in accordance with Item 601 of Regulation S-K).

(b) Exhibits

The exhibits listed below on the Exhibit Index are filed herewith or are incorporated by reference to exhibits previously filed with the SEC.

EXHIBIT INDEX

Number	Description
2.1*	Agreement and Plan of Merger by and between Aquinox Pharmaceuticals, Inc., Apollo Sub, Inc., and Neoleukin Therapeutics, Inc., dated August 5, 2019—Incorporated by reference to Exhibit 2.1 to our Current Report on Form 8-K filed with the Securities and Exchange Commission on August 6, 2019
3.1	Amended and Restated Certificate of Incorporation of Neoleukin Therapeutics, Inc.—Incorporated by reference to Exhibit 3.1 to our Current Report on Form 8-K filed with the Securities and Exchange Commission on March 12, 2014
3.2	Amended and Restated Bylaws of Neoleukin Therapeutics, Inc.—Incorporated by reference to Exhibit 3.1 to our Current Report on Form 8-K, filed with the Securities and Exchange Commission on April 13, 2020
3.3	Certificate of Designation of Preferences, Rights and Limitations of Series A Convertible Stock, filed August 8, 2019—Incorporated by reference to Exhibit 3.1 to our Current Report on Form 8-K filed with the Securities and Exchange Commission August 12, 2019
3.4	Certificate of Amendment to Amended and Restated Certificate of Incorporation of Neoleukin Therapeutics, Inc., filed August 9, 2019—Incorporated by reference to Exhibit 3.4 to our Quarterly Report on Form 10-Q for the quarter ended September 30, 2019 filed with the Securities and Exchange Commission on November 13, 2019.
3.5	Certificate of Amendment to Amended and Restated Certificate of Incorporation of Neoleukin Therapeutics, Inc., filed November 13, 2019—Incorporated by reference to Exhibit 3.5 to our Quarterly Report on Form 10-Q for the quarter ended September 30, 2019 filed with the Securities and Exchange Commission on November 13, 2019.
4.1	Specimen Common Stock Certificate of the Registrant—Incorporated by reference to Exhibit 4.1 to our Quarterly Report on Form 10-Q for the quarter ended March 31, 2014 filed with the Securities and Exchange Commission on May 13, 2014

Number	Description
4.2	Registration Rights Agreement, dated September 19, 2016, by and between Aquinox Pharmaceuticals, Inc. and the persons listed on Schedule A attached thereto—Incorporated by reference to Exhibit 10.1 to our Current Report on Form 8-K filed with the Securities and Exchange Commission on September 20, 2016
4.3	Description of Securities Registered Under Section 12 of the Securities Exchange Act of 1934, as amended—Incorporated by reference to Exhibit 4.3 to our Annual Report on Form 10-K for the year ended December 31, 2019 filed with the Securities and Exchange Commission on March 12, 2020
4.4	Form of Pre-Funded Warrant—Incorporated by reference to Exhibit 4.1 to our Current Report on Form 8-K filed with the Securities and Exchange Commission on December 19, 2019
4.5	Form of Pre-Funded Warrant— Incorporated by reference to Exhibit 4.1 to our Current Report on Form 8-K filed with the Securities and Exchange Commission on July 2, 2020.
10.1	Exclusive Start-Up License Agreement, dated July 8, 2019, by and between the University of Washington and Neoleukin Therapeutics, Inc.—Incorporated by reference to Exhibit 10.1 to our Current Report on Form 8-K filed with the Securities and Exchange Commission August 12, 2019
10.2	Lease Agreement, dated September 23, 2019, by and between Neoleukin Therapeutics, Inc. and ARE-Eastlake Avenue No. 3, LLC.—Incorporated by reference to Exhibit 10.7 to our Quarterly Report on Form 10-Q for the quarter ended September 30, 2019 filed with the Securities and Exchange Commission on November 13, 2019
10.3	Lease Agreement, dated December 23, 2019, by and between Neoleukin Therapeutics, Inc. and ARE-Eastlake Avenue No. 3, LLC—Incorporated by reference to Exhibit 10.8 to our Annual Report on Form 10-K for the year ended December 31, 2019 filed with the Securities and Exchange Commission on March 12, 2020
10.4+	Joint Canadian Stock Option Plan—Incorporated by reference to Exhibit 10.1 to our Registration Statement on Form S-1 (File No. 333-193615) filed with the Securities and Exchange Commission on January 28, 2014
10.5+	Forms of Option Agreement for Registrant's Joint Canadian Stock Option Plan—Incorporated by reference to Exhibit 10.2 to our Registration Statement on Form S-1 (File No. 333-193615) filed with the Securities and Exchange Commission on January 28, 2014
10.6+	Neoleukin Therapeutics, Inc. Amended and Restated 2014 Equity Incentive Plan, as amended and restated on May 13, 2021—Incorporated by reference to Exhibit 10.1 to our Current Report on Form 8-K filed with the Securities and Exchange Commission on May 14, 2021
10.7+	Forms of Option Agreement and Option Grant Notice for Registrant's 2014 Equity Incentive Plan—Incorporated by reference to Exhibit 10.4 to our Registration Statement on Form S-1 (File No. 333-193615) filed with the Securities and Exchange Commission on January 28, 2014
10.8+	Neoleukin Therapeutics, Inc. 2020 Employee Stock Purchase Plan—Incorporated by reference to Exhibit 10.1 to our Current Report on Form 8-K filed with the Securities and Exchange Commission on May 6, 2020.
10.9	Form of Indemnity Agreement entered into between the Registrant and each of its directors and its executive officers—Incorporated by reference to Exhibit 10.5 to our Registration Statement on Form S-1 (File No. 333-193615) filed with the Securities and Exchange Commission on January 28, 2014
10.10*	Exchange Agreement, dated December 17, 2019, by and among Neoleukin Therapeutics, Inc., 667, L.P. and Baker Brothers Life Sciences, L.P.—Incorporated by reference to Exhibit 10.1 to our Current Report on Form 8-K filed with the Securities and Exchange Commission on December 19, 2019

Number	Description
10.11	Lease Agreement, dated February 5, 2016, by and between Aquinox Pharmaceuticals (Canada) Inc. and 560677 B.C. Ltd. Incorporated by reference to Exhibit 10.1 to our Current Report on Form 8-K filed with the Securities and Exchange Commission on February 10, 2016
10.12+	Executive Employment Agreement, dated March 16, 2020, Neoleukin Therapeutics, Inc. and Robert Ho—Incorporated by reference to Exhibit 10.1 to our Quarterly Report on Form 10-Q for the quarter ended March 31, 2020 filed with the Securities and Exchange Commission on May 6, 2020.
10.13+	Amended and Restated Executive Employment Agreement, dated April 15, 2020, by and between Neoleukin Therapeutics, Inc., and Jonathan G. Drachman—Incorporated by reference to Exhibit 10.1 to our Current Report on Form 8-K filed with the Securities and Exchange Commission on April 17, 2020
10.14	First Amendment to Lease, dated June 18, 2020, by and between Neoleukin Therapeutics, Inc. and ARE-Eastlake Avenue No. 3, LLC—Incorporated by reference to Exhibit 10.1 to our Quarterly Report on Form 10-Q for the quarter ended June 30, 2020 filed with the Securities and Exchange Commission on August 12, 2020.
10.15+	Form of Restricted Stock Unit Grant Notice for Registrant's 2014 Equity Incentive Plan— Incorporated by reference to Exhibit 10.1 to our Quarterly Report on Form 10-Q for the quarter ended June 30, 2020 filed with the Securities and Exchange Commission on August 12, 2020
10.16	Amendment No. 1 to Exclusive Start-Up License Agreement, dated July 24, 2020, by and between the University of Washington and Neoleukin Therapeutics, Inc.—Incorporated by reference to Exhibit 10.21 to our Annual Report on Form 10-K for the year ended December 31, 2020 filed with the Securities and Exchange Commission on March 25, 2021
10.17	First Amendment to Lease, dated November 5, 2020, by and between Neoleukin Therapeutics, Inc. and ARE-Seattle No. 28, LLC—Incorporated by reference to Exhibit 10.24 to our Annual Report on Form 10-K for the year ended December 31, 2020 filed with the Securities and Exchange Commission on March 25, 2021
10.18	Second Amendment to Lease, dated March 24, 2021, by and between Neoleukin Therapeutics, Inc. and ARE-Seattle No. 28, LLC—Incorporated by reference to Exhibit 10.1 to our Quarterly Report on Form 10-Q for the quarter ended March 31, 2021 filed with the Securities and Exchange Commission on May 12, 2021
10.19	Amendment No. 2 to Exclusive Start-Up License Agreement, dated December 15, 2021, by and between the University of Washington and Neoleukin Therapeutics, Inc.
10.20	ATM Equity Offering Sales Agreement, dated November 4, 2021, by and between Neoleukin Therapeutics, Inc. and BofA Securities, Inc. – Incorporated by reference to Exhibit 1.1 to Current Report on Form 8-K filed with the Securities Exchange Commission on November 4, 2021.
10.21+	Employment Agreement, dated April 14, 2021, by and between Neoleukin Therapeutics, Inc. and Priti Patel.
21.1	List of subsidiaries of the Registrant
23.1	Consent of Deloitte & Touche LLP, Independent Registered Public Accounting Firm
31.1	Certification of Chief Executive Officer pursuant to Rule 13a-14(a).
31.2	Certification of Chief Financial Officer pursuant to Rule 13a-14(a).
32.1#	Certification of Chief Executive Officer and Chief Financial Officer pursuant to 18 U.S.C. Section 1350.
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document.
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document.
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document.
101.LAB	XBRL Taxonomy Extension Labels Linkbase Document.
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document.

+ Indicates a management contract or compensatory plan.

This certification is deemed not filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (Exchange Act), or otherwise subject to the liability of that section, nor shall it be deemed incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act.

* Schedules and exhibits have been omitted pursuant to Item 601(b)(2) 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.

N/A

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.

Neoleukin Therapeutics, Inc.

Date: March 1, 2022

By: /s/ Jonathan G. Drachman

Jonathan G. Drachman
President & Chief Executive Officer
(Principal Executive Officer)

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Jonathan G. Drachman Jonathan G. Drachman	Director, President & Chief Executive Officer (Principal Executive Officer)	March 1, 2022
/s/ Robert Ho Robert Ho	Chief Financial Officer (Principal Financial and Accounting Officer)	March 1, 2022
/s/ Martin Babler Martin Babler	Director	March 1, 2022
/s/ M. Cantey Boyd M. Cantey Boyd	Director	March 1, 2022
/s/ Erin Lavelle Erin Lavelle	Director	March 1, 2022
/s/ Sarah Noonberg Sarah Noonberg	Director	March 1, 2022
/s/ Todd Simpson Todd Simpson	Director	March 1, 2022
/s/ Lewis T. Williams Lewis T. Williams	Director	March 1, 2022

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