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, 2020

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 001-38130

Aileron Therapeutics, Inc.

(Exact name of Registrant as specified in its Charter)

Delaware **(State or other jurisdiction of incorporation or organization)**	**13-4196017** **(I.R.S. Employer Identification No.)**
290 Pleasant Street, Unit 112 **Watertown, MA** **(Address of principal executive offices)**	**02472** **(Zip Code)**

Registrant's telephone number, including area code: (617) 995-0900

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

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

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

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

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

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

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

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

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

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

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

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

As of June 30, 2020, the last business day of the Registrant's most recently completed second fiscal quarter, the aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant, based on the last reported sale price of the shares of common stock on The Nasdaq Global Market was $36,630,063.

As of March 19, 2021, the Registrant has 90,210,557 shares of Common Stock, $0.001 par value per share, outstanding.

Portions of the Registrant's definitive proxy statement for its 2021 Annual Meeting of Stockholders, which the Registrant intends to file pursuant to Regulation 14A with the Securities and Exchange Commission not later than 120 days after the end of the Registrant's fiscal year ended December 31, 2020, are incorporated by reference into Part III of this Annual Report on Form 10-K.

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Aileron and the other trademarks or service marks of Aileron appearing in this Annual Report on Form 10-K are the property of Aileron. All other trademarks, service marks or other trade names appearing in this Annual Report on Form 10-K are the property of their respective owners.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This Annual Report on Form 10-K contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Annual Report on Form 10-K, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management and expected market growth are forward-looking statements. The words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

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

- our plans to develop and commercialize ALRN-6924, including the potential benefits thereof;
- our ongoing and future clinical trials for ALRN-6924, whether conducted by us or by any future collaborators, including the timing of initiation of these trials and of the anticipated results;
- our expectations regarding our ability to fund our operating expenses and capital expenditure requirements with our cash, cash equivalents and investments;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- the timing of and our ability to obtain and maintain marketing approvals for our product candidates;
- the rate and degree of market acceptance and clinical utility of any products for which we receive marketing approval;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position and strategy;
- our ability to identify additional product candidates with significant commercial potential;
- our plans to enter into collaborations for the development and commercialization of product candidates;
- potential benefits of any future collaboration;
- developments relating to our competitors and our industry;
- the impact of government laws and regulations;
- the impact the coronavirus pandemic may have on the timing of our clinical development and on our operations; and
- our ability to maintain our listing on the Nasdaq Capital Market.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements in this Annual Report on Form 10-K, particularly in the “Risk Factors” section, that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, collaborations, joint ventures or investments that we may make or enter into.

You should read this Annual Report on Form 10-K and the documents that we reference herein and have filed or incorporated by reference hereto completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

This Annual Report on Form 10-K includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties. Industry publications and

third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information.

SUMMARY RISK FACTORS

Our business is subject to a number of risks of which you should be aware in evaluating our company and our business. These risks are discussed more fully in the "Risk Factors" section of this Annual Report on Form 10-K for the year ended December 31, 2020. These risks include the following:

- Our business depends entirely on the successful development and commercialization of our product candidate, ALRN-6924. Our clinical trials of ALRN-6924 may not be successful. If our trials prove unsuccessful or if we are unable to obtain approval for and commercialize ALRN-6924 or experience significant delays in doing so, our business will be materially harmed.
- We will need substantial additional funding to continue our operations. Our cash, cash equivalents and investments are not sufficient to enable us to complete the development of or commercialize ALRN-6924. If we are unable to raise capital when needed, we may be forced to delay, reduce and/or eliminate our research and drug development programs, reduce headcount, and future commercialization efforts, or take other actions that could adversely affect our business.
- We have incurred significant losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability. Even if we are able to develop and commercialize ALRN-6924, we may never generate revenues that are significant or large enough to achieve profitability.
- The COVID-19 pandemic has affected and may continue to affect our ability to conduct our ongoing and planned clinical trials, disrupt regulatory activities, or have other adverse effects on our business and operations. In addition, this pandemic has caused substantial disruption in the financial markets and may adversely impact economies worldwide, which could result in adverse effects on our business and operations.
- The approach we are taking to discover and develop novel drugs is unproven and may never lead to marketable products.
- We are pursuing the development of ALRN-6924 in combination with approved chemotherapeutics. If the U.S. Food and Drug Administration, or the FDA, revokes approval of any such therapeutic, or if safety, efficacy, manufacturing or supply issues arise with any therapeutic that we use in combination with ALRN-6924 in the future, we may be unable to further develop and/or market ALRN-6924, or we may experience significant regulatory delays, and our business could be materially harmed.
- The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, interim results of a clinical trial, such as the interim results of our Phase 1b clinical trial of ALRN-6924 in patients with p53-mutated small cell lung cancer that we announced in October 2020, do not necessarily predict final results and the results of our clinical trials may not satisfy the requirements of the FDA or comparable foreign regulatory authorities. In addition, results of clinical trials of ALRN-6924 when used with one chemotherapy or in one patient population may not be predictive of the results of other clinical trials of ALRN-6924 when used with a different chemotherapy or in a different patient population.
- Clinical drug development is a lengthy and expensive process, with an uncertain outcome. If clinical trials of ALRN-6924 or any other product candidate that we may develop fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs, experience delays in completing, or ultimately be unable to complete, the development of ALRN-6924 or any other product candidate that we may develop or be unable to obtain marketing approval.

- We are conducting a clinical trial of ALRN-6924 and plan to conduct additional clinical trials of ALRN-6924 at sites outside the United States. The FDA's acceptance of data from clinical trials outside of the United States is subject to conditions. Accordingly, the FDA may not accept data from trials conducted in such locations and the conduct of trials outside the United States could subject us to additional delays and expense.
- We may not be able to initiate or continue clinical trials for ALRN-6924 or any other product candidate that we may develop if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or comparable foreign regulatory authorities. Patient enrollment is a significant factor in the timing of clinical trials. We do not yet know exactly how many patients will have the genetic profile that ALRN-6924 or other future product candidates are designed to address. In particular, because our clinical trials are targeted at a subset of patients in indications with p53-mutated cancers, our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate.
- If serious adverse or unacceptable side effects are identified during the development of ALRN-6924 or any other product candidate that we may develop or we observe limited efficacy of ALRN-6924 or any other product candidate that we may develop, we may need to abandon or limit the development of ALRN-6924 or other product candidates that we may develop.
- The FDA or comparable foreign regulatory authorities may, under certain circumstances, require that a companion diagnostic be approved for use with ALRN-6924. If we are unable to successfully develop and obtain approval for such a diagnostic, either on our own or through a third party, or if we experience significant delays in doing so, we may not obtain marketing approval for ALRN-6924 in a timely manner, or at all.
- We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.
- We rely on third parties to conduct our clinical trials and some aspects of our research and preclinical studies, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research and studies.
- We contract with third parties for the manufacture of our ALRN-6924 for our ongoing clinical trials and expect to continue to do so for additional clinical trials and ultimately for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of ALRN-6924 or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.
- We may seek to enter into strategic collaborations for the development, marketing and commercialization of ALRN-6924 or other product candidates. If we are unable to enter into collaborations or those collaborations into which we enter are not successful, the development, marketing and/or commercialization of ALRN-6924 or such other product candidates that are the subject of such collaborations would be harmed.
- Our success depends in part on our ability to protect our intellectual property. It is difficult and costly to protect our proprietary rights and technology, and we may not be able to ensure their protection.
- If we fail to comply with our obligations under our patent licenses with third parties, we could lose license rights that are important to our business.
- Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us, or any future collaborators, from obtaining approvals for the commercialization of ALRN-6924 or any other product candidate that we may develop. As a result, we cannot predict when or if, and in which territories, we, or any future collaborators, will obtain marketing approval to commercialize ALRN-6924 or any other product candidate that we may develop.

PART I

Item 1. Business

Overview

We are a clinical-stage chemoprotection oncology company focused on fundamentally transforming the experience of chemotherapy for cancer patients, enabling them to fight cancer without the fear or burden of chemotherapy-induced side effects. ALRN-6924, our first-in-class MDM2/MDMX dual inhibitor activating p53, is the only reported therapeutic agent in clinical development to employ a biomarker strategy, in which we exclusively focus on treating patients with p53-mutated cancers. With this targeted strategy of treating patients with p53-mutated cancers, ALRN-6924 is designed to selectively protect multiple healthy cell types throughout the body from chemotherapy while ensuring we do not protect cancer cells.

Based on its mechanism of action and reported data from our Phase 1b clinical trial evaluating ALRN-6924 in patients with p53-mutated small cell lung cancer, or SCLC, who are being treated with the chemotherapy topotecan, we believe that there may be a significant opportunity to develop ALRN-6924 as an agent to reduce the toxic side effects of chemotherapy in the bone marrow of cancer patients without adversely impacting the anti-cancer activity of chemotherapy against p53-mutant tumors. This is a concept known as “chemoprotection”. Biologically, the same mechanism of action may potentially lead to protection of healthy normal cells outside of the bone marrow, which may lead to a form of protection against side effects such as alopecia, mucositis, nausea and other side effects. We plan to explore the chemoprotective effects of ALRN-6924 in other normal tissues and organs, such as the skin, hair follicles and the gastrointestinal tract in future, randomized clinical studies.

Our clinical development program for ALRN-6924 includes our recently completed Phase 1b clinical trial evaluating ALRN-6924 as a chemoprotective agent in patients with SCLC being treated with the chemotherapy topotecan, our ongoing Phase 1 clinical trial of ALRN-6924 in healthy volunteers and a planned Phase 1b placebo-controlled clinical trial evaluating ALRN-6924 as a chemoprotective agent in patients with non-small cell lung cancer, or NSCLC, being treated with frontline chemotherapy- or immunochemotherapy. In addition, we are now investing in chemistry, manufacturing and controls or CMC, development of ALRN-6924 and in the development of a p53 companion diagnostic to accelerate our entry into late-stage development of ALRN-6924 in NSCLC. To that purpose, we plan to engage as appropriate with the U.S. Food and Drug Administration, or FDA, in 2021 to discuss the ALRN-6924 development program.

Subject to obtaining additional funding, we plan to expand our chemoprotection clinical program to other cancer indications and pursue a development path that aims at a tumor-agnostic label for ALRN-6924 as a chemoprotective agent, across many p53-mutated tumor types and chemotherapy regimens.

Chemoprotection

Millions of cancer patients across the world receive chemotherapy each year. Based on published literature, p53 mutations are present in about 50% of all cancer patients. p53-mutation testing is available using standard gene tests such as FoundationOne. Since ALRN-6924 is designed to selectively act only on cells with non-mutated or wild-type p53, our precision medicine approach is to use mutated p53 as a biomarker to identify and treat cancer patients with ALRN-6924 as a chemoprotective agent.

Chemotherapies used to treat cancer patients cause toxicities in normal tissues and organs, thereby limiting the dose and schedule of these drugs and potentially reducing their efficacy. Chemotherapy-related toxicities of the bone marrow, which can be life threatening, include neutropenia, thrombocytopenia and anemia. These toxicities can also lead to increased risk of infection, sepsis, bleeding and fatigue. This is because chemotherapies preferentially act on all proliferating cells as those cells proceed through the cell replication cycle, but chemotherapy lacks specificity for cancer cells and, consequently, can damage normal, healthy cells. In non-clinical studies our product candidate, ALRN-6924, arrested cell proliferation in normal bone marrow cells with wild-type p53 while leaving cancer cells with mutations in p53 unaffected and, therefore, susceptible to chemotherapy. As a result, we believe that treatment of cancer patients with ALRN-6924 may reduce the toxic effects of chemotherapy in the bone marrow and in other

normal tissues and organs without adversely impacting the anti-cancer activity of chemotherapy against p53-mutant tumor cells.

Our Strategy

Our goal is to improve the outcomes and the quality of life of cancer patients by selectively protecting healthy cells from harmful effects of chemotherapy, a concept that we refer to as chemoprotection. Key elements of our strategy to achieve this goal include the following:

Pursue a development strategy, using a precision-medicine approach, for our product candidate, ALRN-6924, as a chemoprotective agent aiming to achieve a tumor-agnostic label for multiple chemotherapies and p53-mutant tumor types.

We have recently completed a Phase 1b clinical trial that demonstrated proof-of-concept of ALRN-6924 as a chemoprotective agent in patients with p53-mutated SCLC being treated with the chemotherapy topotecan. In this trial we are testing multiple dose levels and dosing schedules of ALRN-6924 when administered before topotecan. The key data from the trial was presented as late-breaking presentation at the EORTC-NCI-AACR 2020 conference in October 2020, and additional data from that trial will be submitted for a presentation at a medical conference in the second half of 2021. Reported data from this trial have informed our choice of the recommended dose of ALRN-6924 for subsequent clinical trials, including a Phase 1b trial in patients with NSCLC.

In the second quarter of 2021 we plan to initiate a new Phase 1b clinical trial to assess ALRN-6924 as a chemoprotective agent in advanced patients with p53-mutated NSCLC being treated with first-line chemotherapy with carboplatin and pemetrexed with or without an immune checkpoint inhibitor. This trial is randomized, placebo-controlled, double-blinded, and it is designed to evaluate the potential chemoprotective effects of ALRN-6924 in this patient population. We plan to begin enrolling patients in the NSCLC trial in the second quarter of 2021 and we anticipate reporting interim data (10-20 patients) at the end of 2021 and topline results (60 patients) in mid-2022.

We are also conducting a trial of ALRN-6924 in healthy human volunteers to characterize the time to onset, magnitude, and duration of cell cycle arrest in human bone marrow relative to ALRN-6924 administration, with the goal of developing a universal dosing regimen for ALRN-6924 for use as a chemoprotection agent across a range of additional chemotherapies and tumor indications. Results from the trial remain on track to be reported in mid-2021 and will be submitted for a presentation at a medical conference in second half of 2021.

In addition, we are now investing in CMC development of ALRN-6924 and in the development of a p53 companion diagnostic to support initiation of registrational trials following our Phase 1b clinical trial in NSCLC. To that purpose, we plan to engage as appropriate with the FDA in 2021 to discuss the ALRN-6924 development program.

Subject to obtaining additional funding, we plan to expand our chemoprotection clinical program to other cancer indications and pursue a development path that could lead to a tumor-agnostic label for ALRN-6924 as a chemoprotective agent, across many tumor types and chemotherapy regimens.

Maximize the global commercial value of ALRN-6924.

We have all commercial rights to ALRN-6924, and we may enter into strategic collaborations for the development, marketing, and commercialization of ALRN-6924 and any other product candidates we may develop, particularly those directed towards indications with larger patient populations and in certain geographies where we believe a collaboration could bring additional resources and expertise to maximize the value of our product candidates.

Protect ALRN-6924 and our proprietary technologies that we believe are important to our business.

We strive to maintain patent protection intended to cover the composition of matter of ALRN-6924, its methods of use, related platform technology and other inventions. As of March 1, 2021, we owned or had an exclusive license to at least 206 patents and at least 52 provisional or non-provisional patent applications throughout the world directed toward various aspects of our product candidates and research programs.

Chemotherapy and the Need for Novel and Improved Treatment Options to Reduce Chemotherapy-Induced Toxicity

Cancer is a major public health problem in the United States and worldwide. The U.S. National Cancer Institute estimated that approximately 40% of all men and women in the United States will be diagnosed with cancer during their lifetime. According to the U.S. Centers for Disease Control, cancer is currently the second leading cause of death in the United States and is expected to surpass heart disease as the leading cause of death in the next several years. Although progress has been made in the diagnosis and treatment of cancer, the American Cancer Society estimates that approximately 1.8 million new cancer cases will be diagnosed in the United States and more than 600,000 people will die from cancer in 2021.

Chemotherapies are a critical therapeutic pillar to treat cancer patients, but they cause toxicities in normal tissues and organs that limit the dose and schedule of these drugs, thus reducing their efficacy. These toxicities are due to the lack of specificity of chemotherapies, which act on all proliferating cells as they proceed through the cell replication cycle. Consequently, these chemotherapies can damage normal, healthy cells. Chemotherapy-related toxicities of the bone marrow include anemia, neutropenia and thrombocytopenia, which may lead to fatigue, increased risk of infection, sepsis and bleeding, and can be life threatening. We believe arresting the cell cycle of bone marrow cells prior to systemic treatment with chemotherapy will reduce or mitigate the toxic effect on those cells.

Chemotherapy-induced toxicity clinically presents as neutropenia, thrombocytopenia and anemia, and represents one of key dose-limiting toxicities occurring in the course of treatment of cancer patients. Two major consequences of chemotherapy-induced toxicity are increased risk to patient safety and reduced efficacy of chemotherapy due to dose reductions and dose delays.

Available treatment strategies for clinical management of chemotherapy-induced toxicity include the use of growth factors, transfusions, and dose reductions and dose delays of therapy. While growth factors can be effective in addressing their respective indication, such as neutropenia or anemia, they are known to increase the risk of tumor progression, and carry the risk of other side effects. Transfusions are limited by availability and supply, as well as transfusion reactions that may require medical treatment. Therefore, management of chemotherapy-induced toxicity remains a significant unmet medical need for hundreds of thousands of cancer patients worldwide.

Granulocyte-colony-stimulating-factor, or G-CSF, is a glycoprotein that stimulates the bone marrow to produce granulocytes and stem cells and release them into the bloodstream. Platelet growth factors or thrombopoietin (TPO) receptor agonists, including romiplostim (Nplate) and eltrombopag (Promacta/Revolade), stimulate megakaryocytes in the bone marrow and increase platelet production, but fail to protect patients from chemotherapy-induced thrombocytopenia. Erythropoietin, is a glycoprotein cytokine secreted by the kidney in response to cellular hypoxia and it stimulates red blood cell production, or erythropoiesis, in the bone marrow. Additionally, blood products such as donated red blood cells and platelets can be transfused to patients with anemia and thrombocytopenia, respectively.

While growth factors are widely used in the medical management of cancer patients who experience cytopenias, their prescribing information indicates that those drugs may stimulate the growth and aggressiveness of cancer cells Another important consideration is that those supportive care measures are used to treat patients once they experience cytopenias and are already at risk of infection and bleeding.

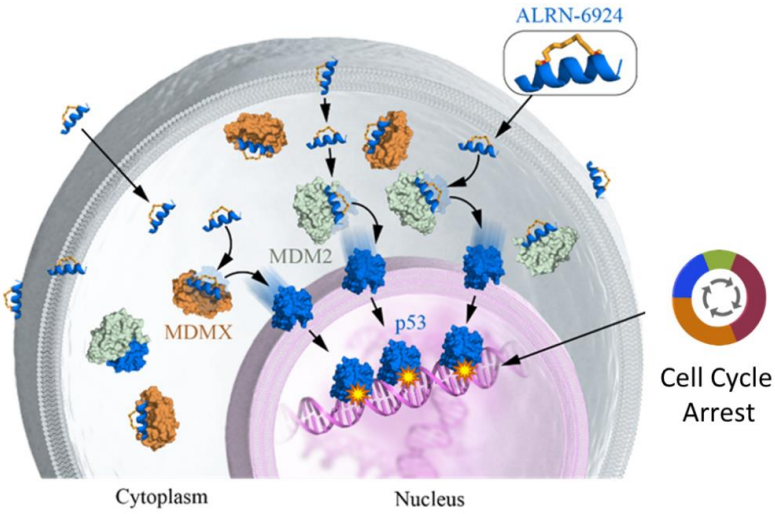
Novel and optimized supportive care drugs should ideally have mechanisms of action that selectively protect normal healthy cells without protecting cancer cells from chemotherapy-related toxicities (thus rendering cancer cells fully vulnerable to chemotherapy).

We believe ALRN-6924 with its specific mechanism of p53 release is positioned to address both requirements. When used in patients with cancers harboring p53 mutations, ALRN-6924 is expected to release functional p53 in normal healthy cells only, and thus will functionally not affect cancer cells. Due to lack of effect in cancer cells, ALRN-6924 could be used safely in a prophylactic manner, mitigating and reducing cytopenias and potentially other chemotherapy-related side effects caused by anti-cancer drugs.

p53 and its Control of the Cell Replication Cycle

One of the main functions of p53 is to control genes that regulate the cell replication cycle. Chemotherapy preferentially acts on cells that are cycling, i.e. undergoing the process of cell division. In cancer cells, the cell cycle is unchecked, which leads to uncontrolled cell proliferation, a hallmark of cancer. Certain types of healthy cells also naturally need to cycle, such as bone marrow cells, hair follicle cells, skin cells, and cells lining the oral cavity and the gastrointestinal tract. As a result, chemotherapy preferentially targets and kills both cycling healthy cells and cycling cancer cells. This, in turn, can lead to a spectrum of chemotherapy-induced side effects, from unpleasant to life-threatening and fatal. In cells with DNA damage from radiation or chemical modification by a carcinogen, cell cycle arrest by p53, which is the activation of normal p53 protein in patients' healthy cells, temporarily and reversibly pauses cell cycling ensuring that damaged cells do not continue to propagate uncontrollably and form cancerous lesions. This is why functional p53 is critical to human health and the main reason it has been called the "guardian of the genome." When p53 itself is mutated or pathologically inhibited by its natural regulators, cells can grow uncontrollably and may eventually form a tumor. Approximately half of all cancer patients at initial diagnosis have cancers that harbor mutations in the p53 gene, thus causing loss of function of p53 in cancer cells. Healthy cells in cancer patients retain normal p53 function.

Because of its importance in the cell replication cycle, p53 activity is carefully regulated in normal, healthy cells. As depicted in the figure below, the most important regulatory elements for p53 are MDM2 and MDMX, two proteins that bind to p53 and play non-redundant roles in modulating p53 activity. In normal healthy cells, MDM2 primarily acts to shuttle p53 out of the nucleus and target it for degradation, whereas MDMX generally acts to sequester p53. By playing these roles, MDM2 and MDMX collectively suppress p53's activity so that normal healthy cells can function as expected. In healthy cells that rapidly replicate under normal circumstances, such as bone marrow cells that divide and transform into blood cells, p53 activation can induce cell cycle arrest. ALRN-6924 is designed to achieve this effect by entering the cell and mimicking the p53 protein to disrupt p53's interactions with its endogenous inhibitors, MDMX and MDM2. ALRN-6924 thereby activates the mechanisms used by p53 in normal healthy cells with non-mutant, or "wild-type" p53 to regulate cell division and progression through the cell replication cycle. We have shown that ALRN-6924 can temporarily and reversibly arrest cell cycling in normal, p53-wild-type cells to selectively shield them from chemotherapy.



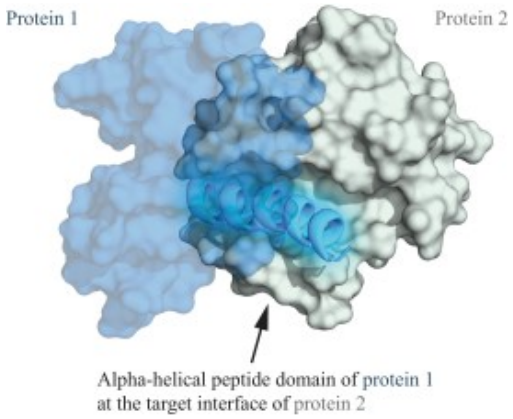
Our Platform – Stabilized Cell-Permeating Peptides

We stabilize peptides by "stapling" them with hydrocarbon bonds into their natural alpha-helical conformation. We achieve this by inserting into the peptides two or more non-natural amino acids that, when catalyzed by a chemical reaction, form a bridge to provide comparable stability to the endogenous protein structure and maintain the biological activity of the peptide.

Our platform enables us to chemically stabilize and improve the performance and activity of a broad range of alpha-helical peptides that we believe may have benefit in oncology and other diseases. We believe that our stabilized peptides can potentially activate and inhibit key cellular functions that underlie disease and that are otherwise difficult to target with existing drug technologies, including small molecules and monoclonal antibodies.

The Value and Intrinsic Limitations of Peptide Drugs

Nature's evolutionarily optimized molecular template to control cellular functions via protein-protein interactions is the peptide. Peptides are functional subunits of proteins that act as nature's locks and keys and enable two proteins to interact. The alpha-helical structure is the most common peptide structure found at these protein interfaces.

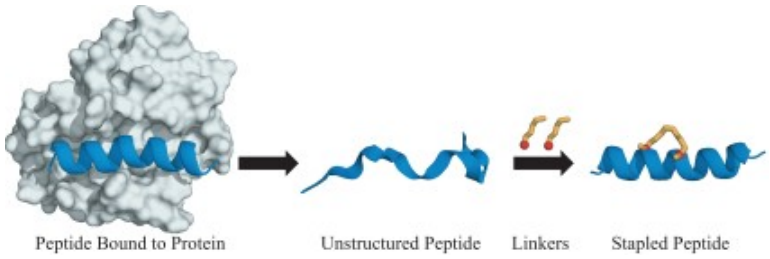


There are presently more than 60 approved peptide drugs, including insulin, liraglutide (Victoza), exenatide (Byetta), teriparatide (Forteo) and Linaclotide (Linzess), that have benefitted patients and improved their quality of life. Attractive attributes of peptide drugs include high specificity and low off-target toxicity, high potency, wide systemic distribution with limited accumulation in specific organs, ready synthesis and rational optimization. Despite these advantages, and the information regarding over 3,000 known alpha-helical protein structures contained in publicly available protein data banks, small molecules remain the primary approach by which drug developers attempt to modulate protein functionality. Drug developers have tended to avoid developing peptide drugs in favor of small molecule drugs because peptide drugs, while highly effective in certain applications, have intrinsic liabilities that limit their applications as therapeutics, including poor biological stability (due to protein degradation), poor chemical stability (due to loss of helical configuration when removed from their natural protein scaffold), short plasma half-lives and the inability to effectively penetrate cell membranes to access desirable intracellular targets.

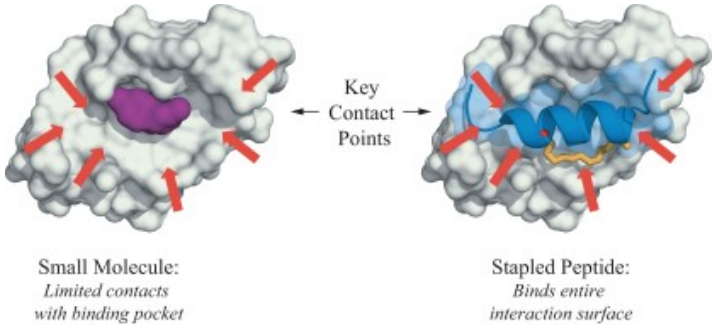
Small molecules currently represent the dominant therapeutic modality underlying the majority of approved drugs and are the only modality that can directly engage protein targets and protein-protein interactions that are contained inside our cells. However, protein-protein interactions are still viewed as difficult targets for small molecule drugs due to the fact that these protein targets often present relatively large and flat interacting surfaces that are not readily addressed by small molecule drugs. In addition, many of the emerging therapeutically important pathways have been found to require engagement of multiple proteins, like MDM2 and MDMX, or multiple binding sites in order to fully engage the mechanism and drive the desired biological activity. Multiple binding sites and complex mechanisms have to date proven to be challenging to small molecules due to their small size and physiochemical properties. We believe that limitations of existing drug technologies like small molecules will become increasingly apparent as the scientific and medical fields continue to understand and reveal the complexity of protein interactions, cellular pathways and disease etiology.

Our Solution

We believe our platform addresses and solves many of the inherent limitations of peptides. Because peptides lose their shape by unwinding when removed from their natural protein scaffold, developing chemical interventions to stabilize peptides into their bioactive structure has been and remains an active area of research. Although there have been several published examples of peptide stabilization strategies, these strategies have not translated into clinically relevant drugs for intracellular targets. Our all-hydrocarbon linker, or "staple", has emerged as a solution that stabilizes the alpha-helical structure, improves protease resistance, enables cellular penetrance and maintains biological activity.



Unlike large proteins that do not penetrate cell membranes due to their size and biophysical properties, such as monoclonal antibodies or other naturally occurring proteins, stabilized alpha-helical peptides can in many circumstances penetrate cells and still maintain high affinity to their large protein surface targets. Our peptides typically retain the molecular target specificity of their underlying native protein structure. As depicted below, we believe that the larger protein structure provides multiple surface contact points accessible to the stabilized peptide, while the small molecule drugs have difficulty binding to the larger, shallower contact points. In addition, as has been demonstrated in third-party publications, the multiple surface contact points mean that the binding may be less likely to be disrupted by single point mutation in the underlying genetic code.



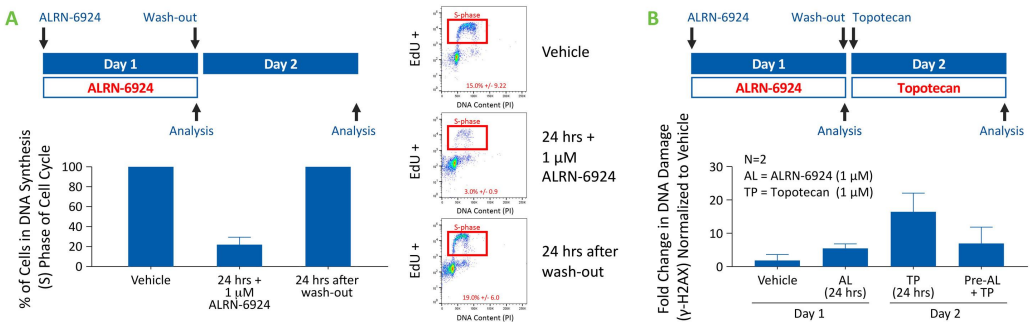
ALRN-6924 as a Chemoprotective Agent

Chemotherapies used to treat cancer patients can cause toxicities in normal tissues and organs, thereby limiting the dose and schedule of these drugs and reducing their efficacy. These toxicities are due to the lack of specificity of chemotherapies, which act on all proliferating cells as they proceed through the cell replication cycle. Consequently, these chemotherapies can damage normal, healthy cells. Chemotherapy-related toxicities of the bone marrow include anemia, neutropenia and thrombocytopenia, which may lead to fatigue, increased risk of infection, sepsis and bleeding, and can be life threatening. We believe arresting proliferation of bone marrow cells prior to systemic treatment with chemotherapy should reduce or mitigate the toxic effect on those cells. ALRN-6924 can pause cell division in cells with wild type (WT) p53, including normal bone marrow cells, and ALRN-6924 has no activity against cancer cells with mutations in p53. As a result, we believe that treatment of patients with ALRN-6924 may reduce the toxic effects of chemotherapy in the bone marrow without adversely impacting the anti-cancer activity of chemotherapy against p53-mutant tumor cells.

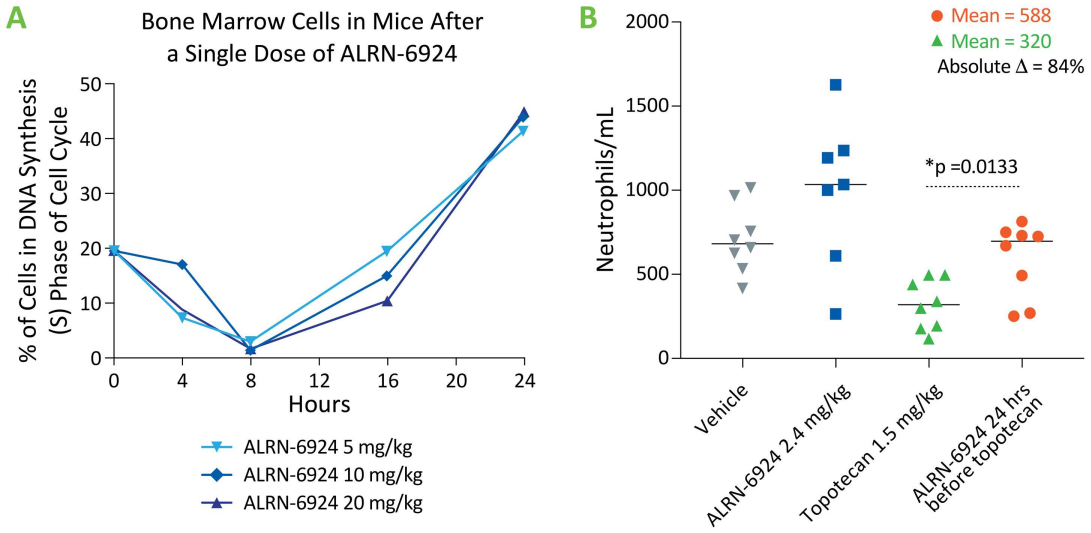
We believe there is a significant opportunity for the use of ALRN-6924 as a chemoprotective agent. In preclinical studies, ALRN-6924 successfully activated WT p53 and induced cell-cycle arrest in normal tissues, including bone marrow cells, in a dose and schedule dependent manner. However, ALRN-6924 did not induce apoptosis or cell-cycle arrest in mutant p53 cancer cells. Bone marrow toxicity is the dose-limiting safety concern of many chemotherapeutics, and cell-cycle arrest prior to administration of chemotherapy has been shown to reduce bone marrow toxicity. As such, we believe ALRN-6924 may serve as a chemoprotective agent in bone marrow cells, without adversely impacting the cell cycle of mutant p53 cancer cells. Therefore, p53-mutant cancer cells remain fully susceptible to chemotherapy following dosing with ALRN-6924.

Preclinical Studies

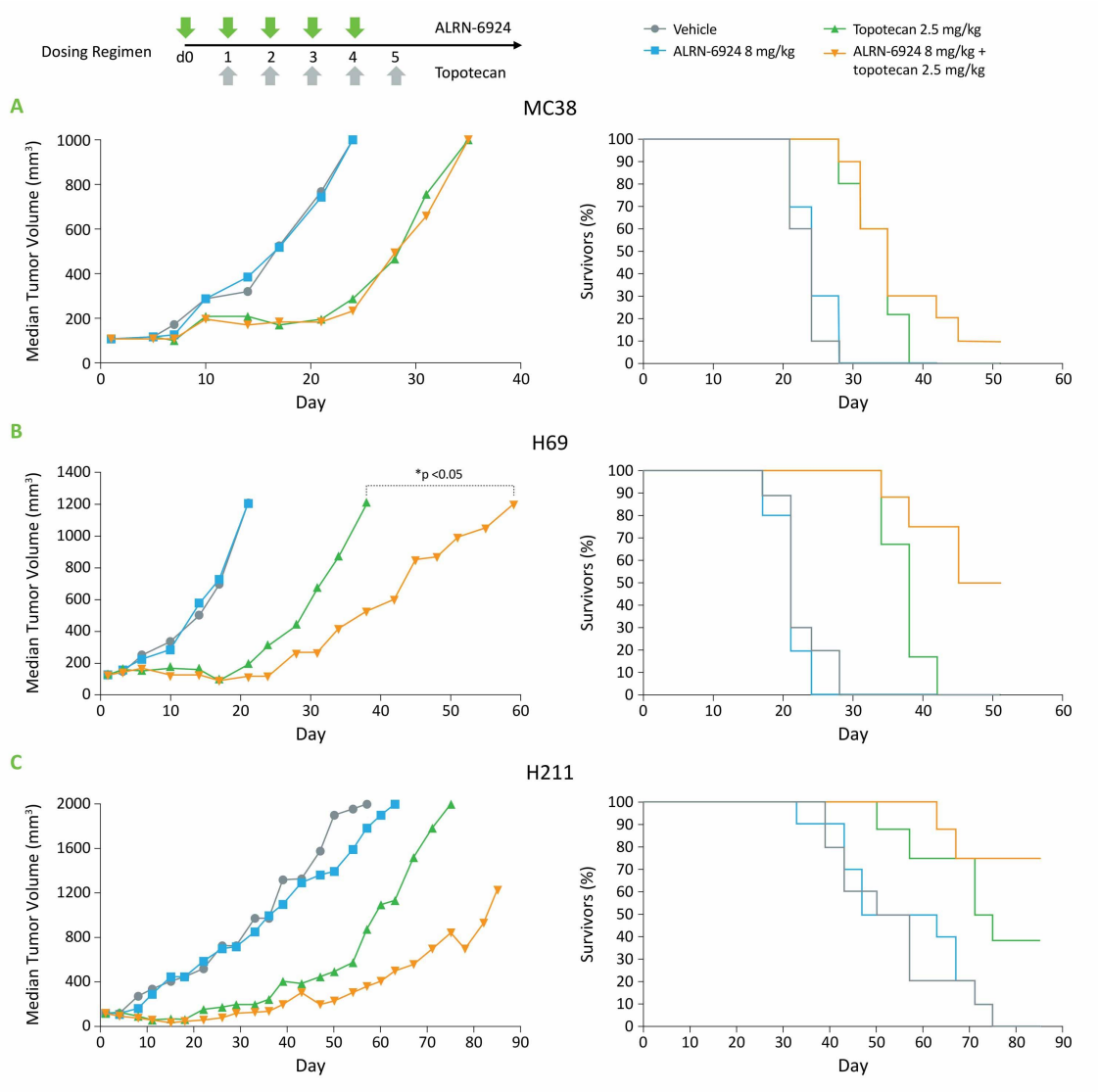
In nonclinical research that we presented at the October 2019 AACR-NCI-EORTC Conference on Molecular Targets and Cancer Therapeutics, ALRN-6924 prevented the toxic side effects of chemotherapy in normal healthy cells while enhancing the anti-cancer activity of chemotherapy. The figures below show that ALRN-6924 reversibly induced cell cycle arrest in normal human bone marrow cells in vitro, and protected bone marrow cells from chemotherapy-induced DNA damage when administered in advance of topotecan, a chemotherapy used in small-cell lung cancer and other cancer indications. In Figure (A), ALRN-6924-induced cell cycle arrest was measured by flow cytometry in human bone marrow cells following incubation with ALRN-6924 ex vivo for 24 hours. In Figure (B), topotecan-induced DNA damage was measured in human bone marrow by γH2AX incorporation following exposure to vehicle or ALRN-6924 for 24 hours to induce cell cycle arrest, then incubated with topotecan for an additional 24 hours following a wash-out step.



In addition, as shown in the figures below in other nonclinical studies, low doses of ALRN-6924 triggered reversible cell-cycle arrest in bone marrow cells in a mouse model of topotecan-induced toxicity and reduced neutropenia caused by topotecan in vivo. In Figure (A), cell cycle arrest in the bone marrow of ALRN-6924-treated C57BL/6 mice was measured by flow cytometry using EdU incorporation in lineage negative, c-Kit positive hematopoietic stem and progenitor cells. In Figure (B), topotecan-induced neutropenia was measured in female C57BL/6 mice following topotecan treatment on days 1-5 and either ALRN-6924 or vehicle on days 0-4.



In three different mouse models of p53-mutant cancer shown below, ALRN-6924 did not diminish topotecan's anti-tumor activity. In addition, ALRN-6924 in combination with topotecan yielded enhancement of tumor growth inhibition and/or improved overall survival in all three models. In these studies, C57BL/6 mice (n=10) bearing established syngeneic MC38 colon cancer tumors (A) or athymic nu/nu mice bearing established H69 (B) or H211 (C) small-cell lung cancer xenograft tumors were treated with topotecan on days 1-5 and either ALRN-6924 or vehicle on days 0-4.



Based on these results, we believe ALRN-6924 has the potential to be an effective chemoprotective agent for bone marrow cells of patients without affecting the anti-cancer activity of chemotherapy in p53-mutant cancers.

Clinical Development of ALRN-6924 as a Chemoprotective Agent

In September 2019, we initiated a Phase 1b trial of ALRN-6924 in patients with advanced p53-mutated SCLC receiving second line topotecan to assess the ability of ALRN-6924 to reduce the proportion of patients with Grade 3/4 treatment emergent adverse events, or TEAEs, and to mitigate and reduce severe anemia, thrombocytopenia and neutropenia related to treatment with topotecan. In the dose optimization part of the trial, ALRN-6924 was administered 24 hours before each dose of topotecan at different dose levels in order to determine the optimal chemoprotective dose of ALRN-6924. The schedule optimization part of the trial was intended to determine the time window when ALRN-6924 should be given prior to topotecan.

On October 24, 2020, we announced positive data demonstrating clinical proof of concept that treatment with ALRN-6924 prior to second-line topotecan administration provides a protective effect against severe anemia, thrombocytopenia and neutropenia. The results were featured as a late-breaking poster presentation at the 32nd EORTC-NCI-AACR Annual Symposium on Molecular Targets and Cancer Therapeutics in October 2020. As of an August 31, 2020 data cut-off, a total of 26 SCLC patients were enrolled in the dose optimization part of the trial. Of these patients, 18 were enrolled across three ALRN-6924 dose levels (1.2 mg/kg, 0.6 mg/kg and 0.3 mg/kg) and an additional eight patients were enrolled in a 0.3 mg/kg expansion cohort. 25 of the 26 patients were evaluable per the trial protocol. ALRN-6924 was administered 24 hours before each dose of topotecan. Topotecan (1.5 mg/m2) was administered on days 1 through 5 of every 21-day treatment cycle. In the trial, toxicities were evaluated using laboratory analyses and the National Cancer Institute's, or NCI, Common Terminology Criteria for Adverse Events, or CTCAE. Per the Phase 1b trial protocol, patients were not permitted to receive prophylactic granulocyte-colony stimulating factor, or G-CSF, treatment in cycle 1.

Key findings from the interim data include the following:

- A protective effect against severe chemotherapy-induced toxicities was observed across all ALRN-6924 dose levels.
- Across all ALRN-6924 dose levels, Grade 3/4 anemia, Grade 3/4 thrombocytopenia and Grade 4 neutropenia were limited to 24%, 36% and 48% of patients, respectively.
- While chemoprotection effects were observed across all ALRN-6924 dose levels, the 0.3 mg/kg dose level showed the most robust chemoprotection results, with Grade 3/4 anemia, Grade 3/4 thrombocytopenia and Grade 4 neutropenia limited to 21%, 36% and 43% of patients, respectively.
- None of the patients treated at 0.3 mg/kg dose level had hematological serious adverse events. One patient (7%) treated at 0.3 mg/kg dose level required one red blood cell transfusion and one platelet transfusion.
- At the 0.3 mg/kg ALRN-6924 dose level, no patients required erythropoiesis-stimulating agents, and seven patients (50%) required G-CSF treatment.
- Across all ALRN-6924 dose levels, no patients experienced febrile neutropenia which is a life-threatening side effect commonly observed with topotecan treatment in this patient population.

We completed the trial, including enrolling an additional 11 SCLC patients in order to complete the evaluation of the dose-response relationship. A preliminary evaluation of data from those 11 patients (seven patients receiving 0.3 mg/kg ALRN-6924 six hours before topotecan and four patients receiving 0.2 mg/kg ALRN-6924 twenty-four hours before topotecan) supports our belief that administering ALRN-6924 at 0.3mg/kg and 24 hours before topotecan remains the optimal schedule. We expect to submit final results for presentation at a scientific conference in the second half of 2021.

We are also conducting a trial of ALRN-6924 in healthy human volunteers to characterize the time to onset, and magnitude and duration of cell cycle arrest in human bone marrow relative to ALRN-6924 administration. The aim of the healthy volunteer study is to develop a universal dosing regimen for ALRN-6924 for use as a chemoprotection agent across a range of additional chemotherapies and tumor indications. Results from the trial will be submitted for presentation at a medical conference in the second half of 2021.

In the second quarter of 2021, we expect to initiate a randomized, double-blind, placebo-controlled clinical Phase 1b trial of ALRN-6924 in patients with advanced NSCLC receiving treatment with the chemotherapy regimen carboplatin/pemetrexed. This clinical trial is designed to enroll 60 patients who will be randomized 1:1 to receive either 0.3 mg/kg of ALRN-6924 or placebo in addition to the standard of care chemo- or immunochemotherapy. The

trial is designed to evaluate the chemoprotective effects of ALRN-6924, including potential reductions in bone marrow toxicity and other toxicities. The clinical trial protocol prespecifies two interim data analyses, for safety and futility, and a final analysis once all 60 patients are enrolled and complete at least four cycles of study treatment.

Past Clinical Trials

We have evaluated high dose therapy with ALRN-6924 (up to 5 mg/kg bodyweight) in earlier clinical trials in more than 200 patients to test ALRN-6924 as a direct anti-cancer agent in a single-agent Phase 1 trial in solid tumor and lymphoma patients; a Phase 2a trial for the treatment of peripheral T-cell lymphoma, or PTCL; a single-agent Phase 1 trial for the treatment of acute myeloid leukemia, or AML, and advanced high-risk myelodysplastic syndrome, or MDS; a Phase 1b trial testing the combination of ALRN-6924 and cytarabine, or Ara-C, in patients with MDS; and a Phase 2a combination trial of ALRN-6924 and palbociclib in patients with tumors harboring MDM2 amplifications or MDM2/CDK4 co-amplifications. We ceased further clinical development for those indications in light of our resources and our assessment of the commercial opportunities and competitive landscape in these indications.

Manufacturing

We contract with third parties for the GMP manufacture of our product candidates for certain preclinical studies and clinical trial materials, including raw materials and consumables necessary for their manufacture. We intend to continue to contract for these materials in the future, including commercial manufacture if our product candidates receive marketing approval. We do not own or operate GMP manufacturing facilities, nor do we currently plan to build our own GMP manufacturing capabilities for the production of ALRN-6924 for clinical or commercial use. Although we rely upon contract manufacturers for the manufacture of our product candidates for clinical trials, we have personnel with extensive manufacturing experience who oversee our contract manufacturers. In the future, we may also rely upon collaboration partners, in addition to contract manufacturers, for the manufacture of our product candidates or any products for which we obtain marketing approval.

The active pharmaceutical ingredient, or API, for ALRN-6924 is currently manufactured by a single contract manufacturer. Although we may do so in the future, we do not currently have arrangements in place for redundant supply of the API for ALRN-6924. We contract with a different manufacturer to conduct fill-and-finish and labeling services, as well as for the storage and distribution of ALRN-6924 to clinical sites. We believe that these third parties have sufficient capacity to meet our current demand and, in the event they fail to meet our demand, we believe that adequate alternative sources for the supply of materials for ALRN-6924 exist. We intend to identify and qualify additional manufacturers to provide the API and fill-and-finish services for ALRN-6924 prior to seeking marketing approval for ALRN-6924.

We believe that, because ALRN-6924 is a peptide, it can be manufactured through reliable and reproducible synthetic processes from readily available raw materials and then purified and packaged for clinical use. We believe that the chemistry process is amenable to scale-up and does not require unusual equipment in the manufacturing process.

We have agreed to purchase all of our olefin metathesis catalyst compositions, which are used in the manufacturing process to cross-link, or “staple,” our API precursors into the final stapled peptides, under a license agreement with Materia, Inc. which has later merged with Umicore Precious Metals Chemistry USA, LLC, or Umicore. If Umicore is unable to meet our requirements for such olefin metathesis catalyst compositions in terms of amount or delivery date, then under the license agreement, we are permitted to procure such olefin metathesis catalyst compositions from a third party until such time that Umicore can meet our requirements.

Manufacturing clinical products is subject to extensive regulations that impose various procedural and documentation requirements, which govern record keeping, manufacturing processes and controls, personnel, quality control and quality assurance. Our contract manufacturers are required to comply with current good manufacturing practice regulations, which are regulatory requirements for the production of pharmaceuticals that will be used in humans.

Companion Diagnostic

We expect to be required to have a companion *in vitro* diagnostic, to identify patients with mutated p53 cancer cells, approved for use with ALRN-6924. We may also be required to obtain similar approvals from comparable foreign regulatory authorities. We are in the process of evaluating a third party for the development and supply of a commercially available diagnostic to identify patients with mutated p53, requiring approval of the diagnostic by regulatory authorities. We currently rely upon commercially available third-party assays and employ a central laboratory to test both archived tumor tissue samples and fresh biopsy samples from patients taken prior to enrollment in our clinical trials to identify mutated p53.

Competition

The pharmaceutical and biotechnology industries generally, and the cancer drug sector specifically, are highly competitive and characterized by rapidly advancing technologies, evolving understanding of disease etiology and a strong emphasis on proprietary drugs. While we believe that ALRN-6924, development capabilities, experience and scientific knowledge provide us with competitive advantages, we face significant potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research institutions. If we successfully develop and commercialize ALRN-6924, it will compete with existing therapies and new therapies that may become available in the future.

There are a large number of companies developing or marketing treatments for cancer, including the indications for which we may develop product candidates. Many of the companies that we compete or may compete against in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved drugs than we do. Small or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or that may be necessary for, our programs.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any drugs that we may develop. Our competitors also may obtain FDA or other regulatory approval for their drugs more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. The key competitive factors affecting the success of any product candidate, if approved, are likely to be its efficacy, safety, convenience, price, the effectiveness of companion diagnostics in guiding the use of related therapeutics, the level of generic competition and the availability of reimbursement from government and other third-party payors.

The most common methods of treating patients with cancer are surgery, radiation and drug therapy. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. Some of the currently-approved drug therapies are branded and subject to patent protection and may be established as the standard of care for the treatment of indications for which we may choose to seek regulatory approvals. Many of these approved drugs are well-established therapies and are widely accepted by physicians, patients and third-party payors, and, even if our product candidates were to be approved, there can be no assurance that our drugs would displace existing treatments. In addition to currently marketed therapies, there are also a number of drugs in late-stage clinical development to treat cancer, including the indications for which we are developing ALRN-6924. These clinical-stage drug candidates may provide efficacy, safety, convenience and other benefits that are not provided by currently-marketed therapies. As a result, they may provide significant competition for ALRN-6924 any of our future product candidates for which we obtain regulatory approval.

We designed ALRN-6924, our product candidate, to act as a reactivator of p53 and initially focused on development for the treatment of various cancers. We are aware of other product candidates that are in clinical development for the treatment of various cancers through the reactivation of p53. Although there is a subset of drugs that directly target the p53 pathway, there are many cancer drugs that claim to affect the p53 pathway by upstream or complementary pathways. We are aware of selective small molecule inhibitors that are designed to target the p53-MDM2 interaction in various stages of clinical development being tested by F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc., or collectively Roche, Novartis AG, Daiichi Sankyo Co., Ltd., Boehringer Ingelheim, Ascentage Pharma Group Corporation, Ltd, Kartos Therapeutics, Inc. and Unity Biotechnology, Inc. including testing MDM2 inhibitors in combination with a variety of other anti-cancer agents.

In February 2021, the FDA approved trilaciclib (COSELA™), a short-acting intravenous CDK4/6 inhibitor developed by G1 Therapeutics, Inc., or GTHX, to decrease chemotherapy-induced myelosuppression in adult patients when administered prior to a platinum/etoposide-containing regimen or topotecan-containing regimen for extensive-stage SCLC. GTHX is conducting additional clinical trials of trilaciclib in other cancer indications. In addition, ALRN-6924 may compete with multiple approved drugs or drugs that may be approved in the future, such as plinabulin which is in development for chemotherapy-induced neutropenia.

Intellectual Property

We strive to protect the proprietary technologies that we believe are important to our business, including seeking and maintaining patent protection intended to cover the composition of matter of our product candidates, including ALRN-6924, their methods of use, related technology, and other inventions that are important to our business. In addition to patent protection, we rely on trade secrets and confidentiality agreements to protect our technology, know-how and other aspects our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions, and know-how related to our business, defend and enforce our patents, maintain our licenses to use intellectual property owned by third parties, preserve the confidentiality of our trade secrets, and operate without infringing the valid and enforceable patents and other proprietary rights of third parties.

A third party may hold intellectual property, including patent rights, which are important or necessary to the development or commercialization of our product candidates. If it becomes necessary for us to use patented or proprietary technology of third parties to develop or commercialize our product candidates, we may need to seek a license from such third parties. Our business could be harmed, possibly materially, if we are unable to obtain such a license on terms that are commercially reasonable, or at all.

We may seek to expand our intellectual property estate by filing patent applications directed to dosage forms, methods of treatment, diagnostics, and additional compounds and their derivatives. Specifically, we have sought and continue to seek patent protection in the United States and internationally for novel compositions of matter covering the compounds, the chemistries and processes for manufacturing these compounds, and the use of these compounds in a variety of therapies.

The patent positions of biopharmaceutical companies like us are generally uncertain and involve complex legal, scientific and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Consequently, we do not know whether any of our product candidates will be protectable or remain protected by enforceable patents. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient proprietary protection from competitors. Any patents that we hold may be challenged, circumvented or invalidated by third parties.

Because patent applications in the United States and certain other jurisdictions are maintained in secrecy for 18 months, and since publication of discoveries in the scientific or patent literature often lags actual discoveries, we cannot be certain of the priority of inventions covered by pending patent applications. Moreover, we may have to participate in interference proceedings declared by the United States Patent and Trademark Office, or USPTO, to determine priority of invention or in post-grant challenge proceedings at the USPTO or at a foreign patent office,

such as inter partes review and post grant review proceedings at the USPTO and opposition proceedings at the European Patent Office, that challenge priority of invention or other features of patentability. Such proceedings could result in substantial cost, even if the eventual outcome is favorable to us.

We generally file a provisional patent application with the USPTO first and then subsequently file a corresponding non-provisional patent application, which enables us to establish an earlier effective filing date in the subsequently filed non-provisional patent application. In order to benefit from the earlier effective filing date, we must file a corresponding non-provisional patent application, such as a utility application in the United States or an international application under the Patent Cooperation Treaty, or PCT, within 12 months of the date of the provisional patent application filing. Based on a PCT filing, we may file national and regional patent applications in the United States or foreign jurisdictions, such as the European Union, the United Kingdom, China, Japan, Australia, Canada, Brazil, India, Indonesia, Israel, Mexico, New Zealand, South Korea, Singapore, South Africa or the Eurasian Patent Organization. To date, we have not filed for patent protection in all national and regional jurisdictions where such protection may be available, and we may decide to abandon national and regional patent applications before a patent is granted. In addition, the patent grant proceeding for each national or regional patent application that we file is an independent proceeding. As a result, it is possible for a patent application to be granted in one jurisdiction and denied in another jurisdiction, and depending on the jurisdiction, the scope of patent protection may vary.

Patent Portfolio

We have rights in patents and patent applications directed to the composition of matter and/or use of our product candidate, ALRN-6924, in the United States and in other countries. We also have an exclusive license to patents that are directed to a class of compounds that includes ALRN-6924. The composition of matter patents that are directed towards the specific chemical structure of ALRN-6924 are wholly-owned by us and are expected to expire in 2033, absent any potential patent term extension under the Hatch-Waxman Act, which is discussed in greater detail below. In addition, we have granted patents and pending patent applications directed towards the composition of matter for ALRN-6924 in foreign jurisdictions, including the United Kingdom, France, Germany, Australia, Canada, China, Japan, Singapore, Taiwan, India and Hong Kong, among others. Our patent portfolio also includes wholly-owned patents and patent applications that cover uses for ALRN-6924 in both the US and foreign jurisdictions.

As of March 1, 2021, we owned or had an exclusive license to 48 U.S. patents, 11 pending U.S. provisional or non-provisional patent applications, 158 foreign patents and 41 pending foreign applications. The claims of these owned or in-licensed patents and patent applications are directed toward various aspects of ALRN-6924 and research programs. Specifically, the claims of these patents and patent applications include compositions of matter, methods of use, drug product formulations, diagnostics, methods of manufacture and methods of identifying active compounds. Such owned and in-licensed patents and patent applications, if issued, are expected to expire on various dates from 2021 through 2037, without taking into account any possible patent term adjustments or extensions. In addition, within our patent portfolio, as of March 1, 2021, we owned or had an exclusive license to 24 U.S. patents, 12 pending U.S. provisional or non-provisional patent applications, 116 foreign patents and 45 pending foreign applications that include claims covering ALRN-6924, such as its composition of matter, formulations, manufacturing processes, manufacturing precursors or uses thereof. Such owned and in-licensed patents and patent applications, if issued, are expected to expire on various dates from 2021 through 2037, with the owned patents and patent applications, if issued, expiring on various dates from 2029 to 2037, in each case without taking into account any possible patent term adjustment or extensions. More specifically, such owned and in-licensed patents claiming compositions of matter covering ALRN-6924 are expected to expire on various dates from 2021 through 2033, with the owned patents and patent applications, if issued, expiring on various dates from 2029 to 2033, in each case without taking into account any possible patent term adjustments or extensions. Lastly, within our patent portfolio, as of March 1, 2021, nine U.S. patents, 34 foreign patents and one foreign patent applications are licensed to us by President and Fellows of Harvard College, or Harvard, and Dana-Farber Cancer Institute, or DFCI, pursuant to our license agreement with such parties, which patents and patent applications, if issued, are expected to expire on various dates from 2021 through 2028, without taking into account any possible patent term adjustments or extensions. We also have rights to certain patents and pending patent applications throughout the world licensed on a non-exclusive basis to us by Materia and other third parties pursuant to our license agreements with such parties.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application.

In the United States, the Hatch-Waxman Act permits a patent holder to apply for patent term extension of a patent that covers an FDA-approved drug, which, if granted, can extend the patent term of such patent to compensate for the patent term lost during the FDA regulatory review process. This extension can be for up to five years beyond the original expiration date of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Similar provisions are available in Europe and other non-United States jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our product candidates receive FDA approval, we expect to apply for patent term extensions on patents covering those product candidates. While we intend to seek patent term extensions to any of our patents in any jurisdiction where such extensions are available, there is no guarantee that the applicable authorities, including the FDA in the United States, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions.

In addition to our reliance on patent protection for our inventions, product candidates and research programs, we also rely on trade secret protection for our confidential and proprietary information. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees and consultants, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology. Thus, we may not be able to meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual or entity during the course of the party's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual, and which are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property.

License Agreements

Harvard and Dana-Farber License Agreement

In August 2006, we entered into a license agreement with Harvard and DFCI. This agreement was amended and restated in February 2010. Pursuant to the amended and restated agreement, Harvard and DFCI granted us an exclusive worldwide license, with the right to sublicense, under certain patents and patent applications to develop, make, have made, market, use, sell, offer for sale, and import products covered by the patents and patent rights. Pursuant to this agreement, we have an exclusive license to patents that are directed to a class of compounds that includes ALRN-6924, which is in addition to the composition of matter patents directed towards the specific chemical structure of ALRN-6924 that are wholly-owned by us. We also generally have the first right to enforce the licensed patents against third-party infringers.

Under the terms of the amended and restated agreement, we are obligated to use commercially reasonable efforts to develop licensed products in accordance with a development plan and to develop and commercialize licensed products. We are also required to achieve specified milestone events by specified dates. Depending on the failure, Harvard may terminate the agreement either in its entirety or as to categories of licensed patent rights if we fail to achieve such milestone events and do not cure such failure within a specified termination notice period.

In addition, under the license agreement, if a third party makes a proposal to Harvard or DFCI to develop a licensed product that does not contain a peptide that is substantially similar to a peptide in a licensed product we are developing, that would be developed for an indication for which we are not interested in developing a licensed product and that would not present a material risk of competing through off-label use with a licensed product we are developing or plan to develop, and Harvard is interested in having such product developed and commercialized, Harvard is to notify us of the proposal. Following such notification, we then have the right to decide to develop such product ourselves, subject to agreement with Harvard upon a development plan and milestones, to directly negotiate a sublicense with such third party of the licensed intellectual property only or to give Harvard the right to negotiate such a sublicense with the third party in which case we will be entitled to a portion of the income to Harvard from the sublicense. Harvard may also terminate the agreement upon our breach of our payment obligations by us under the agreement if we do not cure such breach within a specified period. Harvard and DFCI may terminate the agreement upon other material breaches by us under the agreement if we do not cure such breach within a specified period or our bankruptcy or insolvency. We may terminate the agreement upon any breach by Harvard or DFCI if not cured within a specified notice period or at any time for any reason upon written notice to Harvard and DFCI. If not earlier terminated, the agreement will remain in force on a licensed product-by-licensed product and country-by-country basis until the expiration of the last-to-expire applicable licensed patent.

As of December 31, 2020, we have paid non-refundable fees, consisting of license and maintenance fees, milestone payments and sublicense fees, of $5.1 million. We are obligated to pay annual maintenance fees totaling $145,000, which on an annual basis are creditable against royalties due for commercial sales of licensed products. We are obligated to make additional milestone payments of up to a maximum of $7.5 million upon our achievement of certain specified clinical, regulatory and sales milestones with respect to ALRN-6924. In the future, we may be obligated to pay up to a maximum of $7.7 million per additional licensed therapeutic product upon our achievement of certain specified clinical, regulatory and sales milestones with respect to such product with the first milestone being payable upon initiation of clinical development of the product. We may also be obligated to pay up to a maximum of $700,000 per licensed diagnostic product upon our achievement of certain specified regulatory and sales milestones with respect to such product. We also have agreed to pay low single-digit percentage royalties on aggregate worldwide net sales of licensed products, including sales by our sublicensees, on a licensed product-by-licensed product and country-by-country basis until the expiration of the last-to-expire applicable licensed patent. Our royalty obligations are subject to specified reductions in the event that we are required to obtain additional licenses from third parties and to make payments to such third parties under such licenses. We must also pay a percentage, up to the mid-twenties, of all sublicense income received from sublicensees, less certain costs, such as research and development costs and, in the event our patent rights are licensed to the sublicensee as part of the same transaction, less the portion of sublicense income allocated to our licensed patent rights. Under specified circumstances, portions of our sublicense payments may be creditable against royalty payments payable for sales of a licensed product. Finally, we must also reimburse all future patent expenses related to the prosecution and maintenance of the licensed patents and applications in-licensed.

Umicore License Agreement

In December 2006, we entered into a license agreement with Materia. Pursuant to the agreement, Materia granted us a non-exclusive worldwide license, with the right to sublicense, under certain of its patents and patent applications covering olefin metathesis catalyst compositions, to develop, make, have made, use, sell, offer for sale, import and export certain conformationally restricted peptides, which are crosslinked, or “stapled,” peptides, for the prevention, diagnosis, treatment or control of any human or animal disease, disorder or condition. Materia subsequently assigned the license agreement to Umicore, and Umicore agreed to continue to supply catalyst for the manufacture of ALRN-6924 under the agreement.

During the term of the agreement, we have agreed to purchase all of our olefin metathesis catalyst compositions from Umicore at agreed prices, subject to potential cost-based increases over time. If Umicore is unable or unwilling to meet our requirements for such olefin metathesis catalyst compositions in terms of amount or delivery date, then a process is provided by which we can procure such olefin metathesis catalyst compositions from a third party until such time that Umicore can meet our requirements and notifies us in writing.

As of December 31, 2020, we paid non-refundable fees, consisting of an up-front technology access fee and annual maintenance payments and milestone payments, of $1.0 million. We are obligated to pay Umicore an annual maintenance fee of $50,000. We are obligated to make additional milestone payments up to a maximum of $6.25 million upon our achievement of certain specified clinical, regulatory and sales milestones with respect to ALRN-6924. In the future, we may be obligated to pay to Umicore up to a maximum of $6.25 million per additional licensed product upon our achievement of certain specified clinical, regulatory and sales milestones with respect to such licensed product. We must also pay Umicore tiered royalties ranging in the low single-digit percentages on aggregate worldwide net sales of licensed products, including sales by our sublicensees, on a licensed product-by-licensed product and country-by-country basis until the expiration of the last-to-expire applicable licensed patent. Our royalty obligations are subject to specified reductions in the event that we are required to obtain additional licenses from third parties and to make payments to such third parties under such licenses.

Either party may terminate the agreement upon material breach by the other party under the agreement if the breaching party does not cure such breach within a specified notice period. We may also terminate the agreement at any time with specified prior notice to Umicore.

Government Regulation and Product Approvals

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

Approval and Regulation of Drugs in the United States

In the United States, the FDA approves drug products under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. Biological products, on the other hand, are licensed by the FDA under the Public Health Service Act, or PHSA. With passage of the Biologics Price Competition and Innovation Act of 2009, Congress amended the definition of “biological product” in the PHSA so as to exclude a chemically synthesized polypeptide from licensure under the PHSA. Rather, the Act provided that such products would be treated as drugs under the FDCA. Through companion guidance issued in April 2015, FDA considers any polymer composed of 40 or fewer amino acids to be a peptide and not a protein. Therefore, unless a peptide otherwise meets the statutory definition of a “biological product” (e.g., a peptide vaccine), it will be regulated as a drug under the FDCA. Accordingly, based on this FDA guidance, we believe that our products will not be treated as biologics subject to approval of a biologics license application, or BLA, by the FDA, and rather will be treated as drug products subject to approval of a new drug application, or NDA, by the FDA pursuant to the FDCA.

The failure to comply with applicable requirements under the FDCA and other applicable laws at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by the FDA and the Department of Justice or other governmental entities.

An applicant seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA’s good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND, which must take effect before human clinical trials may begin;

- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug product for each proposed indication;
- preparation and submission to the FDA of an NDA requesting marketing for one or more proposed indications;
- review by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with cGMP requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- completion of the manufacture, under current Good Manufacturing Practices, or cGMP, conditions, of the drug substance and drug product that the sponsor intends to use in human clinical trials along with required analytical and stability testing;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;
- payment of user fees and securing FDA approval of the NDA; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct post-approval studies.

Preclinical Studies

Before an applicant begins testing a compound with potential therapeutic value in humans, the drug candidate enters the preclinical testing stage. Preclinical studies include *in vitro* laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and activity of the drug for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. The results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue or may be conducted after the IND is submitted.

The IND and IRB Processes

An IND is a request for an exemption from restrictions under the FDCA that allows an unapproved drug to be shipped in interstate commerce for use in an investigational clinical trial, and also a request for FDA authorization to administer an investigational drug to humans. Such authorization must be secured prior to interstate shipment and administration of any new drug that is not the subject of an approved NDA. In support of a request for an IND, applicants must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the filing of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research subjects will be exposed to unreasonable health risks. At any time during this 30-day period, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin.

Following commencement of a clinical trial under an IND, based upon reported safety-related information, the FDA may also place a clinical hold or partial clinical hold on that trial. Clinical holds are imposed by the FDA

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

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all IND requirements must be met unless waived. When the foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain FDA regulatory requirements in order to use the study as support for an IND or application for marketing approval. Specifically, FDA has promulgated regulations governing the acceptance of foreign clinical studies not conducted under an IND, establishing that such studies will be accepted as support for an IND or application for marketing approval if the study was conducted in accordance with GCP including review and approval by an independent ethics committee, or IEC, and informed consent from subjects, and the FDA is able to validate the data from the study through an on-site inspection if FDA deems such inspection necessary. The GCP requirements encompass both ethical and data integrity standards for clinical studies. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies. If a marketing application is based solely on foreign clinical data, the FDA requires that the foreign data be applicable to the U.S. population and U.S. medical practice; the studies must have been performed by clinical investigators of recognized competence; and the FDA must be able to validate the data through an on-site inspection or other appropriate means, if the FDA deems such an inspection to be necessary.

In addition to the foregoing IND requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board, or DSMB, or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the study. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk. Suspension or termination decisions, for reasons unrelated to patient safety, may be made by us based on evolving business objectives and/or competitive climate.

Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on its ClinicalTrials.gov website.

Expanded Access to an Investigational Drug for Treatment Use

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

treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the drug under a treatment protocol or Treatment IND Application.

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

On December 13, 2016, the 21st Century Cures Act established (and the 2017 Food and Drug Administration Reauthorization Act later amended) a requirement that sponsors of one or more investigational drugs for the treatment of a serious disease(s) or condition(s) make publicly available their policy for evaluating and responding to requests for expanded access for individual patients. Although these requirements were rolled out over time, they have now come into full effect. This provision requires drug and biologic companies to make publicly available their policies for expanded access for individual patient access to products intended for serious diseases. Sponsors are required to make such policies publicly available upon the earlier of initiation of a Phase 2 or Phase 3 study; or 15 days after the drug or biologic receives designation as a breakthrough therapy, fast track product, or regenerative medicine advanced therapy.

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

Human Clinical Studies in Support of an NDA

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

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

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

evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

- *Phase 4:* Post-approval studies, which are conducted following initial approval, are typically conducted to gain additional experience and data from treatment of patients in the intended therapeutic indication.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if unexpected serious adverse events suspected of being related to the drug occur. IND safety reports must be submitted to the FDA for serious and unexpected suspected adverse reactions, or SUSARs, occurring during the trial; and any clinically important increase in the number or severity of serious suspected adverse reactions over that listed in the protocol or investigator brochure. In addition, findings from other clinical studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the drug should also be reported. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

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

Pediatric Studies

Under the Pediatric Research Equity Act of 2003, an NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug 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. With enactment of the FDASIA in 2012, sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

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

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in FDASIA. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

The FDA Reauthorization Act of 2017 established new requirements to govern certain molecularly targeted cancer indications. Any company that submits an NDA three years after the date of enactment of that statute must submit pediatric assessments with the NDA if the drug is intended for the treatment of an adult cancer and is directed at a molecular target that FDA determines to be substantially relevant to the growth or progression of a

pediatric cancer. The investigation must be designed to yield clinically meaningful pediatric study data regarding the dosing, safety and preliminary efficacy to inform pediatric labeling for the product.

Submission of an NDA to the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the drug product for one or more indications. Under federal law, the submission of NDAs is subject to an application user fee, which for federal fiscal year 2020 is $2,942,965, unless a partial or full fee waiver is granted as may occur for the first NDA of a small business or an NDA for drug intended to treat a rare, or "orphan" disease. The sponsor of an approved NDA may also be subject to an annual program fee, which for fiscal year 2020 is $325,424 per product, per approved indication up to 5 indications.

The FDA conducts a preliminary review of an NDA within 60 days of its receipt and informs the sponsor by the 74th day after the FDA's receipt of the submission to determine whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review process of NDAs. Most such applications are meant to be reviewed within ten months from the filing date, and most applications for "priority review" products are meant to be reviewed within six months of the filing date. The review process and the Prescription Drug User Fee Act goal date may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA submission, including drug component manufacturing (such as active pharmaceutical ingredients), finished drug product manufacturing, and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Under the FDA Reauthorization Act of 2017, the FDA must implement a protocol to expedite review of responses to inspection reports pertaining to certain applications, including applications for products in shortage or those for which approval is dependent on remediation of conditions identified in the inspection report.

In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events, and whether the product is a new molecular entity. REMS can include medication guides, physician communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU may include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The FDA may require a REMS before approval or post-approval if it becomes aware of a serious risk associated with use of the product. The requirement for a REMS can materially affect the potential market and profitability of a product.

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

Fast Track, Breakthrough Therapy and Priority Review Designations and Regenerative Advanced Therapy Designations

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as fast track designation, breakthrough therapy designation, priority review designation and regenerative advanced therapy designation.

Specifically, the FDA may designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a Fast Track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a Fast Track application does not begin until the last section of the application is submitted. In addition, the Fast Track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

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

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

With passage of the 21st Century Cures Act, or the Cures Act, in December 2016, Congress authorized the FDA to accelerate review and approval of products designated as regenerative advanced therapies. A product is eligible for this designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product has the potential to address unmet medical needs for such disease or condition. The benefits of a regenerative advanced therapy designation include early interactions with FDA to expedite development and review, benefits available to breakthrough therapies, potential eligibility for priority review and accelerated approval based on surrogate or intermediate endpoints.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a drug for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely

to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. Drugs granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

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

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a drug, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of drugs for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit.

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

The FDA's Decision on an NDA

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, 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. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

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

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are

subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

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

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

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

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability. In the United States, health care professionals are generally permitted to prescribe drugs for such uses not described in the drug's labeling, known as off-label uses, because the FDA does not regulate the practice of medicine. However, FDA regulations impose rigorous restrictions on manufacturers' communications, prohibiting the promotion of off-label uses. It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in nonpromotional, non-misleading communication regarding off-label information, such as distributing scientific or medical journal information.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, and its implementing regulations, as well as the Drug Supply Chain Security Act, or DSCA, which regulate the distribution and tracing of prescription drug samples at the federal level, and set minimum standards for the regulation of distributors by the states. The PDMA, its implementing regulations and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution and to identify and remove counterfeit and other illegitimate products from the market.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress established an abbreviated regulatory scheme allowing the FDA to approve generic drugs that are shown to contain the same active ingredients as, and to be bioequivalent to, drugs previously approved by the FDA pursuant to NDAs. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. An ANDA is a comprehensive submission that contains, among other things, data and information pertaining to the active pharmaceutical ingredient, bioequivalence, drug product formulation, specifications and stability of the generic drug, as well as analytical methods, manufacturing process validation data and quality control procedures. ANDAs

are “abbreviated” because they generally do not include preclinical and clinical data to demonstrate safety and effectiveness. Instead, in support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference-listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, and the strength of the drug. At the same time, the FDA must also determine that the generic drug is “bioequivalent” to the innovator drug. Under the statute, a generic drug is bioequivalent to a RLD if “the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug.

Upon approval of an ANDA, the FDA indicates whether the generic product is “therapeutically equivalent” to the RLD in its publication “Approved Drug Products with Therapeutic Equivalence Evaluations,” also referred to as the “Orange Book.” Physicians and pharmacists consider a therapeutic equivalent generic drug to be fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA’s designation of therapeutic equivalence often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

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

The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication. Three-year exclusivity would be available for a drug product that contains a previously approved active moiety, provided the statutory requirement for a new clinical investigation is satisfied. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product. The FDA typically makes decisions about awards of data exclusivity shortly before a product is approved.

The FDA must establish a priority review track for certain generic drugs, requiring the FDA to review a drug application within eight (8) months for a drug that has three (3) or fewer approved drugs listed in the Orange Book and is no longer protected by any patent or regulatory exclusivities, or is on the FDA’s drug shortage list. The new legislation also authorizes FDA to expedite review of ‘‘competitor generic therapies’’ or drugs with inadequate generic competition, including holding meetings with or providing advice to the drug sponsor prior to submission of the application.

505(b)(2) NDAs

As an alternative path to FDA approval for modifications to formulations or uses of products previously approved by the FDA pursuant to an NDA, an applicant may submit an NDA under Section 505(b)(2) of the FDCA. Section 505(b)(2) was enacted as part of the Hatch-Waxman Amendments and permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by, or for, the applicant. If the 505(b)(2) applicant can establish that reliance on FDA’s previous findings of safety and effectiveness is scientifically and legally appropriate, it may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements, including

clinical trials, to support the change from the previously approved reference drug. The FDA may then approve the new product candidate for all, or some, of the label indications for which the reference drug has been approved, as well as for any new indication sought by the 505(b)(2) applicant.

Hatch-Waxman Patent Certification and the 30-Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would.

Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the application will not be approved until all the listed patents claiming the referenced product have expired (other than method of use patents involving indications for which the applicant is not seeking approval).

If the ANDA or 505(b)(2) applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA or 505(b)(2) application has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the application until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent, or a decision in the infringement case that is favorable to the applicant. The ANDA or 505(b)(2) application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the branded reference drug has expired.

Pediatric Exclusivity

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

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition (generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the

product). A company must request orphan product designation before submitting an NDA. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process, although it does convey certain advantages such as tax benefits and exemption from PDUFA application fee.

If a product with orphan status receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will be receiving orphan product exclusivity. Orphan product exclusivity means that the FDA may not approve any other applications for the same product for the same indication for seven years, except in certain limited circumstances. If a drug or drug product designated as an orphan product ultimately receives marketing approval for an indication broader than what was designated in its orphan product application, it may not be entitled to exclusivity. Orphan exclusivity will not bar approval of another product under certain circumstances, including if a subsequent product with the same active ingredient for the same indication is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. This is the case despite an earlier court opinion holding that the Orphan Drug Act unambiguously required the FDA to recognize orphan exclusivity regardless of a showing of clinical superiority.

Further, the FDA may approve more than one product for the same orphan indication or disease as long as the products contain different active ingredients. Moreover, competitors may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity.

Patent Term Restoration and Extension

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

FDA Approval and Regulation of Companion Diagnostics

We believe that it is the FDA's current view that, in the event that we decide to seek marketing approval of ALRN-6924 with a label limited to mutant p53 cancer patients, we may be required to have a companion *in vitro* diagnostic approved for use with ALRN-6924. If safe and effective use of a therapeutic depends on an *in vitro* diagnostic, then the FDA generally will require approval or clearance of that diagnostic, known as a companion diagnostic, at the same time that the FDA approves the therapeutic product. In August 2014, the FDA issued final guidance clarifying the requirements that will apply to approval of therapeutic products and *in vitro* companion diagnostics. According to the guidance, for novel drugs, a companion diagnostic device and its corresponding therapeutic should be approved or cleared contemporaneously by the FDA for the use indicated in the therapeutic product's labeling. In July 2016, the FDA issued a draft guidance intended to assist sponsors of the drug therapeutic and *in vitro* companion diagnostic device on issues related to co-development of the products.

If FDA determines that a companion diagnostic device is essential to the safe and effective use of a novel therapeutic product or indication, FDA generally will not approve the therapeutic product or new therapeutic product indication if the companion diagnostic device is not approved or cleared for that indication. Approval or clearance of the companion diagnostic device will ensure that the device has been adequately evaluated and has adequate performance characteristics in the intended population. The review of *in vitro* companion diagnostics in conjunction with the review of our therapeutic treatments for cancer will, therefore, likely involve coordination of

review by the FDA's Center for Drug Evaluation and Research and the FDA's Center for Devices and Radiological Health Office of In Vitro Diagnostics Device Evaluation and Safety.

Under the FDCA, *in vitro* diagnostics, including companion diagnostics, are regulated as medical devices. In the United States, the FDCA and its implementing regulations, and other federal and state statutes and regulations govern, among other things, medical device design and development, preclinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import, and post-market surveillance. Unless an exemption applies, diagnostic tests require marketing clearance or approval from the FDA prior to commercial distribution. The two primary types of FDA marketing authorization applicable to a medical device are premarket notification, also called 510(k) clearance, and premarket approval, or PMA approval. The FDA has generally required *in vitro* companion diagnostics intended to select the patients who will respond to cancer treatment to obtain a PMA, for that diagnostic simultaneously with approval of the drug. We expect that any companion diagnostic developed for use with ALRN-6924 will utilize the PMA pathway.

The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, can take several years or longer. It involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications are subject to fees for medical device product review; for federal fiscal year 2021, the standard fee for review of a PMA is $365,657 and the small business fee is $91,414.

In addition, PMAs for certain devices must generally include the results from extensive preclinical and adequate and well-controlled clinical trials to establish the safety and effectiveness of the device for each indication for which FDA approval is sought. In particular, for a diagnostic, a PMA application typically requires data regarding analytical and clinical validation studies. As part of the PMA review, the FDA will typically inspect the manufacturer's facilities for compliance with the Quality System Regulation, or QSR, which imposes elaborate testing, control, documentation and other quality assurance requirements.

PMA approval is not guaranteed, and the FDA may ultimately respond to a PMA submission with a not approvable determination based on deficiencies in the application and require additional clinical trial or other data that may be expensive and time-consuming to generate and that can substantially delay approval. If the FDA's evaluation of the PMA application is favorable, the FDA typically issues an approvable letter requiring the applicant's agreement to specific conditions, such as changes in labeling, or specific additional information, such as submission of final labeling, in order to secure final approval of the PMA. If the FDA's evaluation of the PMA or manufacturing facilities is not favorable, the FDA will deny approval of the PMA or issue a not approvable letter. A not approvable letter will outline the deficiencies in the application and, where practical, will identify what is necessary to make the PMA approvable. The FDA may also determine that additional clinical trials are necessary, in which case the PMA approval may be delayed for several months or years while the trials are conducted and then the data submitted in an amendment to the PMA. If the FDA concludes that the applicable criteria have been met, the FDA will issue a PMA for the approved indications, which can be more limited than those originally sought by the applicant. The PMA can include post-approval conditions that the FDA believes necessary to ensure the safety and effectiveness of the device, including, among other things, restrictions on labeling, promotion, sale and distribution. Once granted, PMA approval may be withdrawn by the FDA if compliance with post approval requirements, conditions of approval or other regulatory standards are not maintained or problems are identified following initial marketing.

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

Regulation Outside the United States

Regulation and Procedures Governing Approval of Medicinal Products in the European Union

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of products. Whether or not it obtains FDA approval for a product, the company would need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. Specifically, the process governing approval of medicinal products in the European Union generally follows the same lines as in the United States and involves satisfactorily completing preclinical studies and adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each proposed indication, as well as the submission to the relevant competent authorities of a marketing authorisation application, or MAA, and actual granting of a marketing authorization by these authorities before the product can be marketed and sold in the European Union.

Clinical Trial Approval. Pursuant to the currently applicable Clinical Trials Directive 2001/20/EC and the Directive 2005/28/EC on Good Clinical Practice, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the member states. Under this system, an applicant must obtain approval from the competent national authority of a European Union member state in which the clinical trial is to be conducted, or in multiple member states if the clinical trial is to be conducted in a number of member states. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion. The clinical trial application must be accompanied by an investigational medicinal product dossier with supporting information prescribed by Directive 2001/20/EC and Directive 2005/28/EC and corresponding national laws of the member states and further detailed in applicable guidance documents.

In April 2014, the European Union passed a new Clinical Trials Regulation, (EU) No 536/2014, which will replace the current Clinical Trials Directive 2001/20/EC. To ensure that the rules for clinical trials are identical throughout the European Union, the new European Union clinical trials legislation was passed as a regulation that is directly applicable in all European Union member states without the need for implementation into the member states' national laws. All clinical trials performed in the European Union are required to be conducted in accordance with the Clinical Trials Directive 2001/20/EC until the new Clinical Trials Regulation (EU) No 536/2014 becomes applicable. The Clinical Trials Directive 2001/20/EC will, however, still apply three years from the date of entry into application of the Clinical Trials Regulation to (i) clinical trials applications submitted before the entry into application and (ii) clinical trials applications submitted within one year after the entry into application if the sponsor opts for old system.

The new Clinical Trials Regulation aims to simplify and streamline the approval of clinical trial in the European Union. The main characteristics of the regulation include: a streamlined application procedure via a single entry point, the European Union portal; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures that will spare sponsors from submitting broadly identical information separately to various bodies and different member states; a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed jointly by all member states concerned. Part II is assessed separately by each member state concerned; strictly defined deadlines for the assessment of clinical trial applications; and the involvement of the ethics committees in the assessment procedure in accordance with the national law of the member state concerned but within the overall timelines defined by the Clinical Trials Regulation.

As of January 1, 2020, the website of the European Commission reported that the implementation of the new Clinical Trials Regulation was dependent on the development of a fully functional clinical trials portal and database, which would be confirmed by an independent audit, and that the new legislation would come into effect six months after the European Commission publishes a notice of this confirmation. The website indicated that audit findings are expected to be released in 2021.

Similar requirements to those in the US for posting clinical trial information are present in the European Union (EudraCT) website: https://eudract.ema.europa.eu/ and other countries, as well. Specifically, the EMA has adopted transparency requirements that apply to clinical trials conducted in the European Union (EMA Policy/0070 on the publication of clinical data for medicinal products for human use, effective as of January 1, 2015). The EMA will implement this policy on the publication of clinical data in two phases. Phase 1 concerns the publication of clinical reports submitted to the EMA as part of a marketing authorization application and through the centralized procedure. It entered into force on January 1, 2015, but publication by the EMA is currently suspended until further notice due to the relocation of the EMA to Amsterdam.

PRIME Designation in the EU

In March 2016, the European Medicines Agency, or EMA, launched an initiative to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIority MEdicines, or PRIME, scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises, or SMEs, may qualify for earlier entry into the PRIME scheme than larger companies. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated marketing authorization application assessment once a dossier has been submitted. Importantly, a dedicated Agency contact and rapporteur from the Committee for Human Medicinal Products (CHMP) or Committee for Advanced Therapies (CAT) are appointed early in PRIME scheme facilitating increased understanding of the product at EMA's Committee level. A kick-off meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies.

Marketing Authorization. To obtain a marketing authorization for a product under European Union regulatory systems, an applicant must submit an MAA either under a centralized procedure administered by the EMA or one of the procedures administered by competent authorities in European Union member states (decentralized procedure, national procedure or mutual recognition procedure). A marketing authorization may be granted only to an applicant established in the European Union. In the case of pediatric patients, Regulation (EC) No 1901/2006 provides that prior to obtaining a marketing authorization in the European Union, applicants have to demonstrate compliance with all measures included in an EMA-approved Paediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted (1) a product-specific waiver, (2) a class waiver or (3) a deferral for one or more of the measures included in the PIP.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all European Union member states. Pursuant to Regulation (EC) No 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases, including products for the treatment of cancer. For products with a new active substance indicated for the treatment of other diseases and

products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional.

Under the centralized procedure, the Committee for Medicinal Products for Human Use, or the CHMP, established at the EMA is responsible for conducting the initial assessment of a product. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. If the CHMP accepts such request, the time limit of 210 days will be reduced to 150 days but it is possible that the CHMP can revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment.

Regulatory Data Protection in the EU. In the EU, innovative medicinal products approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity pursuant to Directive 2001/83/EC. Regulation (EC) No 726/2004 repeats this entitlement for medicinal products authorized in accordance with the centralized authorization procedure. Data exclusivity prevents applicants for authorization of generics of these innovative products from referencing the innovator's data to assess a generic (abridged) application for a period of eight years. During an additional two-year period of market exclusivity, a generic marketing authorization application can be submitted and authorized, and the innovator's data may be referenced, but no generic medicinal product can be placed on the EU market until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company nevertheless could also market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Periods of Authorization and Renewals. A marketing authorization shall be valid for five years in principle and the marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the authorizing member state. To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization shall be valid for an unlimited period, unless the European Commission or the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal. Any authorization which is not followed by the actual placing of the drug on the European Union market (in case of centralized procedure) or on the market of the authorizing member state within three years after authorization ceases to be valid (the so-called sunset clause).

Orphan Drug Designation and Exclusivity. Regulation 141/2000 provides that a drug shall be designated as an orphan drug if its sponsor can establish that the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the European Community when the application is made, or that the product is intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition in the European Community and that without incentives it is unlikely that the marketing of the drug in the European Community would generate sufficient return to justify the necessary investment. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the European Community or, if such method exists, the drug will be of significant benefit to those affected by that condition.

Regulation 847/2000 sets out criteria and procedures governing designation of orphan drugs in the European Union. Specifically, an application for designation as an orphan product can be made any time prior to the filing of

an application for approval to market the product. Marketing authorization for an orphan drug leads to a ten-year period of market exclusivity. During this market exclusivity period, the EMA or the member state competent authorities, cannot accept another application for a marketing authorization, or grant a marketing authorization, for a similar medicinal product for the same indication. The period of market exclusivity is extended by two years for medicines that have also complied with an agreed PIP.

This period may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan drug designation, for example because the product is sufficiently profitable not to justify market exclusivity. Market exclusivity can be revoked only in very selected cases, such as consent from the marketing authorization holder, inability to supply sufficient quantities of the product, demonstration of "clinical superiority" by a similar medicinal product, or, after a review by the Committee for Orphan Medicinal Products, requested by a member state in the fifth year of the marketing exclusivity period (if the designation criteria are believed to no longer apply). Medicinal products designated as orphan drugs pursuant to Regulation 141/2000 shall be eligible for incentives made available by the European Community and by the member states to support research into, and the development and availability of, orphan drugs.

Regulatory Requirements after a Marketing Authorization has been Obtained. In case an authorization for a medicinal product in the European Union is obtained, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include:

- Compliance with the European Union's stringent pharmacovigilance or safety reporting rules, pursuant to which post-authorization studies and additional monitoring obligations can be imposed, has to be ensured.
- The manufacturing of authorized drugs, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the EMA's GMP requirements and comparable requirements of other regulatory bodies in the European Union, which mandate the methods, facilities and controls used in manufacturing, processing and packing of drugs to assure their safety and identity.
- The marketing and promotion of authorized drugs, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the European Union notably under Directive 2001/83EC, as amended, and European Union member state laws.

Patent Term Extensions in the European Union and Other Jurisdictions

The European Union also provides for patent term extension through Supplementary Protection Certificates, or SPCs. The rules and requirements for obtaining an SPC are similar to those in the United States. An SPC may extend the term of a patent for up to five years after its originally scheduled expiration date and can provide up to a maximum of fifteen years of marketing exclusivity for a drug. These periods can be extended for six additional months if pediatric exclusivity is obtained, which is described in detail below. Although SPCs are available throughout the European Union, sponsors must apply on a country-by-country basis. Similar patent term extension rights exist in certain other foreign jurisdictions outside the European Union

Authorization to Market Companion Diagnostics in the European Union.

In the European Economic Area, or EEA, *in vitro* medical devices are currently required to conform with the essential requirements of the European Union Directive on *in vitro* diagnostic medical devices (Directive No 98/79/EC, as amended). To demonstrate compliance with the essential requirements, the manufacturer must undergo a conformity assessment procedure. The conformity assessment varies according to the type of medical device and its classification. The conformity assessment of *in vitro* diagnostic medical devices can require the intervention of an accredited EEA Notified Body. If successful, the conformity assessment concludes with the drawing up by the manufacturer of an EC Declaration of Conformity entitling the manufacturer to affix the CE mark to its products and to sell them throughout the EEA. On April 5, 2017, the European Parliament passed the In Vitro Device Regulation, or IVDR, which repeals and replaces Directive No 98/79/EC. Unlike directives, which must be implemented into the national laws of the EU member states, a regulation is directly applicable, i.e., without the need for adoption of EU member state laws implementing them, in all EEA member states. The IVDR, among other things, is intended to

establish a uniform, transparent, predictable and sustainable regulatory framework across the EU for *in vitro* diagnostic medical devices and ensure a high level of safety and health while supporting innovation. The IVDR will not become fully applicable until five years following its entry into force. Once applicable, the IVDR will among other things:

- strengthen the rules on placing devices on the market and reinforce surveillance once they are available;
- establish explicit provisions on manufacturers' responsibilities for the follow-up of the quality, performance and safety of devices placed on the market;
- improve the traceability of medical devices throughout the supply chain to the end-user or patient through a unique identification number; and
- set up a central database to provide patients, healthcare professionals and the public with comprehensive information on products available in the EU.

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. Following protracted negotiations, the United Kingdom left the European Union on January 31, 2020. Under the withdrawal agreement, there is a transitional period until December 31, 2020 (extendable up to two years). Discussions between the United Kingdom and the European Union have so far mainly focused on finalizing withdrawal issues and transition agreements but have been extremely difficult to date. On December 24, 2020, the United Kingdom and European Union entered into a Trade and Cooperation Agreement, which set out certain procedures for approval and recognition of medical products in each jurisdiction. Pursuant to the formal withdrawal arrangements agreed between the United Kingdom and the European Union, the United Kingdom withdrew from the European Union, effective December 31, 2020. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of the Trade and Cooperation Agreement or otherwise, may force us to restrict or delay efforts to seek regulatory approval in the United Kingdom for our product candidates, which could significantly and materially harm our business.

Pharmaceutical Coverage, Pricing and Reimbursement

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

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

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

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

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular drug candidate to currently available therapies (so called health technology assessment, or HTA) in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on healthcare costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states, and parallel trade (arbitrage between low-priced and high-priced member states), can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products, if approved in those countries.

Healthcare Law and Regulation

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

- the federal anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing any remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good, facility, item or service, for which payment may be made, in whole or in part, by a federal healthcare program such as Medicare and Medicaid;
- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government.

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the Affordable Care Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the U.S. Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, can apply to sales or marketing arrangements and claims involving healthcare items or services and are reimbursed by non-governmental third-party payors, including private insurers.

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

Pharmaceutical Insurance Coverage and Health Care Reform

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

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

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

There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and biologics and other medical products, government control and other changes to the health care system in the United States. In March 2010, the ACA was enacted, which includes measures that have significantly changed health care financing by both governmental and private insurers. The provisions of the ACA of importance to the pharmaceutical and biotechnology industry are, among others, the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drug agents or biologic agents, which is apportioned among these entities according to their market share in certain government health care programs;
- an increase in the rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for branded and generic drugs, respectively;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts to negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations, unless the drug is subject to discounts under the 340B drug discount program;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- 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 certain 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;
- new requirements under the federal Physician Payments Sunshine Act for drug manufacturers to report information related to payments and other transfers of value made to physicians and teaching hospitals as well as ownership or investment interests held by physicians and their immediate family members;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- creation of the Independent Payment Advisory Board, which, if and when impaneled, will have authority to recommend certain changes to the Medicare program that could result in reduced payments for prescription drugs; and
- establishment of a Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the

legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers up to 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments, will remain in effect through 2030 pursuant to the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by President Trump on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Additionally, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminated the health insurer tax. Further, the Bipartisan Budget Act of 2018, among other things, amended the ACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." The Congress may consider other legislation to replace elements of the ACA during the next Congressional session.

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

On November 10, 2020, the Supreme Court heard oral arguments as to whether the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. On February 10, 2021, the Biden Administration withdrew DOJ's support for this lawsuit. A ruling by the Supreme Court is expected sometime this year. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The costs of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. To date, there have been several recent U.S. congressional inquiries, as well as proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. To those ends, President Trump issued five Executive Orders intended to lower the costs of prescription drug products but it is unclear whether, and to what extent, these orders will remain in force under the Biden Administration.

Further, on September 24, 2020, the Trump Administration finalized a rulemaking allowing states or certain other non-federal government entities to submit importation program proposals to FDA for review and approval. Applicants are required to demonstrate that their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. The FDA has issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

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

Employees and Human Capital Resources

As of December 31, 2020 we had eight full-time employees, including a total of three employees with M.D. or Ph.D. degrees. Of these full-time employees, five employees are engaged in research and development and three employees are engaged in general and administrative activities. None of our employees are represented by labor unions or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

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

Corporate Information

We were incorporated under the laws of the State of Delaware on August 6, 2001 under the name Renegade Therapeutics, Inc. We changed our name to Aileron Therapeutics, Inc. on February 5, 2007. Our principal executive office is located at 290 Pleasant Street, Unit 112, Watertown, MA 02472, and our telephone number is (617) 995-0900.

Information Available on the Internet

Our internet website address is *http://www.aileronrx.com*. The information contained on, or that can be accessed through, our website is not a part of this Annual Report on Form 10-K. We have included our website address in this Annual Report on Form 10-K solely as an inactive textual reference. We make available free of charge through our website our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendment to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act. We make these reports available through the “SEC Filings” section of our website as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the Securities and Exchange Commission, or the SEC. We also make available, free of charge on our website, the reports filed with the SEC by our executive officers, directors and 10% stockholders pursuant to Section 16 under the Exchange Act as soon as reasonably practicable after copies of those filings are provided to us by those persons. You can review our electronically filed reports and other information that we file with the SEC on the SEC’s website at *http://www.sec.gov.*

Item 1A. Risk Factors.

Careful consideration should be given to the following risk factors, in addition to the other information set forth in this Annual Report on Form 10-K and in other documents that we file with the SEC, in evaluating our company and our business. Investing in our common stock involves a high degree of risk. If any of the following risks actually occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected.

Risks Related to Our Financial Position

We will need substantial additional funding to continue our operations. If we are unable to raise capital when needed, we may be forced to delay, reduce and/or eliminate our research and drug development programs, reduce headcount, and future commercialization efforts, or take other actions that could adversely affect our business.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a time-consuming, expensive and uncertain process that takes years to complete. We will be required to expend significant funds in order to advance the development of, conduct clinical trials of, and seek marketing approval for, our product candidate, ALRN-6924, as well as any other product candidates we may develop. If we are able to obtain marketing approval for ALRN-6924 or for any other product candidate in the future, we expect to incur significant commercialization expenses related to drug sales, marketing, manufacturing and distribution to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of any collaborator that we may have at such time for any such product candidate. We also expect to continue to incur additional costs associated with operating as a public company.

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

- the scope, progress, results and costs of our ongoing, planned and future clinical trials of ALRN-6924;
- the impact of the COVID-19 pandemic on our business and operations;
- the scope, progress, results and costs of drug discovery, preclinical research and clinical trials for other product candidates we may develop;
- the number of future product candidates that we pursue and their development requirements;
- the costs, timing and outcome of regulatory review of our product candidates;
- our ability to establish and maintain collaborations with third parties on favorable terms, if at all;
- the success of any collaborations that we may enter into with third parties;
- the extent to which we acquire or invest in businesses, products and technologies, including entering into licensing or collaboration arrangements for product candidates, although we currently have no commitments or agreements to complete any such transactions;
- the costs and timing of future commercialization activities, including drug sales, marketing, manufacturing and distribution, for any product candidate for which we receive marketing approval, to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of any collaborator that we may have at such time;
- the amount of revenue, if any, received from commercial sales of our product candidates, should any product candidate receive marketing approval;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- our headcount growth and associated costs as we expand our business operations and our research and development activities; and
- the costs of operating as a public company.

We believe that, based on our current operating plan, our cash, cash equivalents and investments as of the date of this Annual Report on Form 10-K will enable us to fund our operating expenses into the second half of 2023. Our funding estimates are based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate. In any event, our cash, cash equivalents and investments will not be sufficient to fund all of the efforts that we plan to undertake or to fund the completion of development or commercialization of ALRN-6924.

Accordingly, we will need to obtain further funding through public or private equity offerings, collaborations and licensing arrangements, or other sources of capital. Adequate additional financing may not be available to us on acceptable terms, if at all. Market conditions are volatile and may continue to be volatile for the foreseeable future, which may limit our ability to raise capital. In addition, while we may seek one or more collaborators for future development of our product candidates for one or more indications, we may not be able to enter into a collaboration for ALRN-6924 for such indications on suitable terms, on a timely basis or at all. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy. If we are unable to raise capital when needed, or on acceptable terms, we may be forced to delay, reduce and/or eliminate some or all of our clinical and drug development programs and future commercialization efforts. We may also be forced to take other actions that could adversely affect our business.

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

We expect our expenses to increase as we will incur significant research and development expenses as we continue our ongoing clinical trials of ALRN-6924, continue our non-clinical research with ALRN-6924, initiate additional clinical trials of ALRN-6924 and pursue later stages of clinical development of ALRN-6924. Until such time, if ever, as we can generate substantial revenues from the sale of our products, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and/or licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our then existing stockholders may be diluted, and the terms of these securities could include liquidation or other preferences and anti-dilution protections that could adversely affect the rights of our common stockholders. In addition, debt financing, if available, would result in fixed payment obligations and may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures, creating liens, redeeming stock or declaring dividends, that could adversely impact our ability to conduct our business. Securing financing may also require a substantial amount of time and attention from our management team and could divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of our product candidates.

We may seek one or more collaborators for future development of ALRN-6924 for one or more indications. However, we may not be able to enter into such collaborations on suitable terms, on a timely basis, or at all. Even if we are able to raise additional funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technology, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us.

If we are unable to raise additional funds when needed, we may be required to delay, reduce and/or eliminate our product development or future commercialization efforts, or grant rights to develop and market product candidates that we might otherwise prefer to develop and market ourselves.

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

We are an early-stage company, and our operations to date have been limited to organizing and staffing our company, business planning, raising capital, developing our stabilized cell-permeating peptide platform, identifying potential product candidates, conducting preclinical studies of our product candidates and conducting clinical trials of our product candidates. Our product candidates other than ALRN-6924 have not advanced beyond the preclinical research stage. In March 2020, we determined to focus our efforts on the development of ALRN-6924 as a chemoprotective agent, and do not plan to advance any development of ALRN-6924 for any other purpose at this time. We have not yet demonstrated our ability to successfully complete any Phase 2 or Phase 3 clinical trials, including large-scale, pivotal clinical trials, obtain marketing approvals, manufacture a commercial-scale drug or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful drug commercialization. Typically, it takes about six to ten years to develop a new drug from the time it is first evaluated in Phase 1 clinical trials to when it is approved for treating patients, but in many cases, it may take longer. Consequently, any predictions made about our future success or viability may not be as accurate as they could be if we had a longer operating history.

As a business with a limited operating history, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. In the future, we may need to transition from a company with a research focus to a company capable of supporting commercial activities. We may not be successful in such a transition. Our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for many years, if at all. If we are unable to obtain product approvals or generate significant commercial revenues, our business will be materially harmed.

As we continue to build our business, we expect our financial condition and operating results may fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, stockholders should not rely upon the results of any particular quarterly or annual periods as indications of future operating performance.

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

Since our inception, we have incurred significant losses on an aggregate basis. Our net loss was $21.2 million and $29.4 million for the years ended December 31, 2020 and 2019, respectively. We have not generated any revenue to date from sales of any drugs and have financed our operations principally through sales of our common stock, through private placements of our preferred stock prior to our initial public offering, and, to a lesser extent, through a collaboration agreement. We have devoted substantially all of our efforts to research and development. Our product candidate, ALRN-6924, is in clinical development and we expect that it will be several years, if ever, before it is ready for commercialization. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if and as we:

- conduct our ongoing, planned and future clinical trials of ALRN-6924;
- initiate and resume research and preclinical development of any other product candidates that we may develop;
- seek to identify additional product candidates;
- seek marketing approvals for any product candidate that successfully completes clinical trials, if any;
- require the manufacture of larger quantities of our product candidates for clinical development and potentially commercialization;
- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
- maintain, expand and protect our intellectual property portfolio;
- acquire or in-license other drugs and technologies;

- hire and retain additional clinical, quality control and scientific personnel;
- build out new facilities or expand existing facilities to support our ongoing development activity; and
- add operational, financial and management information systems and personnel, including personnel to support our drug development, any future commercialization efforts and our compliance with our obligations as a public company.

To become and remain profitable, we must develop, obtain approval for and eventually commercialize a product or products with significant market potential, either on our own or with a collaborator. This will require us to be successful in a range of challenging activities, including completing preclinical studies and clinical trials of our product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those products for which we may obtain marketing approval and establishing and managing any collaborations for the development, marketing and/or commercialization of our product candidates. We may never succeed in these activities and, even if we do, may never generate revenues that are significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business and/or continue our operations. A decline in the value of our company could also cause our stockholders to lose all or part of their investment.

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

We are dependent on the success of our product candidate, ALRN-6924. Our clinical trials of ALRN-6924 may not be successful. If our trials prove unsuccessful or if we are unable to obtain approval for and commercialize ALRN-6924 or experience significant delays in doing so, our business will be materially harmed.

Our future success is substantially dependent on our ability to timely obtain marketing approval for, and then successfully commercialize, ALRN-6924, our product candidate. We are investing a substantial portion of our efforts and financial resources in the research and development of ALRN-6924 as a chemoprotective agent. Our business depends entirely on the successful development and commercialization of ALRN-6924. We currently generate no revenues from sales of any products, and we may never be able to develop a marketable product. We have not identified any other product candidates for development and are not currently conducting any preclinical research to discover and identify new product candidates.

ALRN-6924 will require additional clinical development, evaluation of clinical, preclinical and manufacturing activities, marketing approval in multiple jurisdictions, substantial investment and significant marketing efforts before we generate any revenues from product sales. We are not permitted to market or promote ALRN-6924, or any other product candidates, before we receive marketing approval from the U.S. Food and Drug Administration, or the FDA, and comparable foreign regulatory authorities, and we may never receive such marketing approvals.

The success of ALRN-6924 will depend on several factors, including the following:

- successful and timely patient enrollment and completion of our ongoing and planned clinical trials of ALRN-6924;
- initiation and successful patient enrollment and completion of additional clinical trials on a timely basis;
- safety, tolerability and efficacy profiles that are satisfactory to the FDA or any comparable foreign regulatory authority for marketing approval;
- timely receipt of marketing approvals for both ALRN-6924 and any required companion diagnostic from applicable regulatory authorities;
- the performance of our future collaborators, if any;
- the extent of any required post-marketing approval commitments to applicable regulatory authorities;
- establishment of supply arrangements with third-party raw materials and drug product suppliers and manufacturers;

- establishment of scaled production arrangements with third-party manufacturers to obtain finished products that are appropriately packaged for sale;
- obtaining and maintaining patent protection, trade secret protection and regulatory exclusivity, both in the United States and internationally;
- protection of our rights in our intellectual property portfolio, including our licensed intellectual property;
- successful launch of commercial sales following any marketing approval;
- a continued acceptable safety profile following any marketing approval;
- commercial acceptance by patients, the medical community and third-party payors; and
- our ability to compete with other therapies.

We do not have complete control over many of these factors, including certain aspects of clinical development and the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing, distribution and sales efforts of any future collaborator.

The COVID-19 pandemic, which began in late 2019 and has spread worldwide, has affected and may continue to affect our ability to conduct our ongoing clinical trials, disrupt regulatory activities, or have other adverse effects on our business and operations. In addition, this pandemic has caused substantial disruption in the financial markets and may adversely impact economies worldwide, which could result in adverse effects on our business and operations.

Significant outbreaks of contagious diseases, and other adverse public health developments, could have a material impact on our business operations and operating results. In December 2019, an outbreak of respiratory illness caused by a strain of novel coronavirus, COVID-19, began in China. That outbreak has led to numerous confirmed cases worldwide, including in the United States and other countries where we are conducting clinical trials or activities in support thereof. The World Health Organization declared the outbreak a global pandemic on March 11, 2020. Recently, new variants of the virus that causes COVID-19 have been identified and are spreading around the world, which may worsen or prolong the outbreak. In addition to those who have been directly affected, millions more have been affected by governmental efforts around the world to slow the spread of the outbreak. The outbreak and government measures taken in response have also had a significant impact, both direct and indirect, on businesses and commerce. The future progression of the outbreak and its effects on our business and operations are uncertain.

We and our third-party contract manufacturers, contract research organizations and clinical sites may experience disruptions in supply of product candidates and/or procuring items that are essential for our research and development activities, including, for example, raw materials used in the manufacturing of ALRN-6924, medical and laboratory supplies used in our clinical trials or preclinical studies or animals that are used for preclinical testing, in each case, for which there may be shortages because of ongoing efforts to address the COVID-19 pandemic. While we believe that we currently have sufficient supply of ALRN-6924 to continue our ongoing and planned clinical trials, ALRN-6924 and materials contained therein, come from facilities located in areas impacted by the COVID-19 pandemic. There is no guarantee that the ongoing COVID-19 outbreak, or any potential future outbreak, will not impact our future supply chain, which could have a material adverse impact on our clinical trial plans and business operations.

Additionally, we have enrolled, and are seeking to enroll, cancer patients in our clinical trials at sites located in areas being impacted the COVID-19 pandemic. In the event that clinical trial sites close to enrollment in our trials or shift resources to address COVID-19, this could have a material adverse impact on our clinical trial plans and timelines. We may face difficulties recruiting or retaining patients in our ongoing and planned clinical trials if patients are affected by the virus or are fearful of visiting or traveling to our clinical trial sites because of the COVID-19 pandemic. For instance, the initiation of, and expected timing of reporting data from, our ongoing healthy volunteer study was delayed due to the impact of the COVID-19 pandemic and we experienced a higher than anticipated screen failure rate during our recently completed Phase 1b SCLC trial due to COVID-19 related complications in the patient population that was targeted for enrollment.

Any negative impact that the COVID-19 pandemic has on the ability of our suppliers to provide materials for ALRN-6924 or in the conduct of our clinical trials could cause costly delays to clinical trial activities, which could adversely affect our ability to obtain regulatory approval for and to commercialize ALRN-6924, increase our operating expenses, affect our ability to raise additional capital, and have a material adverse effect on our financial results.

The response to the COVID-19 pandemic may cause governments to redirect resources with respect to regulatory and intellectual property matters in a way that would adversely impact our ability to progress regulatory approvals and protect our intellectual property. In addition, we may face impediments to regulatory meetings and approvals due to measures intended to limit in-person interactions.

The COVID-19 pandemic has significantly impacted economies worldwide, which could result in adverse effects on our business and operations. We cannot be certain what the overall impact of the COVID-19 pandemic will be on our business. It has the potential to adversely affect our business, financial condition, results of operations, and prospects.

The approach we are taking to discover and develop novel drugs is unproven and may never lead to marketable products.

We have concentrated our efforts and therapeutic product research on stabilized cell-permeating alpha-helical peptide technology, and our future success depends on the successful development of this technology and products based on our proprietary peptide technology. Neither we nor any other company has received marketing approval to market therapeutics utilizing cell-permeating peptides. The scientific discoveries that form the basis for our efforts to discover and develop new drugs are relatively new. The scientific evidence to support the feasibility of developing drugs based on these discoveries is both preliminary and limited. Very few drug candidates based on these discoveries have ever been tested in animals, and development of an earlier stabilized cell-permeating peptide product candidate by us was suspended following a clinical trial due to the anticipated costs of required reformulation. Peptides, the class of molecule we are trying to develop into drugs, do not naturally possess the inherent molecular properties typically required of drugs, such as the ability to be stable in the body long enough to reach the tissues in which their effects are required, nor the ability to enter cells within these tissues in order to exert their effects. We currently have only limited data to suggest that we can introduce these properties into peptides. We may spend large amounts of money trying to introduce these properties, and never succeed in doing so. In addition, our stabilized cell-permeating peptide product candidates may not demonstrate in patients the chemical and pharmacological properties ascribed to them in laboratory studies, and they may interact with human biological systems in unforeseen, ineffective or harmful ways. As a result, we may never succeed in developing a marketable product. If we do not successfully develop and commercialize products based upon our technological approach, we will not become profitable and the value of our common stock will decline. Further, our focus on stabilized cell-permeating peptide technology as opposed to multiple technologies increases the risks associated with the ownership of our common stock. If our approach is not successful, we may be required to change the scope and direction of our product development activities. In that case, we may not be able to successfully identify and implement an alternative product development strategy.

Moreover, we believe our product candidate, ALRN-6924, reactivates p53 by disrupting the interactions between p53 and its endogenous inhibitors, MDM2 and MDMX, thereby freeing p53 to transit to its DNA target in the nucleus and initiate cell cycle arrest in healthy cells and/or apoptosis in cancerous cells. We believe that ALRN-6924 is the first and only product candidate in clinical development that can bind to and disrupt the interaction of MDM2 and MDMX with p53 with equivalent effectiveness, or equipotently. Although we have evaluated ALRN-6924 in preclinical studies and early-stage clinical trials, and are aware of published literature supporting the role of MDM2 and MDMX in reactivating non-mutated or wild type, or WT, p53 as well as clinical results for small molecule inhibitors that act to disrupt the interaction of p53 and MDM2, we believe that we are the first to clinically test a molecule that binds directly to both MDM2 and MDMX. As such, the effect of binding to and simultaneously disrupting the interactions of MDM2 and MDMX with WT p53 in cancer patients has not been established in clinical trials. In addition, the role of factors other than MDM2 and MDMX in circumventing the p53 mechanism is still the subject of continued research.

The use of a dual inhibitor of MDM2 and MDMX to reduce chemotherapy-related toxicities in the bone marrow is a novel approach and we believe that we are the only company currently developing in clinical trials a MDM2 and MDMX inhibitor for this purpose. The scientific evidence to support the feasibility of developing this

product candidate for this purpose is both preliminary and limited. Even though ALRN-6924 has demonstrated positive results in preclinical and clinical studies, we may not succeed in demonstrating safety and efficacy of ALRN-6924 as a chemoprotective agent in additional or later-stage clinical trials.

As a result, we do not know whether the mechanism of action of ALRN-6924 will have the expected effect on patients receiving chemotherapy in any cancer indications and whether ALRN-6924 will succeed in demonstrating the safety and efficacy needed to advance in clinical development and obtain marketing approval.

We are pursuing the development of ALRN-6924 in combination with other approved therapeutics. If the FDA revokes approval of any such therapeutic, or if safety, efficacy, manufacturing or supply issues arise with any therapeutic that we use in combination with ALRN-6924 in the future, we may be unable to further develop and/or market ALRN-6924, or we may experience significant regulatory delays, and our business could be materially harmed.

We are pursuing the development of ALRN-6924 in combination with other approved therapeutics. In the future, we may commence additional clinical trials of ALRN-6924 in combination with other approved therapeutics, including, if our ongoing trials are successful, later stage clinical trials of ALRN-6924 in combination with approved therapeutics.

We did not develop or obtain regulatory approval for, and we do not manufacture or sell, any of these approved therapeutics. In addition, these combinations have not been tested before and may, among other things, fail to demonstrate synergistic activity, may fail to achieve superior outcomes relative to the use of single agents or other combination therapies, may exacerbate adverse events associated with one of our product candidates when used as a single agent, or may fail to demonstrate sufficient safety or efficacy traits in clinical trials to enable us to complete those clinical trials or obtain marketing approval for the combination therapy.

If the FDA revokes its approval of any of these therapeutics, we will not be able to continue clinical development of or market ALRN-6924 or any other product candidate in combination with such revoked therapeutic. If safety or efficacy issues arise with these or any other therapeutics that we seek to combine with our product candidates in the future, we may experience significant regulatory delays, and the FDA may require us to redesign or terminate the applicable clinical trials. Moreover, if these therapeutics were to receive regulatory approval in combination with a different therapeutic in any indication for which we are pursuing approval, such approval could impact the feasibility and design of any subsequent clinical trials that we may seek to conduct evaluating ALRN-6924, or any other product candidate, in combination with such therapeutic. If manufacturing, cost or other issues result in a supply shortage of these therapeutics or any other combination therapeutics, we may not be able to complete clinical development of ALRN-6924 on our current timeline or at all, or any other product candidate we may develop in the future.

In addition, we may need, for supply, data referencing or other purposes, to collaborate or otherwise engage with the companies who market these approved therapeutics. If we are unable to do so on a timely basis, on acceptable terms or at all, we may have to curtail the development of a product candidate or indication, reduce or delay its development program, delay its potential commercialization or reduce the scope of any sales or marketing activities.

Even if ALRN-6924 or any other product candidate were to receive regulatory approval and be commercialized for use in combination with an approved therapeutic, we would continue to be subject to the risk that the FDA could revoke its approval of such therapeutic, that safety, efficacy, manufacturing, cost or supply issues could arise with one of these therapeutic agents, or that the current standard of care may be replaced. This could result in ALRN-6924 or any such other product candidate, if approved, being removed from the market or being less successful commercially.

The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, interim results of a clinical trial do not necessarily predict final results and the results of our clinical trials may not satisfy the requirements of the FDA or comparable foreign regulatory authorities.

We currently have no drugs approved for sale and we cannot guarantee that we will ever have marketable drugs. Clinical failure can occur at any stage of clinical development. For instance, our first clinical trial of one of our earlier cell-permeating peptide product candidates did not generate the desired results, and we suspended the development program. Clinical trials may produce negative or inconclusive results, and we or any future collaborators may decide, or regulators may require us, to conduct additional clinical trials or preclinical studies. We will be required to demonstrate with substantial evidence through well-controlled clinical trials that our product candidates are safe and effective for use in a diverse population before we can seek marketing approvals for their commercial sale. Success in preclinical studies and early-stage clinical trials does not mean that future larger registration clinical trials will be successful because product candidates in later-stage clinical trials may fail to demonstrate sufficient safety and efficacy to the satisfaction of the FDA and non-U.S. regulatory authorities despite having progressed through preclinical studies and early-stage clinical trials. Product candidates that have shown promising results in preclinical studies and early-stage clinical trials may still suffer significant setbacks in subsequent registration clinical trials. Additionally, the outcome of preclinical studies and early-stage clinical trials may not be predictive of the success of later-stage clinical trials.

We may publish or report interim or preliminary data from our clinical trials. Interim or preliminary data from clinical trials that we may conduct may not be indicative of the final results of the trial and 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. Interim or preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the interim or preliminary data. As a result, interim or preliminary data should be viewed with caution until the final data are available.

In addition, the design of a clinical trial can determine whether its results will support approval of a drug and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We have limited experience in designing clinical trials and may be unable to design and conduct a clinical trial to support marketing approval. Further, if our product candidates are found to be unsafe or lack efficacy, we will not be able to obtain marketing approval for them and our business would be harmed. A number of companies in the pharmaceutical industry, including those with greater resources and experience than us, have suffered significant setbacks in advanced clinical trials, even after obtaining promising results in preclinical studies and earlier clinical trials.

In some instances, there can be significant variability in safety and efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial protocols, differences in size and type of the patient populations, differences in and adherence to the dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. We do not know whether any clinical trials we may conduct will demonstrate consistent or adequate efficacy and safety sufficient to obtain marketing approval to market our product candidates. We may also determine to discontinue development of our product candidates for certain indications for a variety of other strategic reasons.

In the event that an adverse safety issue, clinical hold or other adverse finding occurs in one or more of our clinical trials of ALRN-6924, such event could adversely affect our other clinical trials of ALRN-6924. Moreover, there is a relatively limited safety data set for product candidates utilizing stabilized cell-permeating peptides or that are designed to reactivate p53. An adverse safety issue or other adverse finding in a clinical trial conducted by a third party with a product candidate utilizing stabilized cell-permeating peptides or that is designed to reactivate p53, such as the small molecules in development that target the p53-MDM2 interaction, could adversely affect our clinical trials of ALRN-6924.

Further, ALRN-6924 or any other product candidate we may develop may not be approved even if they achieve their primary endpoints in Phase 3 clinical trials or registration trials. The FDA or non-U.S. regulatory authorities may disagree with our trial design and our interpretation of data from preclinical studies and clinical trials. In addition, any of these regulatory authorities may change requirements for the approval of a product candidate even after reviewing and providing comments or advice on a protocol for a pivotal clinical trial that has the potential to result in approval by the FDA or another regulatory authority. In addition, any of these regulatory authorities may also approve a product candidate for fewer or more limited indications than we request or may grant approval contingent on the performance of costly post-marketing clinical trials. In addition, the FDA or other non-U.S. regulatory authorities may not approve the labeling claims that we believe would be necessary or desirable for the successful commercialization of our product candidates.

Before obtaining marketing approvals for the commercial sale of any product candidate for a target indication, we must demonstrate with substantial evidence gathered in preclinical studies and well-controlled clinical studies, and, with respect to approval in the United States, to the satisfaction of the FDA, that the product candidate is safe and effective for use for that target indication. There is no assurance that the FDA or non-U.S. regulatory authorities will consider our future clinical trials to be sufficient to serve as the basis for approval of one of our product candidates for any indication. The FDA and non-U.S. regulatory authorities retain broad discretion in evaluating the results of our clinical trials and in determining whether the results demonstrate that a product candidate is safe and effective. If we are required to conduct additional clinical trials of a product candidate than we expect prior to its approval, we will need substantial additional funds and there is no assurance that the results of any such additional clinical trials will be sufficient for approval.

Clinical drug development is a lengthy and expensive process, with an uncertain outcome. If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs, experience delays in completing, or ultimately be unable to complete, the development of our product candidates or be unable to obtain marketing approval.

Before obtaining marketing approval from regulatory authorities for the sale of ALRN-6924 or any other product candidate we may develop, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical studies and early-stage clinical trials may not be predictive of the success of later clinical trials in the same or different indications, and interim results of a clinical trial, such as the interim results of our Phase 1b clinical trial of ALRN-6924 in patients with p53-mutated SCLC that we announced in October 2020, do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their drugs.

We do not know whether our ongoing clinical trials will be completed on schedule or at all, or whether future clinical trials will begin on time, need to be redesigned, enroll patients on time or be completed on schedule, if at all. Moreover, due to the continuing COVID-19 pandemic, patient recruitment and enrollment in our clinical trials may be adversely affected, delayed or interrupted. For instance, the initiation of, and expected timing of reporting data from, our ongoing human volunteer study was delayed due to the impact of the COVID-19 pandemic. Patients may choose to withdraw from our studies or we may choose to or be required to pause enrollment and or patient dosing in our ongoing clinical trials in order to preserve health resources and protect trial participants.

Clinical trials can be delayed for a variety of reasons, including delays related to:

- obtaining marketing approval to commence a trial;
- reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- obtaining institutional review board approval at each clinical trial site;

- recruiting suitable patients to participate in a trial;
- developing and validating any companion diagnostic to be used in the trial, to the extent we are required to do so;
- patients failing to comply with trial protocol or dropping out of a trial;
- clinical trial sites deviating from trial protocol or dropping out of a trial;
- the need to add new clinical trial sites; or
- manufacturing sufficient quantities of product candidate for use in clinical trials.

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

- we may receive feedback from regulatory authorities that requires us to modify the design of our clinical trials;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon drug development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- 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;
- we or our investigators might have to suspend or terminate clinical trials of our product candidates for various reasons, including non-compliance with regulatory requirements, a finding that our product candidates have undesirable side effects or other unexpected characteristics, or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- 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;
- regulators may revise the requirements for approving our product candidates, or such requirements may not be as we anticipate; and
- any future collaborators that conduct clinical trials may face any of the above issues, and may conduct clinical trials in ways they view as advantageous to them but that are suboptimal for us.

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

- incur unplanned costs;
- be delayed in obtaining marketing approval for our product candidates or not obtain marketing approval at all;
- obtain marketing approval in some countries and not in others;
- obtain marketing approval for indications or patient populations that are not as broad as intended or desired;
- obtain marketing approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;

- be subject to additional post-marketing testing requirements; or
- have the drug removed from the market after obtaining marketing approval.

Our drug development costs will also increase if we experience delays in testing or marketing approvals. We do not know whether clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Furthermore, we rely on third-party CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials, and while we have agreements governing their committed activities, we have limited influence over their actual performance. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring drugs to market before we do and impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

We are conducting a clinical trial of ALRN-6924 and plan to conduct additional trials of ALRN-6924 at sites outside the United States. The FDA may not accept data from trials conducted in such locations and the conduct of trials outside the United States could subject us to additional delays and expense.

We are conducting our Phase 1b clinical trial of ALRN-6924 and plan to conduct additional trials of ALRN-6924 at one or more trial sites that are located outside the United States. The FDA's acceptance of data from clinical trials outside of the United States is subject to certain conditions. For example, the clinical trial must be well designed and conducted and performed by qualified investigators in accordance with good clinical practice. The FDA must be able to validate the data from the trial through an onsite inspection if necessary. The trial population must also have a similar profile to the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful, except to the extent the disease being studied does not typically occur in the United States. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will be dependent upon its determination that the trials also complied with all applicable U.S. laws and regulations. There can be no assurance that the FDA will accept data from trials conducted outside of the United States. If the FDA does not accept the data from any trial that we conduct outside the United States, it would likely result in the need for additional trials, which would be costly and time-consuming and delay or permanently halt our development of our product candidates.

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

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or comparable foreign regulatory authorities. Patient enrollment is a significant factor in the timing of clinical trials. We do not yet know exactly how many patients will have the genetic profile that ALRN-6924 or other future product candidates are designed to address. In particular, because our clinical trials are targeted at a subset of patients in indications with p53-mutated cancers, our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate.

Due to the ongoing COVID-19 pandemic, patient recruitment and enrollment in our clinical trials has been and may continue to be adversely affected, delayed or interrupted. Patients may choose to withdraw from our studies or we may choose to or be required to pause enrollment and or patient dosing in our ongoing clinical trials in order to preserve health resources and protect trial participants. It is unknown how long these pauses or disruptions could continue.

Patient enrollment may be affected if our competitors have ongoing clinical trials for product candidates that are under development for the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials instead enroll in clinical trials of our competitors' product candidates. Patient enrollment may also be affected by other factors, including:

- size and nature of the patient population;
- severity of the disease under investigation;
- availability and efficacy of approved drugs for the disease under investigation;
- patient eligibility criteria for the trial in question;
- perceived risks and benefits of the product candidate under study;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- proximity and availability of clinical trial sites for prospective patients; and
- continued enrollment of prospective patients by clinical trial sites.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or may 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, which would cause the value of our company to decline and limit our ability to obtain additional financing.

If serious adverse or unacceptable side effects are identified during the development of our product candidates or we observe limited efficacy of our product candidates, we may need to abandon or limit the development of one or more of our product candidates.

Adverse events or undesirable side effects caused by, or other unexpected properties of, our product candidates could cause us, any future collaborators, an institutional review board, or IRB, or regulatory authorities to interrupt, delay or halt clinical trials of one or more of our product candidates and could result in the delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities or a more restrictive label, if approved.

In general, our clinical trials of ALRN-6924 include cancer patients who are very sick and whose health is deteriorating, and we expect that additional clinical trials of ALRN-6924 and any other product candidates that we may develop will include similar patients with deteriorating health. It is possible that some of these patients might die prior to their completion of our clinical trial. For example, in our Phase 1 trial of single agent ALRN-6924 for the treatment of AML and MDS a patient that was receiving a 3.8 mg/kg dose of ALRN-6924 under our three times per week dosing regimen died of tumor lysis syndrome related to treatment with ALRN-6924. Such deaths may be caused by the cancers from which such patients are suffering, or other causes, unrelated to ALRN-6924 or the other product candidates that may be the subject of the clinical trial. Even if the deaths are not related to our product candidate, the deaths could affect perceptions regarding the safety of our product candidate.

If ALRN-6924 is associated with adverse events or undesirable side effects or has properties that are unexpected such as the aforementioned death we observed in our Phase 1 trial of single agent ALRN-6924 for the treatment of AML and MDS, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. We, or any future collaborators, may abandon development or limit development of that product candidate to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, results of operations, financial condition and prospects significantly.

We have never obtained marketing approval for a product candidate and we may be unable to obtain, or may be delayed in obtaining, marketing approval for any product candidate.

We have never obtained marketing approval for a product candidate. It is possible that the FDA may refuse to accept for substantive review any new drug applications, or NDAs, that we submit for our product candidates or may conclude after review of our data that our application is insufficient to obtain marketing approval of our product candidates. If the FDA does not accept or approve our NDAs for our product candidates, it may require that we conduct additional clinical, nonclinical or manufacturing validation studies and submit that data before it will reconsider our applications. Depending on the extent of these or any other FDA-required studies, approval of any NDA or application that we submit may be delayed by several years, or may require us to expend more resources than we have available. It is also possible that additional studies, if performed and completed, may not be considered sufficient by the FDA to approve our NDAs.

Any delay in obtaining, or an inability to obtain, marketing approvals would prevent us from commercializing our product candidates, generating revenues and achieving and sustaining profitability. If any of these outcomes occur, we may be forced to abandon our development efforts for our product candidates, which could significantly harm our business.

The FDA or comparable foreign regulatory authorities may, under certain circumstances, require that a companion diagnostic be approved for use with ALRN-6924. If we are unable to successfully develop and obtain approval for such a diagnostic, either on our own or through a third party, or if we experience significant delays in doing so, we may not obtain marketing approval for ALRN-6924 in a timely manner, or at all.

We expect that The FDA will, under certain circumstances, require us to have a companion *in vitro* diagnostic to identify patients with mutated p53 cancer cells, approved for use with ALRN-6924. We expect also be required to obtain similar approvals from comparable foreign regulatory authorities. We are in the process of evaluating the third party for the supply of a commercially available diagnostic to identify patients' p53 status, or develop such a diagnostic ourselves, in each case requiring approval of the diagnostic by regulatory authorities. We are currently evaluating the likelihood of such a requirement, given recent FDA actions, as well as the risks and benefits of each approach. We currently rely upon commercially available third-party assays and employ a central laboratory to test both archived tumor tissue samples and fresh biopsy samples from patients taken prior to enrollment in clinical trials of ALRN-6924 to identify p53 status. We do not have experience or capabilities in developing or commercializing companion diagnostics.

Companion diagnostics are subject to regulation by the FDA and comparable foreign regulatory authorities as medical devices and require separate marketing approval prior to commercialization. We or any third party upon which we decide to rely may encounter difficulties in developing and obtaining approval for a companion diagnostic for ALRN-6924, including issues relating to selectivity/specificity, analytical validation, reproducibility or clinical validation. The process of complying with the requirements of the FDA and comparable foreign regulatory authorities to support marketing authorization of a companion diagnostic is costly, time-consuming and burdensome. Any delay or failure to develop or obtain marketing approval of the companion diagnostic could delay or prevent approval of ALRN-6924.

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

Because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs 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 drugs. For instance, we have conducted clinical trials of ALRN-6924 for the treatment of peripheral T-cell lymphoma, acute myeloid leukemia and advanced high-risk myelodysplastic syndrome, SCLC and MDM2-amplified advanced solid tumors in combination with palbociclib (Ibrance) and, in part, due to commercial developments, have ceased clinical development of ALRN-6924 for those

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

One element of our strategy is to leverage our proprietary stabilized cell-permeating peptide platform to develop additional product candidates across oncology and other diseases with unmet medical need. We may not be successful in doing so. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons, including:

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

Research programs to identify new product candidates require substantial technical, financial and human resources. If we are unable to identify suitable compounds for preclinical and clinical development, our business would be harmed.

If ALRN-6924 or any of our future product candidates receives marketing approval and we, or others, later discover that the drug is less effective than previously believed or causes undesirable side effects that were not previously identified, our ability, or that of any future collaborators, to market the drug could be compromised.

Clinical trials of our product candidates must be conducted in carefully defined subsets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials, or those of any future collaborator, may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. If one or more of our product candidates receives marketing approval and we, or others, discover that the drug is less effective than previously believed or causes undesirable side effects that were not previously identified, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw their approval of the drug or seize the drug;
- we, or any future collaborators, may be required to recall the drug, change the way the drug is administered or conduct additional clinical trials;
- additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the particular drug;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication;
- we, or any future collaborators, may be required to create a Medication Guide outlining the risks of the previously unidentified side effects for distribution to patients;
- we, or any future collaborators, could be sued and held liable for harm caused to patients;
- the drug may become less competitive; and
- our reputation may suffer.

Any of these events could have a material and adverse effect on our operations and business and could adversely impact our stock price.

Even if ALRN-6924 or any of our future product candidates receives marketing approval, they may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors and others in the medical community necessary for commercial success.

If ALRN-6924 or any of our future product candidates receives marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, healthcare payors and others in the medical community. For example, current cancer treatments like chemotherapy and radiation therapy are well-established in the medical community, and doctors may continue to rely on these treatments. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant revenues from sales of drugs and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of the product;
- the potential advantages of the product compared to competitive therapies;
- the prevalence and severity of any side effects;
- whether the product is designated under physician treatment guidelines as a first-, second- or third-line therapy;
- our ability, or the ability of any future collaborators, to offer the product for sale at competitive prices;
- the product's convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try, and of physicians to prescribe, the product;
- limitations or warnings, including distribution or use restrictions contained in the product's approved labeling;
- the strength of sales, marketing and distribution support;
- changes in the standard of care for the targeted indications for the product; and
- availability and amount of coverage and reimbursement from government payors, managed care plans and other third-party payors.

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

We do not have a sales or marketing infrastructure and have no experience in the sale or marketing of pharmaceutical drugs. We are not currently a party to a strategic collaboration that provides us with access to a collaborator's resources in selling or marketing drugs. To achieve commercial success for any approved drug for which sales and marketing is not the responsibility of any strategic collaborator that we may have in the future, we must either develop a sales and marketing organization or outsource these functions to other third parties. In the future, we may choose to build a sales and marketing infrastructure to market or co-promote some of our product candidates if and when they are approved or enter into collaborations with respect to the sale and marketing of our product candidates.

There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time-consuming and could delay any commercial launch of a product candidate. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

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

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future drugs;
- the lack of complementary drugs to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive drug lines;
- unforeseen costs and expenses associated with creating an independent sales and marketing organization; and
- inability to obtain sufficient coverage and reimbursement from third-party payors and governmental agencies.

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

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

The pharmaceutical and biotechnology industries generally, and the cancer drug sector specifically, are highly competitive and characterized by rapidly advancing technologies, evolving understanding of disease etiology and a strong emphasis on proprietary drugs. We face competition with respect to ALRN-6924, our product candidate, and will face competition with respect to any product candidates that we may seek to discover and develop or commercialize in the future, from major pharmaceutical, specialty pharmaceutical and biotechnology companies. There are a number of major pharmaceutical, specialty pharmaceutical and biotechnology companies that currently market and sell drugs or are pursuing the development of drugs for the treatment of cancer. Potential competitors also include academic institutions and governmental agencies and public and private research institutions.

There are a large number of companies developing or marketing treatments for cancer, including the indications for which we may develop product candidates. Many of the companies that we compete or may compete against in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved drugs than we do. Small or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or that may be necessary for, our programs.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any drugs that we may develop. Our competitors also may obtain FDA or other regulatory approval for their drugs more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. The key competitive factors affecting the success of our product candidates, if approved, are likely to be their efficacy, safety, convenience, price, the effectiveness of companion diagnostics in guiding the use of related therapeutics, the level of generic competition and the availability of reimbursement from government and other third-party payors.

The most common methods of treating patients with cancer are surgery, radiation and drug therapy. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. Some of the currently-approved drug therapies are branded and subject to patent protection and may be established as the standard of care for the treatment of indications for which we may choose to seek regulatory approvals. Many of these approved drugs are well-established therapies and are widely accepted by physicians, patients and third-party payors, and, even if our product candidates were to be approved, there can be no assurance that our drugs would displace existing treatments. In addition to currently marketed therapies, there are also a number of drugs in late-stage clinical development to treat cancer, including the indications for which we are developing product candidates. These clinical-stage drug candidates may provide efficacy, safety, convenience and other benefits that are not provided by currently-marketed therapies. As a result, they may provide significant competition for ALRN-6924 any of our future product candidates for which we obtain regulatory approval.

We initially designed ALRN-6924, our product candidate, to act as a reactivator of p53 for the treatment of various cancers. We are aware of other product candidates that are in clinical development for the treatment of various cancers through the reactivation of p53. Although there is a subset of drugs that directly target the p53 pathway, there are many cancer drugs that claim to affect the p53 pathway by upstream or complementary pathways. We are aware of selective small molecule inhibitors that are designed to target the p53-MDM2 interaction in various stages of clinical development being tested by F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc., or collectively Roche, Novartis AG, Daiichi Sankyo Co., Ltd., Boehringer Ingelheim, Ascentage Pharma Group Corporation, Ltd, Kartos Therapeutics, Inc. and Unity Biotechnology, Inc. including testing MDM2 inhibitors in combination with a variety of other anti-cancer agents or investigating MDM2 inhibitors and senolytic drugs for the treatment of aging-related diseases such as osteoarthritis of the knee. Roche is currently conducting Phase 3 testing of idasanutlin, a MDM2 inhibiting agent, in combination with high-dose Ara-C in AML patients between the ages of 18 and 60.

We are aware of another company that is actively developing chemoprotective agents, G1 Therapeutics, Inc., or G1. In February 2021, the FDA approved trilaciclib (COSELA), a short-acting intravenous CDK4/6 inhibitor developed by G1, to decrease chemotherapy-induced myelosuppression in adult patients when administered prior to a platinum/etoposide-containing regimen or topotecan-containing regimen for extensive-stage SCLC. G1 is conducting or has to plans to conduct additional clinical trials of trilaciclib in other indications, including colorectal cancer, metastatic triple-negative breast cancer and bladder cancer. In addition, ALRN-6924 may compete with multiple approved drugs or drugs that may be approved in the future, such as plinabulin which is in development for chemotherapy-induced neutropenia.

If the FDA or comparable foreign regulatory authorities approve generic versions of any of our drugs that receive marketing approval, or such authorities do not grant our drugs appropriate periods of data or market exclusivity before approving generic versions of our drugs, the sales of our drugs could be adversely affected.

Once an NDA is approved, the drug covered thereby becomes a “reference-listed drug” in the FDA’s publication, “Approved Drug Products with Therapeutic Equivalence Evaluations.” Manufacturers may seek approval of generic versions of reference-listed drugs through submission of abbreviated new drug applications, or ANDAs, in the United States. In support of an ANDA, a generic manufacturer need not conduct clinical trials demonstrating safety and efficacy. Rather, the applicant generally must show that its drug has the same active ingredient(s), dosage form, strength, route of administration and conditions of use or labeling as the reference-listed drug and that the generic version is bioequivalent to the reference-listed drug, meaning it is absorbed in the body at the same rate and to the same extent. Generic drugs may be significantly less costly to bring to market than the reference-listed drug and companies that produce generic drugs are generally able to offer them at lower prices. Thus, following the introduction of a generic drug, a significant percentage of the sales of any branded product or reference-listed drug is typically lost to the generic drug.

The FDA may not approve an ANDA for a generic drug until any applicable period of non-patent exclusivity for the reference-listed drug has expired. The Federal Food, Drug, and Cosmetic Act, or FDCA, provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity, or NCE. Specifically, in cases where such exclusivity has been granted, an ANDA may not be filed with the FDA and the FDA may not approve the application until the expiration of five years unless the submission is accompanied by a Paragraph IV certification that a patent covering the reference-listed drug is either invalid or will not be infringed by the generic

drug, in which case the applicant may submit its application four years following approval of the reference-listed drug. Manufacturers may seek to launch these generic drugs following the expiration of the marketing exclusivity period, even if we still have patent protection for our drug.

Competition that our drugs may face from generic versions of our drugs could materially and adversely impact our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on the investments we have made in those drug candidates. Our future revenues, profitability and cash flows could also be materially and adversely affected and our ability to obtain a return on the investments we have made in those drug candidates may be substantially limited if our drugs, if and when approved, are not afforded the appropriate periods of non-patent exclusivity.

Even if we are able to commercialize any product candidate, such product candidate may become subject to unfavorable pricing regulations, third-party coverage and reimbursement policies or healthcare reform initiatives, which would harm our business.

The regulations that govern marketing approval, pricing, coverage and reimbursement for new drugs vary widely from country to country. 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 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 in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

Our ability to commercialize any products successfully also will depend in part on the extent to which reimbursement and coverage for these products and related treatments will be available from government authorities, private health insurers and other organizations, and if reimbursement and coverage is available, the level of reimbursement and coverage. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the healthcare industry in the United States and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, the third-party payors who reimburse patients or healthcare providers, such as government and private insurance plans, are requiring that drug companies provide them with predetermined discounts from list prices, and are seeking to reduce the prices charged or the amounts reimbursed for medical products. We cannot be sure that reimbursement will be available for any drug that we commercialize and, if reimbursement is available, we cannot be sure as to the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining 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, eligibility for reimbursement does not imply that any drug will be reimbursed in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs, may be incorporated into existing payments for other services and may reflect budgetary constraints or imperfections in Medicare data. 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. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement rates. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for new products that we develop and for which we obtain marketing approval could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

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

We 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 commercially sell any drugs that we may develop. If we cannot successfully defend ourselves against claims that our product candidates or drugs caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

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

We currently hold clinical trial liability insurance coverage for up to $5.0 million, but that coverage may not be adequate to cover any and all liabilities that we may incur. We would need to increase our insurance coverage when we begin the commercialization of our product candidates, if ever. 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.

Governments outside of the United States tend to impose strict price controls, which may adversely affect our revenues from the sales of our products, if any.

In some countries, particularly member states of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we, or our future collaborators, may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by

third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of any product candidate approved for marketing is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

Risks Related to Our Dependence on Third Parties

We rely on third parties to conduct our clinical trials and some aspects of our research and preclinical studies, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research and studies.

We currently rely on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials of ALRN-6924 and expect to continue to rely upon third parties to conduct additional clinical trials of ALRN-6924 and any other product candidates that we may develop. We currently rely and expect to continue to rely on third parties to conduct some aspects of our research and preclinical studies. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our drug development activities.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our regulatory responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as Good Clinical Practice, or GCP, regulations for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. The European Medicines Agency, or EMA, also requires us to comply with similar standards. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, EMA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. There can be no assurances that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations. Furthermore, we conduct clinical trials in foreign countries, subjecting us to additional risks and challenges, including additional regulatory compliance. We also contract with foreign CROs that may be less experienced with respect to regulatory matters applicable to us. In addition, our clinical trials must be conducted with product produced under current Good Manufacturing Practices, or cGMP, regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the marketing approval process. We also are required to register certain ongoing clinical trials and post the results of certain completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

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

We contract with third parties for the manufacture of ALRN-6924 for our ongoing clinical trials, and expect to continue to do so for additional clinical trials and ultimately for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or drugs or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not have any manufacturing facilities or personnel. We currently rely, and expect to continue to rely, on third-party manufacturers for the manufacture of ALRN-6924 for clinical trials under the guidance of members of our organization. To date, we have obtained the active pharmaceutical ingredient, or API, of ALRN-6924 from one third-party manufacturer. We have engaged a separate third-party manufacturer to conduct fill-and-finish and labeling services, as well as for the storage and distribution of ALRN-6924 to clinical sites. We do not have a long-term supply agreement with either of these third-party manufacturers, and we purchase our required drug supplies on a purchase order basis.

We expect to rely on third-party manufacturers or third-party collaborators for the manufacture of our product candidates for commercial supply of ALRN-6924 or any of our future product candidates for which we or any of our future collaborators obtain marketing approval. We may be unable to establish any agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- the possible failure of the third party to manufacture our product candidate according to our schedule, or at all, including if our third-party contractors give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of the agreements between us and them;
- the possible termination or nonrenewal of agreements by our third-party contractors at a time that is costly or inconvenient for us;
- the possible breach by the third-party contractors of our agreements with them;
- the failure of third-party contractors to comply with applicable regulatory requirements;
- the possible failure of the third party to manufacture our product candidates according to our specifications;
- the possible mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or active drug or placebo not being properly identified;
- the possibility of clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales; and
- the possible misappropriation of our proprietary information, including our trade secrets and know-how.

The facilities used by our contract manufacturers to manufacture our product candidates must be approved by the FDA pursuant to inspections that will be conducted after we submit our NDA to the FDA. We do not have complete control over all aspects of the manufacturing process of, and are dependent on, our contract manufacturing partners for compliance with cGMP regulations for manufacturing both active drug substances and finished drug products. Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside of the United States. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure and/or maintain marketing approval for their manufacturing facilities. In addition, we do not have complete control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain marketing approval for or market our product candidates, if approved. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our drugs and harm our business and results of operations.

Any drugs that we may develop may compete with other product candidates and drugs for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply of the API of ALRN-6924 and we only currently use a different single third-party manufacturer for fill-and-finish services for ALRN-6924. If our current contract manufacturers cannot perform as agreed, we may be required to replace those manufacturers. Although we believe that there are several potential alternative manufacturers who could manufacture our product candidates, we may incur added costs and delays in identifying and qualifying any such replacement.

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

We may enter into strategic collaborations for the development, marketing and commercialization of ALRN-6924. If those collaborations are not successful, the development, marketing and/or commercialization of our product candidates that are the subject of such collaborations would be harmed.

As we further develop ALRN-6924, we may build a commercial infrastructure with the capability to directly market it to a variety of markets and geographies. Although we currently plan to retain all commercial rights to ALRN-6924, we may enter into strategic collaborations for the development, marketing and commercialization of ALRN-6924 and any other product candidates that we may develop. Our likely collaborators for any collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. If we do enter into any such arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development, marketing and/or commercialization of our product candidates. 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. In addition, any future collaborators may have the right to abandon research or development projects and terminate applicable agreements, including funding obligations, prior to or upon the expiration of the agreed upon terms.

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

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development, marketing and/or commercialization of our product candidates or may elect not to continue or renew development, marketing or commercialization programs based on clinical trial results, changes in the collaborator's 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, drugs that compete directly or indirectly with our drugs or product candidates;
- a collaborator with marketing and distribution rights to one or more drugs may not commit sufficient resources to the marketing and distribution of such drug or drugs;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- we may lose certain valuable rights under circumstances identified in any collaboration arrangement that we enter into, such as if we undergo a change of control;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development, marketing and/or commercialization of the applicable product candidates;
- collaborators may learn about our discoveries, data, proprietary information, trade secrets or compounds and use this knowledge to compete with us in the future; and
- the number and type of our collaborations could adversely affect our attractiveness to future collaborators or acquirers.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner, or at all.

If we decide to seek to establish collaborations, but are not able to establish those collaborations, we may have to alter our development and commercialization plans.

Our development of ALRN-6924 and the potential commercialization of ALRN-6924 will require substantial additional cash to fund expenses. We may seek to selectively form collaborations to expand our capabilities, potentially accelerate research and development activities and provide for commercialization activities by third parties.

We would face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a

number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or comparable foreign 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 drugs, the existence of uncertainty with respect to our ownership of intellectual property, 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. The potential collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate.

We may also be restricted under then-existing collaboration agreements from entering into future agreements on certain terms with potential collaborators.

Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all, if and when we seek to enter into collaborations. If we are unable to do so, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms, or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate revenue from sales of drugs.

Risks Related to Our Intellectual Property

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

Our commercial success will depend in large part on obtaining and maintaining patent, trademark and trade secret protection of our proprietary technologies and our product candidates, which include ALRN-6924 and others, their respective components, formulations, methods used to manufacture them and methods of treatment, as well as successfully defending these patents against third-party challenges. Our ability to stop unauthorized third parties from making, using, selling, offering to sell or importing our product candidates is dependent upon the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities.

The patenting process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. In addition, we may not pursue or obtain patent protection in all relevant markets. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Our pending and future patent applications may not result in issued patents that protect our technology or products, in whole or in part. In addition, our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from using our technology or from developing competing products and technologies.

We currently in-license certain intellectual property from President and Fellows of Harvard College, or Harvard, and Dana-Farber Cancer Institute, or DFCI, and others. In the future we may in-license intellectual property from other licensors. We rely on certain of these licensors to file and prosecute patent applications and maintain patents and otherwise protect the intellectual property we license from them. We have limited control over these activities or any other intellectual property that may be related to our in-licensed intellectual property. For example, we cannot be certain that such activities by these licensors have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents and other intellectual property rights. We have limited control over the manner in which our licensors initiate an infringement proceeding against a third-party infringer of the intellectual property rights, or defend certain of the intellectual property that is licensed to us. It is possible that the licensors' infringement proceeding or defense activities may be less vigorous than had we conducted them ourselves.

The growth of our business may depend in part on our ability to acquire or in-license additional proprietary rights. For example, our programs may involve additional product candidates that may require the use of additional proprietary rights held by third parties. Our product candidates may also require specific formulations to work effectively and efficiently. These formulations may be covered by intellectual property rights held by others. We may develop products containing our compounds and pre-existing pharmaceutical compounds. These pharmaceutical compounds may be covered by intellectual property rights held by others. We may be required by the FDA or comparable foreign regulatory authorities to provide a companion diagnostic test or tests with our product candidates. These diagnostic test or tests may be covered by intellectual property rights held by others. We may be unable to acquire or in-license any relevant third-party intellectual property rights that we identify as necessary or important to our business operations. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all, which would harm our business. We may need to cease use of the compositions or methods covered by such third-party intellectual property rights, and may need to seek to develop alternative approaches that do not infringe on such intellectual property rights which may entail additional costs and development delays, even if we were able to develop such alternatives, which may not be feasible. Even if we are able to obtain a license under such intellectual property rights, any such license may be non-exclusive, which may allow our competitors access to the same technologies licensed to us.

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

The licensing and acquisition of third-party intellectual property rights is a competitive practice, 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 larger size and cash resources or greater clinical development and commercialization capabilities. There can be no assurance that we will be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to acquire.

During the course of business we have decided not to pursue certain products or processes and have terminated certain corresponding intellectual property license agreements or removed certain intellectual property from current license agreements, and we may do so again in the future. If it is later determined that our activities or product candidates infringe this intellectual property, then we may be liable for damages, enhanced damages or subjected to an injunction, any of which could have a material adverse effect on our business.

The patent position of pharmaceutical and biotechnology companies generally is highly uncertain and involves complex legal and factual questions for which many legal principles remain unresolved. In recent years patent rights have been the subject of significant litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued in the United States or in other jurisdictions which protect our technology or products or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. 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 patents or pending patent applications, or that we were the first to file for patent protection of such inventions. In addition, the U.S. Patent and Trademark Office, or USPTO, might require that the term of a patent issuing from a pending patent application be disclaimed and limited to the term of another patent that is commonly owned or names a common inventor. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain.

Recent or future patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. In March 2013, under the Leahy-Smith America Invents Act, or America Invents Act, the United States moved from a “first to invent” to a “first-to-file” system. Under a “first-to-file” system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on the invention regardless of whether another inventor had made the invention earlier. The America Invents Act includes a number of other significant changes to U.S. patent law, including provisions that affect the way patent applications are prosecuted, redefine prior art and establish a new post-grant review system. The effects of these changes are currently unclear as the USPTO only recently developed new regulations and procedures in connection with the America Invents Act and many of the substantive changes to patent law, including the “first-to-file” provisions, only became effective in March 2013. In addition, the courts have yet to address many of these provisions and the applicability of the act and new regulations on specific patents discussed herein have not been determined and would need to be reviewed. However, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition. We may become involved in opposition, interference, derivation, *inter partes* review or other proceedings challenging our patent rights or the patent rights of others, and the outcome of any proceedings are highly uncertain. An adverse determination in any such proceeding could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights.

Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner. The issuance of a patent is not conclusive as to its scope, validity or enforceability, and our owned and in-licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in the patent claims of our owned or in-licensed patents being narrowed, invalidated or held unenforceable, which could limit our ability to stop or prevent us from stopping others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours or otherwise provide us with a competitive advantage.

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

- others may be able to make or use compounds that are similar to the pharmaceutical compounds used in our product candidates but that are not covered by the claims of our patents;
- the active pharmaceutical ingredients in our current product candidates will eventually become commercially available in generic drug products, and no patent protection may be available with regard to formulation or method of use;
- we or our licensors, as the case may be, may fail to meet our obligations to the U.S. government in regards to any in-licensed patents and patent applications funded by U.S. government grants, leading to the loss of patent rights;
- we or our licensors, as the case may be, might not have been the first to file patent applications for these inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies;
- it is possible that our pending patent applications will not result in issued patents;
- it is possible that there are prior public disclosures that could invalidate our or our licensors' patents, as the case may be, or parts of our or their patents;
- it is possible that others may circumvent our owned or in-licensed patents;
- it is possible that there are unpublished applications or patent applications maintained in secrecy that may later issue with claims covering our products or technology similar to ours;
- the laws of foreign countries may not protect our or our licensors', as the case may be, proprietary rights to the same extent as the laws of the United States;
- the claims of our owned or in-licensed issued patents or patent applications, if and when issued, may not cover our product candidates;
- our owned or in-licensed issued patents may not provide us with any competitive advantages, may be narrowed in scope or may be held invalid or unenforceable as a result of legal challenges by third parties;
- the inventors of our owned or in-licensed patents or patent applications may become involved with competitors, develop products or processes which design around our patents or become hostile to us or the patents or patent applications on which they are named as inventors;
- we have engaged in scientific collaborations in the past, such as with Roche, and will continue to do so in the future. Such collaborators may develop adjacent or competing products to ours that are outside the scope of our patents;
- we may not develop additional proprietary technologies for which we can obtain patent protection;
- it is possible that product candidates or diagnostic tests we develop may be covered by third parties' patents or other exclusive rights; or
- the patents of others may have an adverse effect on our business.

We also may rely on trade secrets to protect our technology, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect, and we have limited control over the protection of trade secrets used by our licensors, collaborators and suppliers. Although we use reasonable efforts to protect our trade secrets, our employees, consultants, contractors, outside scientific collaborators and other advisors may unintentionally or willfully disclose our information to competitors or use such information to compete with us. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how. If our confidential or proprietary information is divulged to or acquired by third parties, including our competitors, our competitive position in the marketplace will be harmed and this would have a material adverse effect on our business.

If any of our owned or in-licensed patents are found to be invalid or unenforceable, or if we are otherwise unable to adequately protect our rights, it could have a material adverse impact on our business and our ability to commercialize or license our technology and product candidates. Our current owned and in-licensed patents covering our proprietary technologies and our product candidates are expected to expire on various dates from 2021 through 2033, including a composition of matter patent that we own covering our product candidate, ALRN-6924, which expires in the United States in 2033, without taking into account any possible patent term adjustments or extensions. Our earliest in-licensed patents were only filed in the United States and may expire before, or soon after, our first product achieves marketing approval in the United States. Upon the expiration of our current patents, we may lose the right to exclude others from practicing these inventions. The expiration of these patents could also have a similar material adverse effect on our business, results of operations, financial condition and prospects. We own or in-license pending patent applications covering our proprietary technologies or our product candidates that if issued as patents are expected to expire from 2021 through 2037, without taking into account any possible patent term adjustments or extensions. However, we cannot be assured that the USPTO or relevant foreign patent offices will grant any of these patent applications.

If we fail to comply with our obligations under our patent licenses with third parties, we could lose license rights that are important to our business.

We are a party to license agreements with Harvard, DFCI, Umicore Precious Metals Chemistry USA, LLC and others, pursuant to which we in-license key patent and patent applications for our product candidates. These existing licenses impose various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with these obligations, our licensors may have the right to terminate the license, in which event we would not be able to develop or market the products covered by such licensed intellectual property.

In early 2016, Harvard communicated a claim to us that we had not achieved one or more of the diligence milestones set forth in our license agreement with Harvard and DFCI and that we were in material breach of the license agreement. We provided Harvard with a response stating our position that we had fully satisfied the diligence milestones required under the license agreement. Since that time, Harvard has never re-asserted its claim or sought to terminate the license agreement. In making its assertion, Harvard did not seek to terminate the license agreement or interfere with our ongoing p53 program, but instead proposed to convert our exclusive license with respect to certain of the patent families licensed under the license agreement to a non-exclusive license. In any event, Harvard's proposal would not have impeded our development of ALRN-6924 or our other ongoing programs. DFCI did not join Harvard in making this assertion or proposal and has not expressed a similar position to us. We have continued to communicate with Harvard in the ordinary course, including providing periodic reports, and have paid applicable licensing and milestone payments to Harvard pursuant to the terms of the license agreement, and we believe we remain in full compliance with the agreement.

We continue to monitor our compliance with our obligations under our license agreements on an ongoing basis. However, if in the future Harvard or DFCI were to successfully assert a material breach and if we were to lose some or all of our rights under the license agreement, our business would be adversely affected, and it may be difficult to commercialize ALRN-6924 until the applicable patents covered by the license agreement with Harvard and DFCI expired, unless we were able to negotiate a new license arrangement with those parties.

We may incur substantial costs as a result of litigation or other proceedings relating to patents, and we may be unable to protect our rights to our products and technology.

If we or our licensors choose to go to court to stop a third party from using the inventions claimed in our owned or in-licensed patents, that third party may ask the court to rule that the patents are invalid and/or should not be enforced against that third party. These lawsuits are expensive and would consume time and other resources even if we or they, as the case may be, were successful in stopping the infringement of these patents. In addition, there is a risk that the court will decide that these patents are not valid and that we or they, as the case may be, do not have the right to stop others from using the inventions.

There is also the risk that, even if the validity of these patents is upheld, the court will refuse to stop the third party on the ground that such third party's activities do not infringe our owned or in-licensed patents. In addition, the U.S. Supreme Court has recently changed some legal principles that affect patent applications, granted patents and assessment of the eligibility or validity of these patents. As a consequence, issued patents may be found to contain invalid claims according to the newly revised eligibility and validity standards. Some of our owned or in-licensed patents may be subject to challenge and subsequent invalidation or significant narrowing of claim scope in proceedings before the USPTO, or during litigation, under the revised criteria which could also make it more difficult to obtain patents.

We, or our licensors, may not be able to detect infringement against our owned or in-licensed patents, as the case may be, which may be especially difficult for manufacturing processes or formulation patents. Even if we or our licensors detect infringement by a third party of our owned or in-licensed patents, we or our licensors, as the case may be, may choose not to pursue litigation against or settlement with the third party. If we, or our licensors, later sue such third party for patent infringement, the third party may have certain legal defenses available to it, which otherwise would not be available except for the delay between when the infringement was first detected and when the suit was brought. Such legal defenses may make it impossible for us or our licensors to enforce our owned or in-licensed patents, as the case may be, against such third party.

If another party questions the patentability of any of our claims in our owned or in-licensed U.S. patents, the third party can request that the USPTO review the patent claims such as in an *inter partes* review, *ex parte* re-exam or post-grant review proceedings. These proceedings are expensive and may result in a loss of scope of some claims or a loss of the entire patent. In addition to potential USPTO review proceedings, we may become a party to patent opposition proceedings in the European Patent Office, or EPO, or similar proceedings in other foreign patent offices, where either our owned or in-licensed foreign patents are challenged. The costs of these opposition or similar proceedings could be substantial, and may result in a loss of scope of some claims or a loss of the entire patent. An unfavorable result at the USPTO, EPO or other patent office may result in the loss of our right to exclude others from practicing one or more of our inventions in the relevant country or jurisdiction, which could have a material adverse effect on our business.

We may incur substantial costs as a result of litigation or other proceedings relating to intellectual property rights other than patents, and we may be unable to protect our rights to our products and technology.

We may rely on trade secrets and confidentiality agreements to protect our technology and know-how, especially where we do not believe patent protection is appropriate or obtainable. Enforcing a claim that a third party illegally obtained and is using any of our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. If we choose to go to court to stop a third party from using any of our trade secrets, we may incur substantial costs. These lawsuits may consume our time and other resources even if we are successful.

If we are sued for infringing patents or other intellectual property rights of third parties, it will be costly and time consuming, and an unfavorable outcome in that litigation would have a material adverse effect on our business.

Our commercial success depends upon our ability to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields relating to our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that others may assert our product candidates infringe the patent rights of others. Moreover, it is not always clear to industry participants, including us, which patents cover various types of drugs, products or their methods of use or manufacture. Thus, because of the large number of patents issued and patent applications filed in our fields, there may be a risk that third parties may allege they have patent rights encompassing our product candidates, technologies or methods.

In addition, because some patent applications in the United States may be maintained in secrecy until the patents are issued, patent applications in the United States and many foreign jurisdictions are typically not published until 18 months after filing, and publications in the scientific literature often lag behind actual discoveries, we cannot be certain that others have not filed patent applications for technology covered by our owned and in-licensed issued patents or our pending applications, or that we or, if applicable, a licensor were the first to invent the technology. Our competitors may have filed, and may in the future file, patent applications covering our products or

technology similar to ours. Any such patent application may have priority over our owned and in-licensed patent applications or patents, which could require us to obtain rights to issued patents covering such technologies. If another party has filed a U.S. patent application on inventions similar to those owned by or in-licensed to us on or before March 15, 2013, we or, in the case of in-licensed technology, the licensor may have to participate in an interference proceeding initiated by such other party to determine priority of invention in the United States. If another party has filed such patent application after March 15, 2013, a derivation proceeding in the United States can be initiated by such other party to determine whether our, or in the case of in-licensed technology, the licensor's invention was derived from such party's invention. If we or one of our licensors is a party to an interference proceeding involving a U.S. patent application on inventions owned by or in-licensed to us, we may incur substantial costs, divert management's time and expend other resources, even if we are successful.

There is a substantial amount of litigation involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries generally. We may be exposed to, or threatened with, future litigation by third parties having patent or other intellectual property rights alleging that our product candidates and/or proprietary technologies infringe their intellectual property rights.

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

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

Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations or could otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

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

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

Filing, prosecuting and defending patents on all of our product candidates throughout the world would be prohibitively expensive. Competitors may use our technology in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but where enforcement is not as strong as in the United States. These products may compete with our product candidates 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 against third parties in violation of our proprietary rights generally. The initiation of proceedings by third parties to challenge the scope or validity of our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business.

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

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent prosecution process and following the issuance of a patent. Our failure to comply with such requirements could 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 if our patent were in force, which would have a material adverse effect on our business.

We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

As is common in the biotechnology and pharmaceutical industries, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and, if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. This type of litigation or proceeding could substantially increase our operating losses and reduce our resources available for development activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other intellectual property related proceedings could adversely affect our ability to compete in the marketplace.

Risks Related to Marketing Approval and Other Legal Compliance Matters

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

The research, testing, manufacturing, labeling, approval, selling, marketing, promotion and distribution of drugs are subject to extensive regulation by the FDA and comparable foreign regulatory authorities, whose laws and regulations may differ from country to country. We, and any future collaborators, are not permitted to market our product candidates in the United States or in other countries until we or they receive approval of an NDA from the FDA or marketing approval from comparable foreign regulatory authorities. Our product candidates are in early stages of development and are subject to the risks of failure inherent in drug development. We have not submitted an application for or received marketing approval for ALRN-6924 any of our future product candidates in the United States or in any other jurisdiction. We have limited experience in conducting and managing the clinical trials necessary to obtain marketing approvals, including FDA approval of an NDA.

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

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

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

This lengthy approval process as well as the unpredictability of clinical trial results may result in our failing to obtain marketing approval to market ALRN-6924, which would significantly harm our business, results of operations and prospects.

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

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

Failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed abroad. Any approval we are granted for our product candidates in the United States would not assure approval of our product candidates in foreign jurisdictions.

In order to market and sell our products in the European Union and many other foreign jurisdictions, we or our potential third-party collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside of the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside of the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We or our potential third-party collaborators may not obtain approvals from regulatory authorities outside of 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 of the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in other countries. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products candidates in any market.

Additionally, we could face heightened risks with respect to seeking marketing approval in the United Kingdom as a result of the recent withdrawal of the United Kingdom from the European Union. Pursuant to the formal withdrawal arrangements agreed between the United Kingdom and the European Union, the United Kingdom withdrew from the European Union, effective December 31, 2020. On December 24, 2020, the United Kingdom and European Union entered into a Trade and Cooperation Agreement, which set out certain procedures for approval and recognition of medical products in each jurisdiction. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of the Trade and Cooperation Agreement or otherwise, could prevent us from commercializing any product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for any product candidates, which could significantly and materially harm our business.

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

Regulatory authorities in some jurisdictions, including the United States and the European Union, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States, or a patient

population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In April 2017, the FDA granted orphan drug designation to ALRN-6924 for use in the treatment of AML. We may also seek orphan drug designations for ALRN-6924 for other indications, or for other of our product candidates. There can be no assurances that we will be able to obtain such designations.

In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusivity. Orphan drug exclusivity in the United States provides that the FDA may not approve any other applications, including a full NDA, to market the same drug for the same indication for seven years, except in limited circumstances. The applicable exclusivity period is ten years in Europe. The European exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified.

Even if we, or any future collaborators, obtain orphan drug designation for a product candidate as we have obtained for ALRN-6924 for AML, we, or they, may not be able to obtain or maintain orphan drug exclusivity for that product candidate. We may not be the first to obtain marketing approval of any product candidate for which we have obtained orphan drug designation for the orphan-designated indication due to the uncertainties associated with developing pharmaceutical products. In addition, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan-designated indication or may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Further, even if we, or any future collaborators, obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties may be approved for the same condition.

Even after an orphan drug is approved, the FDA can subsequently approve the a different product for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care or the manufacturer of the product with orphan exclusivity is unable to maintain sufficient product quantity. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process. The FDA may reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business.

Even if we, or any collaborators we may have in the future, obtain marketing approvals for our product candidates, the terms of approvals and ongoing regulation of our drugs could require substantial expenditure of resources and may limit how we, or they, manufacture and market our drugs, which could materially impair our ability to generate revenue.

Once marketing approval has been granted, an approved drug and its manufacturer and marketer are subject to ongoing review and extensive regulation. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. We, and any collaborators we may have in the future, must also comply with requirements concerning advertising and promotion for any of our product candidates for which we or they obtain marketing approval. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the drug's approved labeling. Thus, we, and any collaborators we may have in the future, may not be able to promote any drugs we develop for indications or uses for which they are not approved.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a drug. For example, the approval may be subject to limitations on the indicated uses for which the drug may be marketed or to the conditions of approval, including the requirement to implement a Risk Evaluation and Mitigation Strategy, which could include requirements for a restricted distribution system. Manufacturers of approved drugs and those manufacturers' facilities are also required to comply with extensive

FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, our contract manufacturers, our future collaborators and their contract manufacturers could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMPs.

Accordingly, assuming we, or our future collaborators, receive marketing approval for one or more of our product candidates, we, and our future collaborators, and our and their contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control.

If we, and our future collaborators, are not able to comply with post-approval regulatory requirements, we, and our future collaborators, could have the marketing approvals for our drugs withdrawn by regulatory authorities and our, or our future collaborators', ability to market any future drugs could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

The FDA's and other regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates, which would impact our ability to generate revenue.

In December 2016, the 21st Century Cures Act, or Cures Act, was signed into law. The Cures Act, among other things, is intended to modernize the regulation of drugs and spur innovation, but its ultimate implementation is unclear. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the current administration may impact our business and industry. Namely, the current administration has taken several executive actions, including the issuance of a number of executive orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance and review and approval of marketing applications.

ALRN-6924 and any of our future product candidates for which we, or our future collaborators, obtain marketing approval in the future will be subject to substantial penalties if we, or they, fail to comply with regulatory requirements or if we, or they, experience unanticipated problems with our drugs following approval.

ALRN-6924 and any of our future product candidates for which we, or our future collaborators, obtain marketing approval in the future, will be subject to continual review by the FDA and other regulatory authorities.

The FDA and other agencies, including the Department of Justice, or the DOJ, closely regulate and monitor the post-approval marketing and promotion of drugs to ensure that they are manufactured, marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we, or our future collaborators, do not market any of our product candidates for which we, or they, receive marketing approval for only their approved indications, we, or they, may be subject to warnings or enforcement action for off-label marketing. Violation of the FDCA and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations or allegations of violations of federal and state healthcare fraud and abuse laws and state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our drugs or their manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- litigation involving patients taking our drug;
- restrictions on such drugs, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a drug;
- restrictions on drug distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the drugs from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of drugs;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- damage to relationships with any potential collaborators;
- restrictions on coverage by third-party payors;
- unfavorable press coverage and damage to our reputation;
- refusal to permit the import or export of drugs;
- drug seizure; or
- injunctions or the imposition of civil or criminal penalties.

Recently enacted and future legislation may increase the difficulty and cost for us and our future collaborators to obtain marketing approval of and commercialize our product candidates and affect the prices we, or they, may obtain for any products that are approved in the United States or foreign jurisdictions.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability, or the ability of any future collaborators, to profitably sell any product candidates for which we, or they, obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any collaborators, may receive for any approved products. If reimbursement of our products is unavailable or limited in scope, our business could be materially harmed.

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

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the ACA. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. This legislation resulted in aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which will remain in effect through 2030 under the CARES Act. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, or the TCJA, which was signed by President Trump on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019.

On November 10, 2020, the Supreme Court heard oral arguments. On February 10, 2021, the Biden Administration withdrew the federal government's support for overturning the ACA. A ruling by the Supreme Court is expected sometime this year.

The Trump Administration also took executive actions to undermine or delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden issued a new Executive Order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care, and consider actions that will protect and strengthen that access. This Executive Order also directs the U.S. Department of Health and Human Services to create a special enrollment period for the Health Insurance Marketplace in response to the COVID-19 pandemic. We cannot predict how federal agencies will respond to such Executive Orders.

Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

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

The costs of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. To date, there have been several recent U.S. congressional inquiries and proposed and enacted state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for products. To those ends, President Trump issued several executive orders intended to lower the costs of prescription drug products. Certain of these orders are reflected in recently promulgated regulations, including an interim final rule implementing President Trump's most favored nation model, but such final rule is currently subject to a nationwide preliminary injunction. It remains to be seen whether these orders and resulting regulations will remain in force during the Biden Administration. Further, on September 24, 2020, the Trump Administration finalized a rulemaking allowing states or certain other non-federal government entities to submit importation program proposals to the FDA for review and approval. Applicants are required to demonstrate their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. The FDA has issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will

pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

We may seek to obtain certain regulatory designations for ALRN-6924. We may not receive such designations, and even if we do, such designation may not lead to a faster development or regulatory review or approval process.

We may seek to obtain breakthrough therapy designation, fast track designation, or priority review designation for ALRN-6924. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. FDA fast track designation is possible for drugs intended for the treatment of a serious condition and nonclinical or clinical data demonstrate the potential to address unmet medical need for this condition. In addition, if the FDA determines that a product candidate offers a treatment for a serious condition and, if approved, the product would provide a significant improvement in safety or effectiveness, the FDA may designate the product candidate for priority review. Drugs designated as breakthrough therapies by the FDA may also be eligible for priority review if supported by clinical data at the time the NDA is submitted to the FDA.

Such regulatory designations are within the discretion of the FDA, and the FDA may not approve any application that we submit. Even if we were to obtain breakthrough designation or fast track designation, the FDA may subsequently withdraw such designation if the FDA determines that the designation no longer meets the conditions for qualification or is no longer supported by data from our clinical development program. In addition, receipt of any such designations may not result in a faster development or regulatory review or approval process compared to drugs considered for approval under conventional FDA procedures, and does not assure ultimate approval by the FDA of any drug candidates so designated.

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

Our relationships with healthcare providers, physicians and third-party payors will subject us to additional healthcare statutory and regulatory requirements and enforcement by the federal government and the states and foreign governments in which we conduct our business. Our future arrangements with healthcare providers, physicians and third-party payors and patients may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- *Anti-Kickback Statute*—the federal anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing any remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good, facility, item or service, for which payment may be made, in whole or in part, by a federal healthcare program, such as Medicare and Medicaid.
- *False Claims Act*—the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- *HIPAA*—the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- *HIPAA Privacy Provisions*—as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information
- *Transparency Requirements*—the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the Affordable Care Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the U.S. Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and
- *Analogous State and Foreign Laws*—analogous state and foreign fraud and abuse laws and regulations, such as state anti-kickback and false claims laws, can apply to sales or marketing arrangements and claims involving healthcare items or services and are reimbursed by non-governmental third-party payors, including private insurers.

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

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of drugs from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. Although effective compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, these risks cannot be entirely eliminated. Any action against us for an alleged or suspected violation could cause us to incur significant legal expenses and could divert our management's attention from the operation of our business, even if our defense is successful. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, it may be costly to us in terms of money, time and resources, and they may be subject to criminal, civil or administrative sanctions, including exclusions from government-funded healthcare programs.

Our employees may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of employee fraud or other misconduct, 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 may establish, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

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

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of hazardous and flammable materials, including chemicals and biological materials.

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

Laws and regulations governing any international operations we may have in the future 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.

If 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. 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 Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, 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 certain accounting provisions requiring the company 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 DOJ. The Securities and Exchange Commission, or 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 of 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. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain drugs and product candidates outside of 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.

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

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the European Union, including personal health data, is subject to the EU General Data Protection Regulation, or the GDPR, which took effect across all member states of the European Economic Area, or EEA, in May 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR increases our obligations with respect to clinical trials conducted in the EEA by expanding the definition of personal data to include coded data and requiring changes to informed consent practices and more detailed notices for clinical trial subjects and investigators. In addition, the GDPR also imposes strict rules on the transfer of personal data to countries outside the European Union, including the United States and, as a result, increases the scrutiny that clinical trial sites located in the EEA should apply to transfers of personal data from such sites to countries that are considered to lack an adequate level of data protection, such as the United States. The GDPR also permits data protection authorities to require destruction of improperly gathered or used personal information and/or impose substantial fines for violations of the GDPR, which can be up to four percent of global revenues or €20 million, whichever is greater, and it also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR provides that EU member states may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric or health data.

Similar actions are either in place or under way in the United States. There are a broad variety of data protection laws that are applicable to our activities, and a wide range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns based on general consumer protection laws. The Federal Trade Commission and state Attorneys General all are aggressive in reviewing privacy and data security protections for consumers. New laws also are being considered at both the state and federal levels. For example, the California Consumer Privacy Act, which went into effect on January 1, 2020, is creating similar risks and obligations as those created by the GDPR, though the California Consumer Privacy Act does exempt certain information collected as part of a clinical trial subject to the Federal Policy for the Protection of Human Subjects (the Common Rule). Many other states are considering similar legislation. A broad range of legislative measures also have been introduced at the federal level. Accordingly, failure to comply with federal and state laws (both those currently in effect and future legislation) regarding privacy and security of personal information could expose us to fines and penalties under such laws. There also is the threat of consumer class actions related to these laws and the overall protection of personal data.

Given the breadth and depth of changes in data protection obligations, preparing for and complying with these requirements is rigorous and time intensive and requires significant resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the European Union. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities and increase our cost of doing business, and could lead to government enforcement actions, private litigation and significant fines and penalties against us and could have a material adverse effect on our business, financial condition or results of operations. Similarly, failure to comply with federal and state laws regarding privacy and security of personal information could expose us to fines and penalties under such laws. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business.

Risks Related to Employee Matters and Managing Growth

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

We are highly dependent on Manuel Aivado, M.D., Ph.D., our Chief Executive Officer, as well as the other principal members of our management and scientific teams. Our agreements with Dr. Aivado and other key employees do not prevent them from terminating their employment with us at any time. Replacing our executives or other key employees may be extremely difficult, and may take an extended period of time due to the intense competition for qualified personnel in our industry and the limited number of individuals who have the breadth of skills and experience required to develop, gain regulatory approval of, and commercialize products successfully. We do not maintain “key person” insurance for any of our executives or other employees. Accordingly, the loss of the services of Dr. Aivado or any other senior member of our management and scientific teams could impede the achievement of our research, development and commercialization objectives, and harm our business.

Recruiting and retaining qualified personnel in the scientific and clinical fields is also critical to our success. The pool of qualified candidates is limited, and competition in the life sciences industry, particularly in the Greater Boston area, is intense. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. We may be unable to hire, train, retain or motivate additional key personnel on acceptable terms given the degree of competition for similar personnel. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

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

In order to conduct later stage clinical trials and prepare for commercialization, we would need to expand our organization significantly through the hiring of a number of additional employees, particularly in the areas of drug

development, clinical operations, regulatory affairs and, potentially, sales and marketing. To manage this future growth, we must continue to implement and improve our managerial, operational and financial systems, periodically assess the adequacy of our facilities, and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our leadership team in managing a company's growth, we may not be able to effectively manage an expansion of our operations or recruit and train additional qualified personnel. In addition, a physical expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

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

Despite our security measures, our internal computer systems and those of our current and any future collaborators and other contractors or consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such material system failure, accident 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, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed, and the further development and commercialization of our product candidates could be delayed or halted. In addition, we may not have adequate insurance coverage to provide compensation for any losses associated with such events.

We could be subject to risks caused by misappropriation, misuse, leakage, falsification or intentional or accidental release or loss of information maintained in our information systems and networks, including personal information of our employees. In addition, outside parties may attempt to penetrate our systems or those of our vendors or fraudulently induce our employees or employees of our vendors to disclose sensitive information to gain access to our data. Like other companies, we may experience threats to our data and systems, including malicious codes and viruses, and other cyber-attacks. The number and complexity of these threats continue to increase over time. If a material breach of our security or that of our vendors occurs, the market perception of the effectiveness of our security measures could be harmed, we could lose business and our reputation and credibility could be damaged. We could also be required to expend significant amounts of money and other resources to repair or replace information systems or networks.

Risks Related to Our Common Stock

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

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

- establish a classified board of directors such that not all members of the board are elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;

- limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws.

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

An active trading market for our common stock may not be sustained.

Our shares of common stock began trading on The Nasdaq Global Market June 29, 2017 and transferred to The Nasdaq Capital Market, effective December 30, 2019. Given the limited trading history of our common stock, there is a risk that an active trading market for our shares may not be sustained, which could put downward pressure on the market price of our common stock and thereby affect the ability of stockholders to sell their shares. An inactive trading market for our common stock may also impair our ability to raise capital to continue to fund our operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

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

The trading market for our common stock relies in part on the research and reports that industry or financial analysts publish about us or our business. If few analysts commence, or if analysts discontinue, coverage of us, the trading price of our stock would likely decrease. If one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

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

Our stock price is volatile. During the period from June 28, 2017 to March 19, 2021, the closing price of our common stock ranged from a high of $14.91 per share to a low of $0.29 per share. The stock market in general and the market for pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, our stockholders may not be able to sell their shares at or above the price they paid for their shares. The market price for our common stock may be influenced by many factors, including:

- the timing and results of clinical trials of ALRN-6924 and any of our other product candidates that may develop;
- regulatory actions with respect to our product candidates or our competitors' products and product candidates;
- the effect of the COVID-19 pandemic on both the healthcare system and the patient population;

- the success of existing or new competitive products or technologies;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- establishment or termination of collaborations for our product candidates or development programs;
- failure or discontinuation of any of our development programs;
- results of clinical trials of product candidates 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 ALRN-6924 or development programs;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
- actual or anticipated changes in estimates as to financial results or development timelines;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or other stockholders;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts, if any, that cover our stock;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this “Risk Factors” section.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because pharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management’s attention and our resources, which could harm our business.

We are an “emerging growth company,” and a “smaller reporting company” and the reduced disclosure requirements applicable to emerging growth companies and smaller reporting companies may make our common stock less attractive to investors.

We are an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. We may remain an emerging growth company until December 31, 2022, or until such earlier time as we have more than $1.07 billion in annual revenue, the market value of our stock held by non-affiliates is more than $700 million or we issue more than $1 billion of non-convertible debt over a three-year period. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor’s report providing additional information about the audit and the financial statements, reduced disclosure obligations regarding executive compensation and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We are also a smaller reporting company, and we will remain a smaller reporting company until the fiscal year following the determination that our voting and non-voting common stock held by non-affiliates is more than $250

million measured on the last business day of our second fiscal quarter, or our annual revenues are less than $100 million during the most recently completed fiscal year and our voting and non-voting common stock held by non-affiliates is more than $700 million measured on the last business day of our second fiscal quarter. Similar to emerging growth companies, smaller reporting companies are able to provide simplified executive compensation disclosure, are exempt from the auditor attestation requirements of Section 404 and have certain other reduced disclosure obligations, including, among other things, being required to provide only two years of audited financial statements and not being required to provide selected financial data, supplemental financial information or risk factors.

We have elected to take advantage of certain of the reduced reporting obligations. Investors may find our common stock less attractive as a result of our reliance 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.

Our management is required to devote substantial time to new compliance initiatives. Any failure to maintain effective internal control over our financial reporting could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

As a public company, we incur, and particularly after we are no longer an "emerging growth company" or a "smaller reporting company" we will incur, significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act of 2002 and rules subsequently implemented by the SEC and Nasdaq have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. We have had to hire additional accounting, finance, and other personnel in connection with our becoming a public company, and our efforts to comply with the requirements of being a public company, and our management and other personnel devote a substantial amount of time towards maintaining compliance with these requirements. These requirements increase our legal and financial compliance costs and will make some activities more time-consuming and costly.

In addition, Section 404 of the Sarbanes-Oxley Act of 2002 requires us, on an annual basis, to review and evaluate our internal controls. To maintain compliance with Section 404, we are required to document and evaluate our internal control over financial reporting, which is both costly and challenging. We will need to continue to dedicate internal resources, continue to engage outside consultants, and follow a detailed work plan to continue to assess and document the adequacy of internal control over financial reporting, continue to improve control processes as appropriate, validate through testing that controls are functioning as documented, and implement a continuous reporting and improvement process for internal control over financial reporting. There is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

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

Changes in tax law may adversely affect our business or financial condition. On December 22, 2017, the U.S. government enacted the TCJA, which significantly reformed the U.S. Internal Revenue Code of 1986, as amended, or the Code. The TCJA, among other things, contained significant changes to corporate taxation, including a reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, the limitation of the tax deduction for net interest expense to 30% of adjusted taxable income (except for certain small businesses), the limitation of the deduction for net operating losses arising in taxable years beginning after December 31, 2017 to 80% of current year taxable income and elimination of net operating loss carrybacks for losses arising in taxable years ending after December 31, 2017 (though any such net operating losses may be carried forward indefinitely), the imposition of a one-time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, the elimination of U.S. tax on foreign earnings (subject to certain important exceptions), the allowance of immediate deductions for certain new investments instead of deductions for depreciation expense over time, and the modification or repeal of many business deductions and credits.

As part of Congress' response to the COVID-19 pandemic, the Families First Coronavirus Response Act, or FFCR Act, was enacted on March 18, 2020, the Coronavirus Aid, Relief, and Economic Security Act, or CARES Act, was enacted on March 27, 2020 and COVID-19 relief provisions were included in the Consolidated Appropriations Act, 2021, or CAA, which was enacted on December 27, 2020. All contain numerous tax provisions. In particular, the CARES Act retroactively and temporarily (for taxable years beginning before January 1, 2021) suspends application of the 80%-of-income limitation on the use of net operating losses, which was enacted as part of the TCJA. It also provides that net operating losses arising in any taxable year beginning after December 31, 2017, and before January 1, 2021 are generally eligible to be carried back up to five years. The CARES Act also temporarily (for taxable years beginning in 2019 or 2020) relaxes the limitation of the tax deductibility for net interest expense by increasing the limitation from 30 to 50% of adjusted taxable income.

Regulatory guidance under the TCJA, the FFCR Act, the CARES Act and the CAA is and continues to be forthcoming, and such guidance could ultimately increase or lessen impact of these laws on our business and financial condition. It is also likely that Congress will enact additional legislation in connection with the COVID-19 pandemic, some of which could have an impact on our company. In addition, it is uncertain if and to what extent various states will conform to the TCJA, the FFCR Act, the CARES Act and the CAA.

We might not be able to utilize a significant portion of our net operating loss carryforwards and research and development tax credit carryforwards.

As of December 31, 2020, we had federal net operating loss carryforwards of $203.5 million, of which $129.6 million will, if not utilized, begin to expire in 2029. As of December 31, 2020, we had state net operating carryforwards of $197.7 million, which will, if not utilized, begin to expire in 2030. Our federal and state research and development tax credit carryforwards of $2.6 million and $1.8 million, respectively, will, if not utilized, begin to expire in 2025. We also have federal orphan drug tax credit carryforwards of $1.0 million which begin to expire in 2039. These net operating loss and tax credit carryforwards could expire unused and be unavailable to offset future income tax liabilities.

We have a history of cumulative losses and anticipate that we will continue to incur significant losses in the foreseeable future; thus, we do not know whether or when we will generate taxable income necessary to utilize our net operating losses or research and development tax credit carryforwards.

In addition, under Section 382 of the Code and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50% change, by value, in its equity ownership by certain stockholders over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income may be limited. We have not conducted a study to assess whether we have experienced Section 382 ownership changes in the past and if a portion of our net operating loss and tax credit carryforwards are subject to an annual limitation under Section 382. In addition, we may experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which may be outside of our control. If we determine that an ownership change has occurred at any time since our inception and our ability to use our historical net operating loss and tax credit carryforwards is materially limited, it would harm our future operating results by effectively increasing our future tax obligations.

There is also a risk that due to regulatory changes, such as suspensions on the use of net operating losses, or other unforeseen reasons, our existing net operating losses could expire or otherwise become unavailable to offset future income tax liabilities. In addition, state net operating losses generated in one state cannot be used to offset income generated in another state. For these reasons, even if we attain profitability, we may be unable to use a material portion of our net operating losses and other tax attributes.

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

A significant portion of our total outstanding shares may be sold into the market at any time, which could cause the market price of our common stock to drop significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. 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. As of March 19, 2021, we had 90,210,557 shares of common stock outstanding.

We have filed several registration statements covering the resale of shares of our common stock held by several stockholders. In connection with our April 2019 private placement, we filed a registration statement covering the resale of shares purchased by the purchasers in the private placement and shares issuable upon exercise of warrants issued in the private placement. In August 2020 and February 2021, we filed registration statements on Form S-3 covering the resale of an aggregate of 12,700,000 shares of our common stock held by Satter Medical Technology Partners, L.P., or SMTP, and entities affiliated with SMTP. Dr. Nolan Sigal, a partner at Satter Management Co., L.P., an affiliate of SMTP, is a member of our board of directors.

On September 21, 2020, we entered into the Purchase Agreement with LPC pursuant to which LPC has committed to purchase up to $15.0 million of shares of our common stock. We filed a registration statement on Form S-1 covering the sale of shares of common stock that are issued to LPC under the Purchase Agreement, which was declared effective on October 15, 2020. We generally have the right to control the timing and amount of any future sales of shares of our common stock to LPC. Sales of shares of our common stock, if any, to LPC will depend upon market conditions and other factors to be determined by us. We may ultimately decide to sell to LPC all, some or none of the additional shares of our common stock that may be available for us to sell pursuant to the Purchase Agreement. Therefore, sales to Lincoln Park by us could result in substantial dilution to the interests of other holders of our common stock. Additionally, the sale of a substantial number of shares of our common stock to LPC, or the anticipation of such sales, could make it more difficult for us to sell equity or equity-related securities in the future at a time and at a price that we might otherwise wish to effect sales. If and when we do sell shares of our common stock to LPC, after LPC has acquired the shares of common stock, LPC may resell all, some or none of those shares of common stock at any time or in its discretion.

We have also registered all shares of common stock that we may issue under our equity compensation plans, including upon exercise of outstanding options. These shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates.

If we fail to maintain compliance with the requirements for continued listing on the Nasdaq Capital Market, our common stock could be delisted from trading, which would adversely affect the liquidity of our common stock and our ability to raise additional capital or enter into strategic transactions.

On July 12, 2019, we received a deficiency letter from the Listing Qualifications Department of the Nasdaq Stock Market notifying us that, for the last 30 consecutive business days, the bid price for our common stock had closed below the minimum $1.00 per share requirement for continued inclusion on the Nasdaq Global Market, or the Bid Price Rule. On December 20, 2019, we applied to transfer the listing of our stock from the Nasdaq Global Market to the Nasdaq Capital Market. The Nasdaq Capital Market is a continuous trading market that operates in substantially the same manner as the Nasdaq Global Market and listed companies must meet certain financial requirements and comply with Nasdaq's corporate governance requirements.

On December 27, 2019, Nasdaq approved our transfer application. This transfer became effective at the opening of business on December 30, 2019. On June 11, 2020, after our common stock had a closing bid price of at least $1.00 for 10 consecutive trading days, Nasdaq provided written notification to us that we had regained compliance with the Bid Price Rule. We have remained in compliance with the Bid Price Rule since June 2020. However, there can be no assurance that we will continue to maintain compliance with the Bid Price Rule in the future.

Our certificate of incorporation designates the state courts in the State of Delaware or, if no state court located within the State of Delaware has jurisdiction, the federal court for the District of Delaware, as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could discourage lawsuits against the company and our directors, officers and employees.

Our certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Court of Chancery does not have jurisdiction, the federal district court for the District of Delaware) will be the sole and exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or employees to our company or our stockholders, any action asserting a claim against us arising pursuant to any provision of the General Corporation Law of the State of Delaware or our certificate of incorporation or bylaws, or any action asserting a claim against us governed by the internal affairs doctrine. We do not expect this choice of forum provision will apply to suits brought to enforce a duty or liability created by the Securities Act, the Exchange Act of 1934, as amended, or any other claim for which federal courts have exclusive jurisdiction. This exclusive forum provision may limit the ability of our stockholders to bring a claim in a judicial forum that such stockholders find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

The Company has migrated to a remote work environment and is evaluating a new corporate headquarters in the metro Boston, MA area.

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.

Our common stock trades under the symbol "ALRN" on the Nasdaq Capital Market and has been publicly traded since June 29, 2017. Prior to this time, there was no public market for our common stock.

Holders of Our Common Stock

As of March 19, 2021, there were approximately 40 holders of record of shares of our common stock. This number does not include stockholders for whom shares are held in "nominee" or "street" name.

Dividend Policy

We have never declared nor paid cash dividends on our common stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. We do not intend to pay cash dividends in respect of our common stock in the foreseeable future. Any future determination to pay cash dividends will be made at the discretion of our board of directors and will depend on restrictions and other factors our board of directors may deem relevant. Investors should not purchase our common stock with the expectation of receiving cash dividends.

Item 6. Selected Financial Data.

We are a smaller reporting company, as defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended, for this reporting period and are not required to provide the information required under this item.

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

You should read the following discussion and analysis of our financial condition and results of operations together with our audited financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. In addition to historical information, this discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of certain factors. We discuss factors that we believe could cause or contribute to these differences below and elsewhere in this report, including those set forth under Item 1A. "Risk Factors" in this Annual Report on Form 10-K.

We are a clinical-stage chemoprotection oncology company focused on fundamentally transforming the experience of chemotherapy for cancer patients, enabling them to fight cancer without the fear or burden of chemotherapy-induced side effects. ALRN-6924, our first-in-class MDM2/MDMX dual inhibitor activating p53, is the only reported therapeutic agent in clinical development to employ a biomarker strategy, in which we exclusively focus on treating patients with p53-mutated cancers. With this targeted strategy of treating patients with p53-mutated cancers, ALRN-6924 is designed to selectively protect multiple healthy cell types throughout the body from chemotherapy while ensuring we do not protect cancer cells.

Based on its mechanism of action and reported data from our Phase 1b clinical trial evaluating ALRN-6924 in patients with p53-mutated small cell lung cancer, or SCLC, who are being treated with the chemotherapy topotecan, we believe that there may be a significant opportunity to develop ALRN-6924 as an agent to reduce the toxic side effects of chemotherapy in the bone marrow of cancer patients without adversely impacting the anti-cancer activity of chemotherapy against p53-mutant tumors. This is a concept known as "chemoprotection". Biologically, the same mechanism of action can be expected to also lead to protection of healthy normal cells outside of the bone marrow, which may lead to a form of protection against side effects such as alopecia, mucositis, nausea and other side effects. We plan to explore the chemoprotective effects of ALRN-6924 in other normal tissues and organs, such as the skin, hair follicles and the gastrointestinal tract in future, randomized clinical studies.

Our clinical development program for ALRN-6924 includes our recently completed Phase 1b clinical trial evaluating ALRN-6924 as a chemoprotective agent in patients with SCLC being treated with the chemotherapy topotecan, our ongoing Phase 1 clinical trial of ALRN-6924 in healthy volunteers and a planned Phase 1b placebo-controlled clinical trial evaluating ALRN-6924 as a chemoprotective agent in patients with non-small cell lung cancer, or NSCLC, being treated with frontline chemotherapy- or immunochemotherapy.

We completed the trial, including enrolling an additional 11 SCLC patients in order to complete the evaluation of the dose-response relationship. A preliminary evaluation of data from those 11 patients (seven patients receiving 0.3 mg/kg ALRN-6924 six hours before topotecan and four patients receiving 0.2 mg/kg ALRN-6924 twenty-four hours before topotecan) supports our belief that administering ALRN-6924 at 0.3mg/kg and 24 hours before topotecan remains the optimal schedule. We expect to submit final results for presentation at a scientific conference in the second half of 2021.

Reported data from this trial have informed our choice of the recommended dose of ALRN-6924 for subsequent clinical trials, including a Phase 1b trial in patients with NSCLC.

In the second quarter of 2021 we plan to initiate a new Phase 1b clinical trial to assess ALRN-6924 as a chemoprotective agent in advanced patients with p53-mutated NSCLC being treated with first-line chemotherapy with carboplatin and pemetrexed with or without an immune checkpoint inhibitor. This trial is randomized, placebo-controlled, double-blinded, and it is designed to evaluate the potential chemoprotective effects of ALRN-6924 in this patient population. We plan to begin enrolling patients in the NSCLC trial in the second quarter of 2021 and we anticipate reporting interim data (10-20 patients) at the end of 2021 and topline results (60 patients) in mid-2022.

We are also conducting a trial of ALRN-6924 in healthy human volunteers to characterize the time to onset, magnitude, and duration of cell cycle arrest in human bone marrow relative to ALRN-6924 administration, with the goal of developing a universal dosing regimen for ALRN-6924 for use as a chemoprotection agent across a range of additional chemotherapies and tumor indications. Results from the trial remain on track to be reported in mid-2021 and will be submitted for a presentation at a medical conference in second half of 2021.

In addition, we are now investing in CMC development of ALRN-6924 and in the development of a p53 companion diagnostic to support initiation of clinical registration trials upon the completion of our Phase 1b clinical trial in NSCLC. To that purpose, we plan to engage as appropriate with the FDA in 2021 to discuss the ALRN-6924 development program.

Subject to obtaining additional funding, we plan to expand our chemoprotection clinical program to other cancer indications and pursue a development path that aims at a tumor-agnostic label for ALRN-6924 as a chemoprotective agent, across many tumor types and chemotherapy regimens.

We were incorporated in 2001 and commenced principal operations in 2006. We have devoted substantially all of our resources to developing our product candidates, including ALRN-6924, developing our proprietary stabilized cell-permeating peptide platform, building our intellectual property portfolio, business planning, raising capital and providing general and administrative support for these operations.

To date, we have financed our operations primary through $50.0 million in net proceeds from our initial public offering, or IPO, $23.8 million in net proceeds from a private placement in April 2019, $10.2 million in net proceeds from a public offering in June 2020, $33.1 million in net proceeds from a registered direct offering in January 2021, $23.9 million in net proceeds from “at the market” offerings, $4.4 million in net proceeds from sales pursuant to an equity line financing, $131.2 million from our sales of preferred stock prior to our IPO, $0.6 million from the exercise of stock options and $34.9 million from a collaboration agreement.

Since our inception, we have incurred significant losses on an aggregate basis. Our net losses were $21.2 million and $29.4 million for the years ended December 31, 2020 and 2019, respectively. As of December 31, 2020, we had an accumulated deficit of $219.3 million. These losses have resulted primarily from costs incurred in connection with research and development activities, licensing and patent investment and general and administrative costs associated with our operations. We expect to continue to incur significant expenses and operating losses for at least the next several years.

As a result, we will need additional financing to support our continuing operations. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through public or private equity offerings, collaborations and licensing arrangements, or other sources of capital. Adequate additional financing may not be available to us on acceptable terms, if at all. Market conditions are volatile and may continue to be volatile for the foreseeable future, which may limit our ability to raise capital. In addition, while we may seek one or more collaborators for future development of our product candidates for one or more indications, we may not be able to enter into a collaboration for ALRN-6924 for such indications on suitable terms, on a timely basis or at all. Our failure to raise capital as and when needed would have a negative impact on our financial condition and our ability to pursue our business strategy. If we are unable to raise capital when needed, or on acceptable terms, we may be forced to delay, reduce and/or eliminate some or all of our clinical and drug development programs and future commercialization efforts. We may also be forced to take other actions that could adversely affect our business.

Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate revenue from product sales, we may not become profitable. 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 or terminate our operations.

We believe that, based on our current operating plan, our cash, cash equivalents and investments of $13.8 million as of December 31, 2020, together with the net proceeds of approximately $33.1 million from our issuance and sale of shares of common stock in a registered direct public offering on January 8, 2021, net proceeds of approximately $20.0 million from our issuance and sale of shares of common stock in at-market-offerings under Capital on Demand Sales Agreements between January 1, 2021 and the date of this Annual Report on Form 10-K, and net proceeds of approximately $2.6 million from our issuance and sale of shares of common stock from our common stock purchase agreement with Lincoln Park Capital Fund, LLC between January 1, 2021 and the date of this Annual Report on Form 10-K, will enable us to fund our operating expenses into the second half of 2023. Our funding estimates are based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Changing circumstances, some of which may be beyond our control,

could cause us to consume capital significantly faster than we currently anticipate. In any event, our cash, cash equivalents and investments will not be sufficient to fund all of the efforts that we plan to undertake or to fund the completion of development or commercialization of ALRN-6924. See "Liquidity and Capital Resources." Our future viability is dependent on our ability to raise additional capital to finance our operations. In the first half of 2020 we implemented various cost savings measures, including the elimination of previously planned research activities and a shift to a remote work environment, due to our limited cash resources and the uncertainty associated with the coronavirus pandemic.

COVID-19

In March 2020, we began precautionary measures to protect the health and safety of our employees and partners and prospective clinical trial participants during the COVID-19 pandemic. Because COVID-19 infections have been reported throughout the United States and worldwide, certain national, state and local governmental authorities have issued orders, proclamations and/or directives aimed at minimizing the spread of COVID-19. Additional, more restrictive orders, proclamations and/or directives may be issued in the future. As a result, the conduct of our clinical studies with our external partners has been adjusted to institute virtual clinical trial site training and site monitoring, along with partnering with sites to minimize patient visits and institute telemedicine to minimize patient exposure.

While the COVID-19 pandemic did not significantly impact our business or results of operations during the year ended December 31, 2020, the ultimate impact of the COVID-19 pandemic on our operations is unknown and will depend on future developments. Such future events are highly uncertain and cannot be predicted with confidence, including the duration of the COVID-19 outbreak, new information which may emerge concerning the severity of the COVID-19 pandemic, and any additional preventative and protective actions that governments or we may direct, which may result in an extended period of continued business disruption, reduced patient traffic and reduced operations. In particular, the speed of the continued spread of COVID-19 globally, and the magnitude of interventions to contain the spread of the virus, such as government-imposed quarantines, including shelter-in-place mandates, sweeping restrictions on travel, mandatory shutdowns for non-essential businesses, requirements regarding social distancing, and other public health safety measures, will determine the impact of the pandemic on our business. We are continuing to monitor the latest developments regarding the COVID-19 pandemic and its impact on our business, financial condition, results of operations and prospects.

Components of our Results of Operations

Revenue

We have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products in the near future. If our development efforts for ALRN-6924 or other product candidates that we may develop in the future are successful and result in marketing approval or collaboration or license agreements with third parties, we may generate revenue in the future from a combination of product sales or payments from collaboration or license agreements that we may enter into with third parties.

Operating Expenses

Our expenses since inception have consisted solely of research and development costs and general and administrative costs. The ongoing coronavirus pandemic has created substantial uncertainties in the United States and throughout the world, including in the financial markets and in the biopharmaceutical industry. . We are continuing to assess our strategy as the full impact of the coronavirus pandemic is better understood.

In 2021, we raised additional capital through our issuance and sale of shares of common stock in a registered direct public offering on January 8, 2021, from our issuance and sale of shares of common stock in at-market-offerings under Capital on Demand Sales Agreements, and from our issuance and sale of shares of common stock under our common stock purchase agreement with Lincoln Park Capital Fund, LLC. See "Liquidity and Capital Resources. We expect that our operating expenses will increase if and as we use the proceeds of such sales of our common stock to increase our level of clinical development of ALRN-6924 and hire additional personnel to carry out such clinical development.

Research and Development Expenses

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

- expenses incurred under agreements with third parties, including contract research organizations, or CROs, that conduct research, preclinical activities and clinical trials on our behalf as well as contract manufacturing organizations, or CMOs, that manufacture our product candidates for use in our preclinical and clinical trials;
- salaries, benefits and other related costs, including stock-based compensation expense, for personnel engaged in research and development functions;
- costs of outside consultants, including their fees, stock-based compensation and related travel expenses;
- the costs of laboratory supplies and acquiring, developing and manufacturing preclinical study and clinical trial materials;
- third-party license fees;
- costs related to compliance with regulatory requirements; and
- facility-related expenses, which include direct depreciation costs and allocated expenses for rent and maintenance of facilities and other operating costs.

We expense research and development costs as incurred. We recognize costs for certain development activities, such as clinical trials, based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations or information provided to us by our vendors and our clinical investigative sites. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and are reflected in our financial statements as prepaid or accrued research and development expenses.

We typically use our employee and infrastructure resources across our development programs. We track outsourced development costs and milestone payments made under our licensing arrangements by product candidate or development program, but we do not allocate personnel costs, license payments made under our licensing arrangements or other internal costs to specific development programs or product candidates. These costs are included in employee, facility and other development expenses in the table below. Employee, facility and other expenses also includes internal research relating to non-clinical and pipeline compounds in oncology and non-oncology indications.

The following table summarizes our research and development expenses:

	Year Ended December 31,	
	2020	2019
ALRN-6924	$ 7,130	$ 11,284
Other early-stage development programs	18	592
Employee, facility and other development expenses	4,018	5,787
Total research and development expenses	$ 11,166	$ 17,663

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect to incur significant research and development expenses in the foreseeable future as we continue our ongoing clinical trials of ALRN-6924, initiate additional clinical trials of ALRN-6924 and pursue later stages of clinical development of ALRN-6924.

We cannot determine with certainty the duration and costs of the current or future clinical trials of our product candidates or if, when, or to what extent we will generate revenue from the commercialization and sale of any of our product candidates for which we obtain marketing approval. We may never succeed in obtaining marketing approval for any product candidate. The duration, costs and timing of clinical trials and development of ALRN-6924 will depend on a variety of factors, including:

- the scope, rate of progress, expense and results of our ongoing clinical trial of ALRN-6924, as well as of any future clinical trials of ALRN-6924 or other product candidates that we may develop and other research and development activities that we may conduct;
- uncertainties in clinical trial design and patient enrollment rates;
- significant and changing government regulation and regulatory guidance;
- the timing and receipt of any marketing approvals; and
- the expense of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the U.S. Food and Drug Administration, or the FDA, or another regulatory authority were to require us to conduct clinical trials beyond those that we anticipate will be required for the completion of clinical development of a product candidate, or if we experience significant trial delays due to patient enrollment or other reasons, we would be required to expend significant additional financial resources and time on the completion of clinical development.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in our executive, finance and corporate and administrative functions. General and administrative expenses are comprised of professional fees associated with being a public company including costs of accounting, auditing, legal, regulatory, tax and consulting services associated with maintaining compliance with exchange listing and SEC requirements, director and officer insurance costs; and both public and investor relations costs. General and administrative expenses also include legal fees relating to patent and corporate matters; other insurance costs; travel expenses; and facility-related expenses, which include direct depreciation costs and allocated expenses for rent and maintenance of facilities and other operating costs.

Other Income (Expense), net

Other income (expense), net consists of interest income earned on our cash, cash equivalents and investments and other income and expense items that are not classified as operating expenses. Interest expense consists of imputed interest expense related to our construction financing liability associated with the build-out and tenant improvements to our previously leased office and laboratory facility.

Income Taxes

Since our inception in 2001, we have not recorded any U.S. federal or state income tax benefits for the net losses we have incurred in any year or for our earned research and development tax credits, due to our uncertainty of realizing a benefit from those items. As of December 31, 2020, we had federal and state net operating loss carryforwards of $203.5 million and $197.7 million, respectively, which begin to expire in 2029 and 2030, respectively. As of December 31, 2020, we also had federal and state research and development tax credit carryforwards of $2.6 million and $1.8 million, respectively, which begin to expire in 2025. The Company also has federal orphan drug tax credit carryforwards of $1.0 million which begin to expire in 2039.

Utilization of the net operating loss carryforwards and research and development tax credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986 due to ownership changes that have occurred previously or that could occur in the future. These ownership changes may limit the amount of carryforwards that can be utilized annually to offset future taxable income. In general, an ownership change, as defined by Section 382, results from transactions increasing the ownership of certain stockholders or public groups in the stock of a corporation by more than 50% over a three-year period. We have not conducted a study to assess whether a change of control has occurred or whether there have been multiple changes of control since inception due to the significant complexity and cost associated with such a study. If we have experienced a change of control, as defined by Section 382, at any time since inception, utilization of the net operating loss carryforwards or research and development tax credit carryforwards would be subject to an annual limitation under Section 382, which is determined by first multiplying the value of our common stock at the time of the ownership change by the applicable long-term tax-exempt rate, and then could be subject to additional adjustments, as required. Any limitation may result in expiration of a portion of the net operating loss carryforwards or research and development tax credit carryforwards before utilization. Further, until a study is completed and any limitation is known, no amounts are being presented as an uncertain tax position.

Critical Accounting Policies and Use of Estimates

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

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

Accrued Research and Development Expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing open contract and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated costs incurred for the services when we have not yet been invoiced or otherwise notified of the actual costs. The majority of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advanced payments. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. Examples of estimated accrued research and development expenses include fees paid to:

- CROs in connection with performing research activities on our behalf and conducting preclinical studies and clinical trials on our behalf;
- investigative sites or other service providers in connection with clinical trials;
- vendors in connection with preclinical and clinical development activities; and
- vendors related to product manufacturing and development and distribution of preclinical and clinical supplies.

We base our expenses related to preclinical studies and clinical trials on our estimates of the services received and efforts expended pursuant to quotes and contracts with multiple CROs that conduct and manage preclinical studies and clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing fees, we estimate the time period over which services will be performed, enrollment of patients, number of sites activated and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or amount of prepaid expense accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in us reporting amounts that are too high or too low in any particular period. To date, we have not made any material adjustments to our prior estimates of accrued research and development expenses.

Stock-Based Compensation

We measure stock options and other stock-based awards granted to employees and directors based on their fair value on the date of the grant and recognize compensation expense of those awards, net of estimated forfeitures, over the requisite service period, which is generally the vesting period of the respective award. We apply the straight-line method of expense recognition to all awards with only service-based vesting conditions and apply the graded-vesting method to all awards with performance-based vesting conditions or to awards with both service-based and performance-based vesting conditions.

Effective October 1, 2018, we adopted Accounting Standards Update ("ASU") No. 2018-07, Compensation - Stock Compensation (Topic 718): Improvements to Non-employee Share-based Payment Accounting ("ASU 2018-07"), which sets out to simplify the accounting for non-employee share-based awards.

Prior to the adoption of ASU 2018-07 for share-based awards granted to non-employees, including consultants, compensation expense was recognized over the period during which services were rendered by such non-employees until completed. At the end of each financial reporting period prior to completion of the service, the fair value of the unvested awards were remeasured using the then-current fair value of our common stock and updated assumption inputs in the Black-Scholes option-pricing model.

After adoption of ASU 2018-07, the measurement date for non-employee awards is the date of the grant. The compensation expense for awards granted to non-employees is recognized, without changes in the fair value of the award, over the requisite service period, which is the vesting period of the respective award. The compensation expense for awards granted to non-employees was measured as of the adoption date of October 1, 2018, and this amount is the basis for prospective expense recognition.

We estimate the fair value of each stock option grant on the date of grant using the Black-Scholes option-pricing model, which uses as inputs the fair value of our common stock and assumptions we make for the volatility of our common stock, the expected term of our stock options, the risk-free interest rate for a period that approximates the expected term of our stock options and our expected dividend yield.

Emerging Growth Company Status

The Jumpstart Our Business Startups Act of 2012, or the JOBS Act, permits an "emerging growth company" such as us to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have irrevocably elected to "opt out" of this provision and, as a result, we will comply with new or revised accounting standards when they are required to be adopted by public companies that are not emerging growth companies.

Results of Operations

Comparison of the Years Ended December 31, 2020 and 2019

The following table summarizes our results of operations for the years ended December 31, 2020 and 2019:

	Year Ended December 31,		Increase (Decrease)
	2020	2019	
	(in thousands)		
Revenue	$ —	$ —	$ —
Operating expenses:			
Research and development	11,166	17,663	(6,497)
General and administrative	9,330	12,293	(2,963)
Total operating expenses	20,496	29,956	(9,460)
Loss from operations	(20,496)	(29,956)	9,460
Other income (expense), net	(661)	587	(1,248)
Net loss	$ (21,157)	$ (29,369)	$ 8,212

Research and Development Expenses

	Year Ended December 31,		Increase (Decrease)
	2020	2019	
	(in thousands)		
ALRN-6924	$ 7,130	$ 11,284	$ (4,154)
Other early-stage development programs	18	592	(574)
Employee, facility and other development expenses	4,018	5,787	(1,769)
Total research and development expenses	$ 11,166	$ 17,663	$ (6,497)

Research and development expenses for the year ended December 31, 2020 were $11.2 million, compared to $17.7 million for the year ended December 31, 2019. The decrease of $6.5 million was primarily due to a $4.2 million decrease in clinical development cost of ALRN-6924 resulting from the completion of anti-cancer clinical trials in 2019 and early 2020. In addition, employee, facility and other development expenses also decreased by $1.8 million in 2020 compared to 2019. The decrease in employee, facility and other development costs was a result of an early 2020 decision to focus clinical development of ALRN-6924 solely on chemoprotection and as a result we reduced our research and development headcount from seven to five employees.

General and Administrative Expenses

General and administrative expenses were $9.3 million for the year ended December 31, 2020, compared to $12.3 million for the year ended December 31, 2019. The decrease of $3.0 million in general and administrative expense is primarily a result of cost savings initiatives that were implemented in 2019 and in early 2020. The effect of these measures resulted in savings of $1.5 million in headcount related costs, $1.1 million in external spending primarily related to legal expenses and a $0.3 million reduction in stock-based compensation expense.

Other Income (Expense), net

Other expense, net of $0.7 million for the year ended December 31, 2020 consisted of a gain on the sale of fixed assets of $0.1 million and is offset by a non-cash derecognition charge of our former corporate headquarters of $0.8 million. On November 11, 2020, we entered into a lease termination agreement with respect to our former corporate headquarters in Watertown, Massachusetts. In connection with the lease termination we derecognized our right of use assets and operating lease liabilities associated with the lease. The derecognition of these assets and liabilities resulted in a non-cash charge of $0.8 million. We anticipate that our interest income will fluctuate in the future in response to our level of cash, cash equivalents and investments, and then current interest rates.

Other income (expense), net for the year ended December 31, 2019 consisted solely of interest income of $0.6 million.

Liquidity and Capital Resources

Since our inception, we have incurred significant losses on an aggregate basis. We have not yet commercialized any product candidate, including ALRN-6924, which is in clinical development, and we do not expect to generate revenue from sales of any products for several years, if at all. We have financed our operations through sales of common stock in our initial public offering and follow-on public offerings, sales of common stock and warrants in a private placement, sales of common stock in "at-the-market" offerings under the Capital on Demand Sales Agreements, sales of common stock under our equity line with LPC, sales of preferred stock prior to our initial public offering and payments received under a collaboration agreement. As of December 31, 2020, we had cash, cash equivalents and investments of $13.8 million.

Public Offerings

In June 2020, we issued and sold in an underwritten public offering an aggregate of 10,162,059 shares of common stock, including an additional 1,071,149 shares of common stock upon the partial exercise of the option of the underwriter to purchase additional shares of common stock, for a purchase price to the public of $1.10 per share. We received aggregate gross proceeds from the public offering of approximately $11.2 million, before deducting underwriting discounts and commissions and offering expenses of $0.9 million**.**

In January 2021, we issued and sold an aggregate of 32,630,983 shares of common stock in a registered direct offering at a purchase price per share of $1.10. The aggregate gross proceeds of the registered direct offering were $35.9 million, before deducting fees payable to the placement agent and other estimated offering expenses payable by us of approximately $2.8 million.

At-the-Market Offering

In July 2019, we entered into the Sales Agreement with JonesTrading, under which we currently may issue and sell shares of common stock, having an aggregate offering price of up to $15.0 million. Sales of common stock through JonesTrading may be made by any method that is deemed an "at the market" offering as defined in Rule 415(a)(4) under the Securities Act of 1933, as amended. We are not obligated to make any sales of common stock under the Sales Agreement. During the year ended December 31, 2020, we issued and sold an aggregate of 4,160,899 shares of common stock pursuant to the Sales Agreement for gross proceeds of $4.0 million, before deducting commissions and fees. Between January 1, 2021 and January 28, 2021, we sold an additional 7,174,993 shares of common stock pursuant to the Sales Agreement for gross proceeds of $9.7 million, before deducting commissions and fees.

In January 2021, we entered into a Capital on Demand Sales Agreement, or the ATM Sales Agreement, with JonesTrading Institutional Services LLC, or JonesTrading, and William Blair & Company, L.L.C., or William Blair, as agents, under which we may issue and sell shares of common stock, having an aggregate offering price to up to $30.0 million. Sales of common stock through JonesTrading and William Blair may be made by any method that is deemed an "at the market" offering as defined in Rule 415(a)(4) under the Securities Act of 1933, as amended. We are not obligated to make any sales of common stock under the ATM Sales Agreement. Between January 29, 2021 and March 24, 2021, we have issued and sold an aggregate of 5,225,406 shares of common stock pursuant to the ATM Sales Agreement for gross proceeds of $10.6 million, after deducting commissions and fees.

Equity Line Financing

On September 21, 2020, we entered into the Purchase Agreement with Lincoln Park Capital, LLC or LPC for an equity line financing. The Purchase Agreement provides that, subject to the terms and conditions set forth therein, we have the right, but not the obligation, to sell to LPC, and LPC is obligated to purchased up to $15.0 million of shares of common stock at our sole discretion, over a 36-month period that commenced in October 2020. We filed a registration statement on Form S-1 covering the sale of shares of common stock that are issued to LPC under the Purchase Agreement, which was declared effective on October 15, 2020.

Upon entering into the Purchase Agreement, we issued and sold 367,647 shares of common stock, or the Initial Purchase Shares, to LPC at a price per share of $1.36, or $0.5 million, which is part of the $15.0 million of shares of common stock that we may sell to LPC under the Purchase Agreement. Additionally, we issued to LPC as a commitment fee 220,588 shares of common stock as consideration for LPC entering into the Purchase Agreement.

Under the Purchase Agreement, we may, at our discretion, direct LPC to purchase on any single business day, or a Regular Purchase, up to (i) 250,000 shares of common stock if the closing sale price of our common stock is not below $1.50 per share on Nasdaq, (ii) 200,000 shares of common stock if the closing sale price of our common stock is not below $1.00 per share on Nasdaq or (iii) 150,000 shares of common stock if the closing sale price of our common stock is below $1.00 per share on Nasdaq. In any case, LPC's commitment in any single Regular Purchase may not exceed $1,000,000.

The purchase price per share for each such Regular Purchase will be based on prevailing market prices of our common stock immediately preceding the time of sale as computed under the Purchase Agreement. Under the Purchase Agreement, we may not effect any sales of shares of common stock on any purchase date that the closing sale price of our common stock on Nasdaq is less than the floor price of $0.30 per share.

In addition to Regular Purchases, we may also direct LPC to purchase other amounts as accelerated purchases or as additional accelerated purchases on the terms and subject to the conditions set forth in the Purchase Agreement.

The net proceeds under the Purchase Agreement to us will depend on the frequency of sales and the number of shares sold to LPC and prices at which we sell shares to LPC.

The Purchase Agreement contains customary representations, warranties, covenants, indemnification and termination provisions. LPC has covenanted not to cause or engage in any manner whatsoever, any direct or indirect short selling or hedging of our common stock. There are no limitations on use of proceeds, financial or business covenants, restrictions on future financings (other than restrictions on our ability to enter into additional "equity line" or a substantially similar transaction whereby a specific investor is irrevocably bound pursuant to an agreement with us to purchase securities over a period of time from us at a price based on the market price of the common stock at the time of such purchase), rights of first refusal, participation rights, penalties or liquidated damages in the Purchase Agreement. The Purchase Agreement may be terminated by us at any time, at our sole discretion, without any cost or penalty. During any "event of default" under the Purchase Agreement, Lincoln Park does not have the right to terminate the Purchase Agreement; however, we may not initiate any purchase of shares by LPC until such event of default is cured. Through December 31, 2020, we issued and sold an aggregate of 1,417,647 shares of common stock to LPC for gross proceeds of $1,801 million. Between January 1, 2021 and March 24, 2021, we issued and sold an aggregate of 1,375,000 shares of common stock to LPC for gross proceeds of $2.6 million.

Private Placement

On April 2, 2019, we issued and sold in a private placement an aggregate of (i) 11,838,582 units, consisting of 11,838,582 shares of its common stock and associated warrants, or the common warrants, to purchase an aggregate of 11,838,582 shares of common stock, for a combined price of $2.01 per unit and (ii) 1,096,741 units, consisting of (a) pre-funded warrants to purchase 1,096,741 shares of our common stock and (b) associated common warrants to purchase 1,096,741 shares of common stock, for a combined price of $2.01 per unit. The pre-funded warrants had an exercise price of $0.01 per share and had no expiration. The common warrants are exercisable at an exercise price of $2.00 per share and expire five years from the date of issuance. The securities were sold pursuant to a securities purchase agreement entered into with accredited investors on March 28, 2019. We received aggregate gross proceeds from the private placement of approximately $26.0 million before deducting placement agent fees and offering expenses of approximately $2.2 million and excluding the exercise of any warrants. In July 2019, all outstanding pre-funded warrants were exercised for 1,096,741 shares of common stock.

Cash Flows

The following table summarizes our sources and uses of cash for each of the periods presented:

	Year Ended December 31,	
	2020	**2019**
	(in thousands)	
Cash used in operating activities	$ (20,476)	$ (26,474)
Cash (used in) provided by investing activities	6,411	(2,814)
Cash provided by financing activities	15,800	23,964
Net increase (decrease) in cash, cash equivalents and restricted cash	$ 1,735	$ (5,324)

Operating Activities. During the year ended December 31, 2020, operating activities used $20.5 million of cash, primarily resulting from our net loss of $21.2 million and cash provided by the change in operating assets of $1.3 million offset by non-cash charges of $2.0 million. Non-cash charges resulted primarily from stock-based compensation expense. The derecognition of our right-to-use lease assets and operating lease liabilities resulted in operating cash flow usage of $0.8 million. Changes in our operating assets and liabilities during 2020 consisted primarily of a decrease of $1.7 million in accrued expenses and other current liabilities and an increase of $0.7 million in prepaid expense and other assets.

During the year ended December 31, 2019, operating activities used $26.5 million of cash, primarily resulting from our net loss of $29.4 million and cash provided by the change in operating assets of $0.9 million offset by non-cash charges of $2.1 million. Non-cash charges resulted primarily from stock-based compensation expense. Net cash provided by changes in our operating assets and liabilities during the year ended December 31, 2019 consisted primarily of an increase of $0.4 million in accrued expenses and other current liabilities as well as a decrease of $1.3 million in other assets. The increase in accrued expenses and other current liabilities was primarily due to a decrease in payroll-related accruals.

Investing Activities. During the year ended December 31, 2020, investing activities provided $6.4 million of cash. We received $16.2 million of proceeds from the sale of investments and $0.2 million from the sale of property and equipment offset by $10.0 million of purchases of investments.

During the year ended December 31, 2019, investing activities used $2.8 million of cash. We received $24.6 million of proceeds from the sale of investments offset by $27.2 million of purchases of investments and $0.2 million of purchases of property and equipment.

Financing Activities. During the year ended December 31, 2020, net cash provided by financing activities was $15.8 million due to the proceeds received from the sale of common stock in our public offering in June 2020, sales under our Sales Agreement with JonesTrading, funds received from sales of common stock to LPC during 2020 and proceeds from the Paycheck Protection Program Loan of $0.4 million.

During the year ended December 31, 2019, net cash provided by financing activities was $24.0 million due to the proceeds received from the sale of common stock, common warrants and pre-funded warrants in our April 2019 private placement and due to the proceeds from option exercises.

Funding Requirements

We expect our expenses to increase substantially in connection with our ongoing development activities related to ALRN-6924, which is still in clinical development, and any other product candidates and programs that we may pursue in the future. We expect that our expenses will increase substantially if and as we:

- conduct our current, planned and future clinical trials of ALRN-6924;
- initiate and resume research and preclinical and clinical development of any other product candidates that we may develop;
- seek to identify additional product candidates;
- seek marketing approvals for any product candidate that successfully completes clinical trials, if any;
- require the manufacture of larger quantities of our product candidates for clinical development and potentially commercialization;
- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
- maintain, expand and protect our intellectual property portfolio;
- acquire or in-license other drugs and technologies;
- hire and retain additional clinical, quality control and scientific personnel;
- build out new facilities or expand existing facilities to support our ongoing development activity; and
- add operational, financial and management information systems and personnel, including personnel to support our drug development, any future commercialization efforts and our compliance with our obligations as a public company.

We believe that, based on our current operating plan, our cash, cash equivalents and investments of $13.8 million as of December 31, 2020, together with the net proceeds of approximately $33.1 million from our issuance and sale of shares of common stock in a registered direct public offering on January 8, 2021,net proceeds of approximately $20.0 million from our issuance and sale of shares of common stock in at-market-offerings under Capital on Demand Sales Agreements between January 1, 2021 and the date of this Annual Report on Form 10-K, and net proceeds of approximately $2.6 million from our issuance and sale of shares of common stock from our common stock purchase agreement with Lincoln Park Capital Fund, LLC between January 1, 2021 and the date of this Annual Report on Form 10-K, will enable us to fund our operating expenses into the second half of 2023. Our funding estimates are based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate. In any event, our cash, cash equivalents and investments will not be sufficient to fund all of the efforts that we plan to undertake or to fund the completion of development or commercialization of ALRN-6924. Our future viability is dependent on our ability to raise additional capital to finance our operations.

Accordingly, we will be required to obtain further funding through public or private equity offerings, collaborations and licensing arrangements, or other sources of capital. Adequate additional financing may not be available to us on acceptable terms, if at all. In addition, while we may seek one or more collaborators for future development of ALRN-6924 or other product candidates that we may develop, we may not be able to enter into a collaboration for ALRN-6924 or other product candidates that we may develop on suitable terms, on a timely basis or at all.

Because of the numerous risks and uncertainties associated with the development of ALRN-6924 and other product candidates that we may develop and programs we may pursue, and because the extent to which we may enter into collaborations with third parties for development of our product candidates is unknown, we are unable to estimate the timing and amounts of increased capital outlays and operating expenses associated with completing the research and development of ALRN-6924 or other product candidates that we may develop. Our future capital requirements will depend on many factors, including:

- the scope, progress, results and costs of our ongoing, planned and future clinical trials of ALRN-6924;
- the impact of the COVID-19 pandemic on our business and operations;
- the scope, progress, results and costs of drug discovery, preclinical research and clinical trials for any other product candidates that we may develop;
- the number of future product candidates that we pursue and their development requirements;
- the costs, timing and outcome of regulatory review of our product candidates;
- our ability to establish and maintain collaborations on favorable terms, if at all;
- the success of any collaborations that we may enter into with third parties;
- the extent to which we acquire or invest in businesses, products and technologies, including entering into licensing or collaboration arrangements for product candidates, although we currently have no commitments or agreements to complete any such transactions;
- the costs and timing of future commercialization activities, including drug sales, marketing, manufacturing and distribution, for any product candidate for which we receive marketing approval, to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of any collaborator that we may have at such time;
- the amount of revenue, if any, received from commercial sales of our product candidates, should any product candidate receive marketing approval;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- our headcount growth and associated costs, as we expand our business operations and our research and development activities; and
- the costs of operating as a public company.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval for any product candidates or generate revenue from the sale of any products for which we may obtain marketing approval. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of drugs that we do not expect to be commercially available for many years, if ever. Accordingly, we will need to obtain substantial additional funds to achieve our business objectives.

Adequate additional funds may not be available to us on acceptable terms, or at all. Other than the Purchase Agreement with LPC, which is subject to certain limitations and conditions, we do not currently have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our common stockholders may be diluted, and the terms of these securities may include liquidation or other preferences and anti-dilution protections that could adversely affect the rights of our common stockholders. Additional debt or preferred equity financing, if available, may involve agreements that include restrictive covenants that may limit our ability to take specific actions, such as incurring debt, making capital expenditures or declaring dividends, which could adversely impact our ability to conduct our business.

If we raise additional funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technology, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or collaborations, strategic alliances or licensing arrangements with third parties when needed, we may be required to delay, limit, reduce and/or terminate our product development programs or any future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations and Commitments

We are a smaller reporting company, as defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended, for this reporting period and are not required to provide the information required under this item.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined in the rules and regulations of the SEC.

Recently Issued Accounting Pronouncements

We have reviewed all recently issued standards and have determined that, other than as disclosed in Note 2 to our financial statements appearing at the end of this Annual Report on Form 10-K, such standards will not have a material impact on our financial statements or do not otherwise apply to our operations.

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

We are a smaller reporting company, as defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended, for this reporting period and are not required to provide the information required under this item.

Item 8. Financial Statements and Supplementary Data.

The financial statements required to be filed pursuant to this Item 8 are appended to this Annual Report on Form 10-K. An index of those financial statements is found in Item 15 of Part IV of this Annual Report on Form 10-K.

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

None

Item 9A. Controls and Procedures.

Limitations on Effectiveness of Controls and Procedures

The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, refers to controls and procedures that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure.

In designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated, as of the end of the period covered by this Annual Report on Form 10-K, the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act of 1934). Based on that evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2020.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) promulgated under the Exchange Act as a process designed by, or under the supervision of, the company's principal executive and principal financial officers and effected by the company's board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that:

- Pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets of the company;
- Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and
- Provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. 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.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2020. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in *Internal Control—Integrated Framework* (2013 framework)

(COSO). Based on its assessment, management believes that, as of December 31, 2020, our internal control over financial reporting is effective at the reasonable assurance level.

Changes in Internal Control Over Financial Reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) has occurred during the quarter ended December 31, 2020 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this Item 10 will be included under the captions “Executive Officers,” “Election of Directors” and “Delinquent Section 16(a) Reports” in our definitive proxy statement to be filed with the Securities and Exchange Commission, or SEC, with respect to our 2021 Annual Meeting of Stockholders, which is expected to be filed no later than 120 days after the end of our last fiscal year ended December 31, 2020 and is incorporated herein by reference.

We have adopted a Code of Business Conduct and Ethics that applies to our officers, including our principal executive, financial and accounting officers, and our directors and employees. We have posted the text of our Code of Business Conduct and Ethics under the “Investors & Media — Corporate Governance” section of our website, *www.aileronrx.com*. We intend to disclose on our website any amendments to, or waivers from, the Code of Business Conduct and Ethics that are required to be disclosed pursuant to the disclosure requirements of Item 5.05 of Form 8-K.

Item 11. Executive Compensation.

The information required by this Item 11 will be included under the captions “Executive and Director Compensation” and “Compensation Committee Interlocks and Insider Participation” in our definitive proxy statement to be filed with the SEC with respect to our 2021 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this Item 12 will be included under the captions “Security Ownership of Certain Beneficial Owners and Management” and “Securities Authorized for Issuance Under Equity Compensation Plans” in our definitive proxy statement to be filed with the SEC with respect to our 2021Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this Item 13 will be included, as applicable, under the captions “Employment Agreements,” “Director Independence” and “Related Person Transactions” in our definitive proxy statement to be filed with the SEC with respect to our 2021 Annual Meeting of Stockholders and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

The information required by this Item 14 will be included under the captions “Audit Fees and Services” and “Pre-Approval Policies and Procedures” in our definitive proxy statement to be filed with the SEC with respect to our 2021 Annual Meeting of Stockholders and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

The following documents are filed as part of this Report:

(a) *Financial Statements*. The following documents are included in Part II, Item 8 of this Report and are incorporated by reference herein:

INDEX TO FINANCIAL STATEMENTS

c(b) *Financial Statement Schedules*. Schedules have been omitted since they are either not required or not applicable or the information is otherwise included herein.

(c) *Exhibits*.

Exhibit Number	Description	Incorporation by Reference			Filed Herewith
		Form	Date of Filing	Exhibit Number	
3.1	Restated Certificate of Incorporation of the Registrant	8-K	7/5/2017	3.1	
3.2	Amended and Restated By-laws of the Registrant	8-K	7/5/2017	3.2	
4.1	Specimen stock certificate evidencing shares of common stock	S-1^	6/19/2017	4.1	
4.2	Description of Securities of the Registrant	10-K	3/30/2020	4.3	
10.1*	2006 Stock Incentive Plan, as amended	S-1^	6/2/2017	10.1	
10.2*	Form of Incentive Stock Option Agreement under 2006 Stock Incentive Plan	S-1^	6/2/2017	10.2	
10.3*	Form of Nonstatutory Stock Option Agreement under 2006 Stock Incentive Plan	S-1^	6/2/2017	10.3	
10.4*	2016 Stock Incentive Plan	S-1^	6/2/2017	10.4	
10.5*	Form of Incentive Stock Option Agreement under 2016 Stock Incentive Plan	S-1^	6/2/2017	10.5	
10.6*	Form of Nonstatutory Stock Option Agreement under 2016 Stock Incentive Plan	S-1^	6/2/2017	10.6	
10.7*	2017 Stock Incentive Plan	S-1^	6/19/2017	10.8	
10.8*	Form of Incentive Stock Option Agreement under 2017 Stock Incentive Plan	S-1^	6/19/2017	10.9	
10.9*	Form of Nonstatutory Stock Option Agreement under 2017 Stock Incentive Plan	S-1^	6/19/2017	10.10	
10.10*	2017 Employee Stock Purchase Plan	S-1^	6/19/2017	10.11	
10.11	Form of Director and Officer Indemnification Agreement	S-1^	6/19/2017	10.12	
10.12+	License Agreement, dated as of December 31, 2006, by and between the Registrant and Materia, Inc. (now Umicore Precious Metals Chemistry USA, LLC)	S-1^	6/2/2017	10.13	
10.13+	Amended and Restated License Agreement, dated as of February 19, 2010, by and among the Registrant, President and Fellows of Harvard College and Dana-Farber Cancer Institute, Inc.	S-1^	6/19/2017	10.14	
10.14*	Amended and Restated Employment Agreement, dated as of September 6, 2018, between the Registrant and Manuel C. Alves Aivado, M.D., Ph.D.	10-Q	11/7/2018	10.2	

10.15*	Severance Agreement, dated as of September 6, 2018, between the Registrant and Manuel C. Alves Aivado, M.D., Ph.D.	10-Q	11/7/2018	10.3	
10.16*	Offer Letter and Severance Agreement, dated as of November 1, 2018, between the Registrant and Vojislav Vukovic, M.D., Ph.D.	10-K	3/29/2019	10.20	
10.17*	Offer Letter, dated as of November 15, 2007, between the Registrant and D. Allen Annis, Ph.D.	10-K	3/29/2019	10.21	
10.18*	Severance Agreement, dated as of November 5, 2018, between the Registrant and D. Allen Annis, Ph.D.	10-K	3/29/2019	10.22	
10.19*	Offer Letter, dated as of June 7, 2018, between the Registrant and Richard Wanstall.	10-K	3/20/2020	10.26	
10.20*	Severance Agreement, dated as of December 12, 2019, between the Registrant and Richard Wanstall.	10-K	3/20/2020	10.27	
10.21	Securities Purchase Agreement, dated March 28, 2019, by and among the Registrant and the persons party thereto	8-K	4/1/2019	10.1	
10.22	Registration Rights Agreement, dated March 28, 2019, by and among the Registrant and the persons party thereto	8-K	4/1/2019	10.4	
10.23	Form of Warrant to Purchase Common Stock	8-K	4/1/2019	10.3	
10.24	Purchase Agreement, dated as of September 21, 2020, by and between the Company and Lincoln Park Capital Fund, LLC	8-K	9/22/2020	10.1	
10.25	Registration Rights Agreement, dated as of September 21, 2020, by and between the Company and Lincoln Park Capital Fund, LLC	8-K	9/22/2020	10.2	
10.26	Capital on Demand™ Sales Agreement, dated January 29, 2021, by and among Aileron Therapeutics, Inc. and JonesTrading Institutional Services LLC and William Blair & Company, L.L.C.	8-K	1/29/2021	1.1	
23.1	Consent of PricewaterhouseCoopers LLP, independent registered public accounting firm.				X
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				X
31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				X
32.1	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				X

32.2	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	X
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 Label Linkbase Document	
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document	
*	Indicates management contract or compensatory plan.	
+	Confidential treatment has been requested and/or granted as to certain portions, which portions have been omitted and filed separately with the U.S. Securities and Exchange Commission.	
^	SEC File No. 333-218474	

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

Aileron Therapeutics, Inc.

Date: March 24, 2021

By: /s/ Manuel C. Alves Aivado, M.D., Ph.D.

Manuel C. Alves Aivado, M.D., Ph.D.
President and Chief Executive Officer
(principal executive officer)

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

Name	Title	Date
/s/ Manuel C. Alves Aivado, M.D., Ph.D. **Manuel C. Alves Aivado, M.D., Ph.D.**	President, Chief Executive Officer and Director (principal executive officer)	March 24, 2021
/s/ Richard J. Wanstall **Richard J. Wanstall**	Chief Financial Officer & Treasurer (principal financial officer)	March 24, 2021
/s/ Jeffrey A. Bailey **Jeffrey A. Bailey**	Chairman of the Board of Directors	March 24, 2021
/s/ Reinhard J. Ambros, Ph.D. **Reinhard J. Ambros, Ph.D.**	Director	March 24, 2021
/s/ William T. McKee **William T. McKee**	Director	March 24, 2021
/s/ Jodie P. Morrison **Jodie P. Morrison**	Director	March 24, 2021
/s/ Nolan Sigal, M.D., Ph.D. **Nolan Sigal, M.D., Ph.D.**	Director	March 24, 2021
/s/ Joseph H. Von Rickenbach **Joseph H. Von Rickenbach**	Director	March 24, 2021

Report of Independent Registered Public Accounting Firm

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

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Aileron Therapeutics, Inc. (the “Company”) as of December 31, 2020 and 2019, and the related statements of operations and comprehensive loss, of stockholders’ equity (deficit) and of cash flows for the years then ended, including 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, 2020 and 2019, and the results of its operations and its cash flows for the years then ended in conformity with accounting principles generally accepted in the United States of America.

Change in Accounting Principle

As discussed in Note 2 to the consolidated financial statements, the Company changed the manner in which it accounts for leases in 2019.

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

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

/s/ PricewaterhouseCoopers LLP
Boston, Massachusetts
March 24, 2021
We have served as the Company's auditor since 2009.

AILERON THERAPEUTICS, INC.
BALANCE SHEETS

(In thousands, except share and per share data)

	December 31, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 7,046	$ 5,311
Investments	6,759	12,967
Prepaid expenses and other current assets	1,928	1,247
Restricted cash	593	25
Total current assets	16,326	19,550
Operating lease, right-of-use asset	—	6,060
Property and equipment, net	15	295
Restricted cash, non-current	—	568
Total assets	$ 16,341	$ 26,473
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 1,596	$ 1,452
Accrued expenses and other current liabilities	2,196	3,941
Paycheck Protection Program loan, current portion	168	—
Operating lease liabilities, current portion	—	446
Total current liabilities	3,960	5,839
Paycheck Protection Program loan, net of current portion	219	—
Operating lease liabilities, net of current portion	—	4,586
Total liabilities	4,179	10,425
Commitments and contingencies (Note 9)		
Stockholders' equity:		
Preferred stock, $0.001 par value; 5,000,000 shares authorized at December 31, 2020 and December 31, 2019; no shares issued and outstanding at December 31, 2020 and December 31, 2019	—	—
Common stock, $0.001 par value; 150,000,000 shares authorized at December 31, 2020 and December 31, 2019; 43,804,175 and 27,810,358 shares issued and outstanding at December 31, 2020 and December 31, 2019, respectively	44	28
Additional paid-in capital	231,412	214,148
Accumulated other comprehensive income/(loss)	(2)	7
Accumulated deficit	(219,292)	(198,135)
Total stockholders' equity	12,162	16,048
Total liabilities and stockholders' equity	$ 16,341	$ 26,473

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

AILERON THERAPEUTICS, INC.
STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(In thousands, except share and per share data)

	Year Ended December 31,	
	2020	2019
Revenue	$ —	$ —
Operating expenses:		
Research and development	11,166	17,663
General and administrative	9,330	12,293
Total operating expenses	20,496	29,956
Loss from operations	(20,496)	(29,956)
Other income (expense), net	(661)	587
Net loss	$ (21,157)	$ (29,369)
Net loss per share—basic and diluted	$ (0.61)	$ (1.20)
Weighted average common shares outstanding—basic and diluted	34,866,690	24,535,454
Comprehensive loss:		
Net loss	$ (21,157)	$ (29,369)
Other comprehensive gain (loss):		
Unrealized gain (loss) on investments, net of tax of $0	(9)	12
Total other comprehensive gain (loss)	(9)	12
Total comprehensive loss	$ (21,166)	$ (29,357)

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

AILERON THERAPEUTICS, INC.
STATEMENT OF STOCKHOLDERS' EQUITY (DEFICIT)

(In thousands, except share data)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income/(Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Par Value				
Balances at December 31, 2018	14,748,475	$ 15	$ 188,083	$ (5)	$ (168,493)	$ 19,600
Exercise of stock options	126,560	—	165	—	—	165
Sale of common stock and common warrants	11,838,582	12	23,784	—	—	23,796
Sale of pre-funded warrants and common warrants	1,096,741	1	2,202	—	—	2,203
Exercise of pre-funded warrants	—	—	11	—	—	11
Issuance costs	—	—	(2,213)	—	—	(2,213)
Stock-based compensation expense	—	—	2,116	—	—	2,116
Adoption of ASC 842, Leases	—	—	—	—	(273)	(273)
Unrealized gain on investments	—	—	—	12	—	12
Net loss	—	—	—	—	(29,369)	(29,369)
Balances at December 31, 2019	27,810,358	$ 28	$ 214,148	$ 7	$ (198,135)	$ 16,048
Issuance of common stock	15,961,193	16	16,881	—	—	16,897
Issuance costs	—	—	(1,494)	—	—	(1,494)
Stock-based compensation expense	—	—	1,893	—	—	1,893
RSUs vested, net of shares repurchased for tax	32,624	—	(16)	—	—	(16)
Unrealized loss on investments	—	—	—	(9)	—	(9)
Net loss	—	—	—	—	(21,157)	(21,157)
Balances at December 31, 2020	43,804,175	$ 44	$ 231,412	$ (2)	$ (219,292)	$ 12,162

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

AILERON THERAPEUTICS, INC.
STATEMENTS OF CASH FLOWS

(In thousands)

	Year Ended December 31,	
	2020	**2019**
Cash flows from operating activities:		
Net loss	$ (21,157)	$ (29,369)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization expense	163	155
Net amortization of premiums and discounts on investments	(9)	(231)
Stock-based compensation expense	1,893	2,116
(Gain)/loss on disposition of property and equipment	(86)	5
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(682)	(206)
Other assets	6,060	1,318
Accounts payable	116	(277)
Operating lease liabilities	(5,033)	(370)
Accrued expenses and other current liabilities	(1,741)	385
Net cash used in operating activities	(20,476)	(26,474)
Cash flows from investing activities:		
Purchases of investments	(10,034)	(27,237)
Proceeds from sales or maturities of investments	16,242	24,574
Purchases of property and equipment	(5)	(151)
Proceeds from sale of fixed asset	208	—
Net cash (used in) provided by investing activities	6,411	(2,814)
Cash flows from financing activities:		
Proceeds from issuance of common stock, common warrants and pre-funded warrants, net of issuance costs	15,413	23,799
Proceeds from Paycheck Protection Program Loan	387	—
Proceeds from exercise of stock options	—	165
Net cash provided by financing activities	15,800	23,964
Net Increase (decrease) in cash, cash equivalents and restricted cash	1,735	(5,324)
Cash, cash equivalents and restricted cash at beginning of period	5,904	11,228
Cash, cash equivalents and restricted cash at end of period	$ 7,639	$ 5,904
Cash and cash equivalents, end of year	$ 7,046	$ 5,311
Restricted cash, end of year	593	593
Cash and cash equivalents and restricted cash, end of year	$ 7,639	$ 5,904

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

1. Nature of the Business and Basis of Presentation

Aileron Therapeutics, Inc. ("Aileron" or the "Company") is a clinical stage biopharmaceutical company that is focused on transforming the experience of chemotherapy for cancer patients, enabling them to fight cancer without the fear or burden of chemotherapy-induced side effects. ALRN-6924, the Company's first-in-class MDM2/MDMX dual inhibitor activating p53, is the only reported therapeutic agent in clinical development to employ a biomarker strategy, in which the Company exclusively focuses on treating patients with p53-mutated cancers. With this targeted strategy of treating patients with p53-mutated cancers, ALRN-6924 is designed to protect multiple healthy cell types throughout the body from chemotherapy while chemotherapy continues to kill cancer cells. In addition to potentially reducing or eliminating multiple side effects, ALRN-6924 may also improve patients' quality of life and help them better tolerate chemotherapy, potentially allowing patients to complete their treatment without dose reductions or delays. The Company's long-term vision is to provide chemoprotection for patients with p53-mutated cancers, which represents approximately 50% of cancer patients, regardless of cancer type or chemotherapeutic drug.

The Company is subject to risks common to companies in the biotechnology industry, including but not limited to, new technological innovations, protection of proprietary technology, dependence on key personnel, compliance with government regulations, uncertainties in the clinical development of product candidates and in the ability to obtain needed additional financing. ALRN-6924 will require significant additional research and development efforts, including preclinical and clinical testing and regulatory approval prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel infrastructure and extensive compliance-reporting capabilities.

The Company's product candidates are in development. There can be no assurance that the Company's research and development will be successfully completed, that adequate protection for the Company's intellectual property will be obtained, that any products developed will obtain necessary governmental regulatory approval or that any approved products will be commercially viable. Even if the Company's drug development efforts are successful, it is uncertain when, if ever, the Company will generate significant revenue from product sales. The Company operates in an environment of rapid change in technology and substantial competition from pharmaceutical and biotechnology companies. In addition, the Company is dependent upon the services of its key employees and consultants.

The accompanying financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP").

Liquidity

In accordance with Accounting Standards Update ("ASU") No. 2014-15, *Disclosures of Uncertainties about an Entity's Ability to Continue as a Going Concern* (Subtopic 205-40), management must evaluate whether there are conditions or events, considered in the aggregate, that raise substantial doubt about the company's ability to continue as a going concern within one year after the date that the financial statements are issued. This evaluation initially does not take into consideration the potential mitigating effect of management's plans that have not been fully implemented as of the date the financial statements are issued. When substantial doubt exists under this methodology, management evaluates whether the mitigating effect of its plans sufficiently alleviates substantial doubt about the company's ability to continue as a going concern. The mitigating effect of management's plans, however, is only considered if both (1) it is probable that the plans will be effectively implemented within one year after the date that the financial statements are issued, and (2) it is probable that the plans, when implemented, will mitigate the relevant conditions or events that raise substantial doubt about the entity's ability to continue as a going concern within one year after the date that the financial statements are issued. Generally, to be considered probable of being effectively implemented, the plans must have been approved before the date that the financial statements are issued.

The Company's financial statements have been prepared on a going concern basis, which contemplates the continuity of operations, realization of assets and the satisfaction of liabilities in the ordinary course of business. Through December 31, 2020, the Company has financed operations primary through $50,009 in net proceeds from its initial public offering, or IPO, $10,246 in net proceeds from a public offering in June 2020, $3,918 in net proceeds from "at the market" offerings, $1,801 in in net proceeds from sales pursuant to an equity line financing, $23,825 in net proceeds from a private placement in April 2019, $131,211 from sales of preferred stock prior to its IPO, $552 from the exercise of stock options and $34,910 from a collaboration agreement.

As of December 31, 2020, the Company had cash, cash equivalents and investments of $13,805. The Company has incurred losses and negative cash flows from operations and had an accumulated deficit of $219,292 as of December 31, 2020. The Company expects to continue to generate losses for the foreseeable future.

The Company believes that, based on its current operating plan, its cash, cash equivalents and investments of $13,805 as of December 31, 2020, together with the net proceeds of approximately $33,091 from the issuance and sale of shares of common stock in a registered direct public offering on January 8, 2021, net proceeds of approximately $19,962 from the issuance and sale of shares of common stock in at-market-offerings under its Capital on Demand Sales Agreements between January 1, 2021 and the date of this Annual Report on Form 10-K, and net proceeds of approximately $2,614 from the issuance and sale of shares of common stock from its common stock purchase agreement with Lincoln Park Capital Fund, LLC between January 1, 2021 and the date of issuance of these financial statements, will enable the Company to fund its operating expenses for more than twelve months from the date of issuance of these financial statements.

To execute its business plans, the Company will need substantial funding to support its continuing operations and pursue its growth strategy. Until such time as the Company can generate significant revenue from product sales, if ever, it expects to finance its operations through the sale of common stock in public offering and/or private placements, through debt financings or from other capital sources, including collaborations with other companies or other strategic transactions. The Company may not be able to obtain financing on acceptable terms or at all. The terms of any financing may adversely affect the holdings or the rights of the Company's stockholders. If the Company is unable to obtain funding, the Company could be forced to delay, reduce or eliminate some or all of its research and development programs, product portfolio expansion plans or commercialization efforts, which could adversely affect its business prospects. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenue and expenses during the reporting periods. Significant estimates and assumptions reflected in these financial statements include, but are not limited to, the accrual of research and development expenses and the valuation of common stock and stock-based awards. Estimates are periodically reviewed in light of changes in circumstances, facts and experience. Actual results could differ from the Company's estimates.

Cash Equivalents

The Company considers all short-term, highly liquid investments with original maturities of 90 days or less at acquisition date to be cash equivalents. Cash equivalents, which consist of money market accounts, corporate notes and commercial paper are stated at fair value.

Restricted Cash

As of December 31, 2020, current restricted cash of $593 consisted of cash deposited in separate restricted bank accounts as a security deposits for the lease of the Company's facility in Watertown, Massachusetts (see Note 12) and for the Company's corporate credit cards. As of December 31, 2019, current restricted cash consisted of $25 of cash deposited in a separate restricted bank account as a security deposit for the Company's corporate credit cards. As of December 31, 2019, non-current restricted cash consisted of $568 of cash deposited in a separate restricted bank account as a security deposit for the lease of the Company's facility in Watertown, Massachusetts (see Note 12).

Investments

The Company classifies its available-for-sale debt security investments as current assets on the balance sheet if they mature within one year from the balance sheet date.

The Company classifies all of its investments as available-for-sale securities. The Company's investments are measured and reported at fair value using quoted prices in active markets for similar securities or using other inputs that are observable or can be corroborated by observable market data. Unrealized gains and losses on available-for-sale securities are reported as accumulated other comprehensive income (loss), which is a separate component of stockholders' equity (deficit). The cost of securities sold is determined on a specific identification basis, and realized gains and losses are included in other income (expense) within the statements of operations and comprehensive loss.

The Company evaluates its investments with unrealized losses for other-than-temporary impairment. When assessing investments for other-than-temporary declines in value, the Company considers such factors as, among other things, how significant the decline in value is as a percentage of the original cost, how long the market value of the investment has been less than its original cost, the Company's ability and intent to retain the investment for a period of time sufficient to allow for any anticipated recovery in fair value and market conditions in general. If any adjustment to fair value reflects a decline in the value of the investment that the Company considers to be "other than temporary", the Company reduces the investment to fair value through a charge to the statements of operations and comprehensive loss. No such adjustments were necessary during the periods presented.

Concentration of Credit Risk and of Significant Suppliers

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash, cash equivalents and investments. From time to time, the Company has maintained all of its cash, cash equivalents and investment balances at three accredited financial institutions, in amounts that exceed federally insured limits. The Company generally invests its excess cash in money market funds, commercial paper and corporate notes that are subject to minimal credit and market risks. Management has established guidelines relative to credit ratings and maturities intended to safeguard principal balances and maintain liquidity. The investment portfolio is maintained in accordance with the Company's investment policy, which defines allowable investments, specifies credit quality standards and limits the credit exposure of any single issuer.

The Company is dependent on third-party manufacturers to supply products for research and development activities of its programs, including preclinical and clinical testing. In particular, the Company relies and expects to continue to rely on a small number of manufacturers to supply it with its requirements for the active pharmaceutical ingredients and formulated drugs related to these programs. These programs could be adversely affected by a significant interruption in the supply of active pharmaceutical ingredients and formulated drugs.

Fair Value Measurements

Certain assets and liabilities are carried at fair value under GAAP. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable.

- Level 1—Quoted prices in active markets for identical assets or liabilities.
- Level 2—Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.
- Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

The Company's cash equivalents and investments are carried at fair value, determined according to the fair value hierarchy described above (see Note 3). The carrying values of the Company's accounts payable and accrued expenses approximate their fair value due to the short-term nature of these liabilities.

Deferred Offering Costs

The Company capitalizes certain legal, professional accounting and other third-party fees that are directly associated with in-process equity financings as deferred offering costs until such financings are consummated. After consummation of the equity financing, these costs are recorded in stockholders' equity (deficit) as a reduction of additional paid-in capital generated as a result of the offering. Should the planned equity financing be abandoned, the deferred offering costs would be expensed immediately as a charge to operating expenses in the statement of operations and comprehensive loss. During the year ended December 31, 2020, the Company received aggregate gross proceeds from the sale of common stock of approximately $16,881 before deducting placement agent fees and offering expenses of approximately $1,494. During the year ended December 31, 2019, the Company received aggregate gross proceeds from the private placement of approximately $26.0 million before deducting placement agent fees and offering expenses of approximately $2.2 million and excluding the exercise of any warrants.

Property and Equipment

Property and equipment are stated at cost less accumulated depreciation and amortization. Depreciation and amortization expense is recognized using the straight-line method over the following estimated useful lives:

Laboratory equipment	5 years
Computer equipment and software	3 to 5 years
Furniture and fixtures	7 years
Building	30 years
Leasehold improvements	Shorter of 7 years or term of lease

Expenditures for repairs and maintenance of assets are charged to expense as incurred. Upon retirement or sale, the cost and related accumulated depreciation and amortization of assets disposed of are removed from the accounts and any resulting gain or loss is included in the statements of operations and comprehensive loss.

Impairment of Long-Lived Assets

Long-lived assets consist of property and equipment. Long-lived assets to be held and used are tested for recoverability whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends and significant changes or planned changes in the use of the assets. If an impairment review is performed to evaluate a long-lived asset for recoverability, the Company compares forecasts of undiscounted cash flows expected to result from the use and eventual disposition of the long-lived asset to its carrying value. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of an asset are less than its carrying amount. The impairment loss would be based on the excess of the carrying value of the impaired asset over its fair value, determined based on discounted cash flows. To date, the Company has not recorded any impairment losses on long-lived assets.

Research and Development Costs

Research and development expenditures are expensed as incurred. Research and development expenses are comprised of salaries, stock-based compensation and benefits of employees, third-party license fees and other operational costs related to the Company's research and development activities, including allocated facility-related expenses and external costs of outside vendors engaged to conduct both preclinical studies and clinical trials.

Research Contract Costs and Accruals

The Company has entered into various research and development contracts with research institutions and other companies. These agreements are cancelable, and related payments are recorded as research and development expenses as incurred. The Company records accruals for estimated ongoing research costs. This process involves reviewing open contracts and purchase orders, communicating with personnel to identify services that have been performed and estimating level of service performed and the associated costs incurred for the services for which the Company has not yet been invoiced. Significant judgment and estimates are made in determining the accrued balances at the end of any reporting period. Actual results could differ from the Company's estimates. The Company's historical accrual estimates have not been materially different from the actual costs.

Patent Costs

All patent-related costs incurred in connection with filing and prosecuting patent applications are expensed as incurred due to the uncertainty about the recovery of the expenditure. Amounts incurred are classified as general and administrative expenses.

Accounting for Stock-Based Compensation

The Company measures all stock options and other stock-based awards granted to employees and directors based on the fair value on the date of the grant and recognizes compensation expense of those awards, net of estimated forfeitures, over the requisite service period, which is generally the vesting period of the respective award. The Company applies the straight-line method of expense recognition to all awards with only service-based vesting conditions and applies the graded vesting method to all awards with performance-based vesting conditions or both service-based and performance-based vesting conditions.

The Company recognizes compensation expense for only the portion of awards that are expected to vest. In developing a forfeiture rate estimate, the Company has considered its historical experience to estimate pre-vesting forfeitures for awards with service-based vesting conditions. The impact of a forfeiture rate adjustment will be recognized in full in the period of adjustment, and if the actual forfeiture rate is materially different from the Company's estimate, the Company may be required to record adjustments to stock-based compensation expense in future periods.

The Company classifies share-based compensation expense in its statement of operations and comprehensive loss in the same manner in which the award recipient's payroll costs are classified or in which the award recipient's service payments are classified.

The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model. The Company historically has been a private company and lacks company-specific historical and implied volatility information. Therefore, it estimates its expected stock volatility based on the historical volatility of a publicly traded set of peer companies and expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded stock price. For options with service-based vesting conditions, the expected term of the Company's stock options has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. The expected term of stock options granted to non-employees is equal to the contractual term of the option award. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that the Company has never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future.

Income Taxes

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the financial statements or in the Company's tax returns. Deferred taxes are determined based on the difference between the financial statement and tax basis of assets and liabilities using enacted tax rates in effect in the years in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of the deferred tax assets will not be realized, a valuation allowance is established through a charge to income tax expense. Potential for recovery of deferred tax assets is evaluated by estimating the future taxable profits expected and considering prudent and feasible tax planning strategies.

The Company accounts for uncertainty in income taxes recognized in the financial statements by applying a two-step process to determine the amount of tax benefit to be recognized. First, the tax position must be evaluated to determine the likelihood that it will be sustained upon external examination by the taxing authorities. If the tax position is deemed more-likely-than-not to be sustained, the tax position is then assessed to determine the amount of benefit to recognize in the financial statements. The amount of the benefit that may be recognized is the largest amount that has a greater than 50% likelihood of being realized upon ultimate settlement. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate as well as the related net interest and penalties.

Segment Data

The Company manages its operations as a single segment for the purposes of assessing performance and making operating decisions. The Company's singular focus is on developing a novel class of therapeutics for the treatment of cancer and other diseases. All of the Company's tangible assets are held in the United States.

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in stockholders' equity (deficit) that result from transactions and economic events other than those with stockholders. The Company's only element of other comprehensive loss in all periods presented was unrealized gains (losses) on available-for-sale investments.

Net Income (Loss) per Share

The Company follows the two-class method when computing net income (loss) per share as the Company has issued shares that meet the definition of participating securities. The two-class method determines net income (loss) per share for each class of common and participating securities according to dividends declared or accumulated and

participation rights in undistributed earnings. The two-class method requires income available to common stockholders for the period to be allocated between common and participating securities based upon their respective rights to receive dividends as if all income for the period had been distributed.

Basic net income (loss) per share attributable to common stockholders is computed by dividing the net income (loss) attributable to common stockholders by the weighted average number of shares of common stock outstanding for the period. Diluted net income (loss) attributable to common stockholders is computed by adjusting income (loss) per share attributable to common stockholders to reallocate undistributed earnings based on the potential impact of dilutive securities. Diluted net income (loss) per share attributable to common stockholders is computed by dividing the diluted net income (loss) attributable to common stockholders by the weighted average number of shares of common stock outstanding for the period, including potential dilutive common shares. For purpose of this calculation, outstanding options to purchase common stock and shares of redeemable convertible preferred stock are considered potential dilutive common shares.

The Company's redeemable convertible preferred stock contractually entitled the holders of such shares to participate in dividends but contractually did not require the holders of such stock to participate in losses of the Company. Accordingly, in periods in which the Company reports a net loss attributable to common stockholders, diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders, since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive.

Risks and Uncertainties

In December 2019, an outbreak of respiratory illness caused by a strain of novel coronavirus, COVID-19, began in China. That outbreak has led to millions of confirmed cases worldwide, including in the United States and other countries where the Company is conducting clinical trials or activities in support thereof. The World Health Organization declared the outbreak a global pandemic on March 11, 2020. Recently, new variants of the virus that causes COVID-19 have been identified and are spreading around the world, which may worsen or prolong the outbreak. In addition to those who have been directly affected, millions more have been affected by governmental efforts around the world to slow the spread of the outbreak. The outbreak and government measures taken in response have also had a significant impact, both direct and indirect, on businesses and commerce. The future progression of the outbreak and its effects on our business and operations are uncertain.

Potential impacts to the Company's business include disruptions in supply of the Company's product candidate and/or procuring items that are essential for the Company's research and development activities, including, for example, raw materials used in the manufacturing of ALRN-6924, medical and laboratory supplies used in the Company's clinical trials or preclinical studies or animals that are used for preclinical testing, in each case, for which there may be shortages because of ongoing efforts to address the COVID-19 pandemic. While the Company believes that it currently has sufficient supply of its product candidate to continue the Company's ongoing and planned clinical trials, its product candidate, or materials contained therein, come from facilities located in areas impacted by the COVID-19 pandemic.

Additionally, the Company has enrolled, and is seeking to enroll, cancer patients in the Company's clinical trials at sites located both in the United States and Europe, which are areas that continue to be impacted by the COVID-19 pandemic. Enrollment at clinical trial sites may be disrupted as the effects of the COVID-19 pandemic persist. In the event that clinical trial sites close to enrollment in the Company's trials or shift resources to address COVID-19, this could have a material adverse impact on the Company's clinical trial plans and timelines. The Company may face difficulties recruiting or retaining patients in its ongoing and planned clinical trials if patients are affected by the virus or are fearful of visiting or traveling to our clinical trial sites because of the COVID-19 pandemic.

Any negative impact that the COVID-19 outbreak has on the ability of the Company's suppliers to provide materials necessary for the Company's product candidate or on recruiting or retaining patients in the Company's clinical trials could cause costly delays to clinical trial activities, which could adversely affect the Company's ability to obtain regulatory approval for and to commercialize the Company's product candidate, increase the Company's operating expenses, affect the Company's ability to raise additional capital, and impact the Company's operating

and financial results. The capital markets have also experienced significant volatility as a result of the pandemic. Future disruptions in the capital markets could negatively impact the Company's ability to raise capital in the future.

Recently Accounting Pronouncements

In December 2019, the FASB issued ASU 2019-12, *Income Taxes*, or ASC 740, which simplifies the accounting for income taxes. The ASU will be effective for the Company in the first quarter of fiscal 2021, with early adoption permitted. The Company is currently evaluating the impact of the adoption of ASU 2019-12 and does not expect adoption to have a material effect on the Company's consolidated financial statements or disclosures.

In February 2016, the FASB issued ASU No. 2016-02, *Leases*, ("ASU 2016-02"), which sets out the principles for the recognition, measurement, presentation and disclosure of leases for both parties to a contract (i.e. lessees or lessors). The new standard requires lessees to apply a dual approach, classifying leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight-line basis over the term of the lease, respectively. A lessee is also required to record a right-of-use asset and a lease liability for all leases with a term of greater than 12 months, regardless of their classification. Leases with a term of 12 months or less will be accounted for similar to existing guidance for operating leases today. ASU 2016-02 (Accounting Standards Codification ("ASC") Topic 842) supersedes the previous leases standard, ASC 840, *Leases*. The standard is effective for public entities for annual periods beginning after December 15, 2018 and for interim periods within those fiscal years.

The Company adopted the standard effective January 1, 2019. It has implemented the standard using the required modified retrospective approach and has also elected to utilize the package of practical expedients. The expedients used by the Company are as follows: (1) allowing an entity to not reassess the lease classification for any expired or existing leases, (2) allowing an entity to not reassess the treatment of initial direct costs as they related to existing leases, and (3) allowing an entity to not reassess whether expired or existing contracts are or contain leases. The Company elected to adopt the standard at the beginning of the period of adoption.

As a result of the adoption of ASU 2016-02, the Company de-recognized $7,079 of the building asset and $81 of accumulated depreciation related to its former corporate headquarters at 490 Arsenal Way. Prior to the adoption of ASU 2016-02, the Company classified facility improvements associated with the 490 Arsenal Way building as a component of its building asset. Subsequent to the adoption of ASU 2016-02, these improvements were reclassified to leasehold improvements.

Other accounting standards that have been issued or proposed by the FASB or other standards-setting bodies that do not require adoption until a future date are not expected to have a material impact on the Company's financial statements upon adoption.

3. Fair Value of Financial Assets

The following tables present information about the Company's assets that are measured at fair value on a recurring basis and indicate the level of the fair value hierarchy utilized to determine such fair values:

	Fair Value Measurements as of December 31, 2020 using:			
	Level 1	**Level 2**	**Level 3**	**Total**
Cash equivalents:				
Money market funds	$ 4,190	$ —	$ —	$ 4,190
Corporate notes	—	—	—	—
Commercial paper	—	1,001	—	1,001
Investments:				
Corporate notes	—	—	—	—
Treasury bills		1,249		1,249
Agency bonds		3,511		3,511
Commercial paper	—	1,999	—	1,999
	$ 4,190	$ 7,760	$ —	$ 11,950

	Fair Value Measurements as of December 31, 2019 using:			
	Level 1	Level 2	Level 3	Total
Cash equivalents:				
Money market funds	$ 4,208	$—	$—	$ 4,208
Corporate notes	—	—	—	—
Commercial paper	—	—	—	—
Investments:				
Corporate notes	—	5,491	—	5,491
Commercial paper	—	7,476	—	7,476
	$ 4,208	$ 12,967	$—	$ 17,175

As of December 31, 2020 and 2019, the Company's cash equivalents and investments were invested in money market funds, corporate notes and commercial paper and were valued based on Level 1 and Level 2 inputs. In determining the fair value of its corporate notes and commercial paper at each date presented above, the Company relied on quoted prices for similar securities in active markets or using other inputs that are observable or can be corroborated by observable market data. The Company's cash equivalents have original maturities of less than 90 days from the date of purchase. All available-for-sale investments have contractual maturities of less than one year. During the years ended December 31, 2020 and 2019, there were no transfers between Level 1, Level 2 and Level 3.

4. Investments

As of December 31, 2020 and 2019, the fair value of available-for-sale investments by type of security was as follows:

	December 31, 2020			
	Amortized Cost	**Gross Unrealized Gain**	**Gross Unrealized Loss**	**Fair Value**
Investments:				
Corporate notes	$ —	$ —	$ —	$ —
Treasury bills	1,249	—	—	1,249
Agency Bonds	3,511	—	—	3,511
Commercial paper	1,999	—	—	1,999
	$ 6,759	$ —	$ —	$ 6,759

	December 31, 2019			
	Amortized Cost	Gross Unrealized Gain	Gross Unrealized Loss	Fair Value
Investments:				
Corporate notes	$ 5,489	$ 2	$ —	$ 5,491
Commercial paper	7,470	6	—	7,476
	$ 12,959	$ 8	$ —	$ 12,967

5. Property and Equipment, Net

Property and equipment, net consisted of the following:

	December 31,	
	2020	2019
Laboratory equipment	$ -	$ 451
Computer equipment and software	181	177
Furniture and fixtures	-	189
	181	817
Less: Accumulated depreciation and amortization	(166)	(522)
	$ 15	$ 295

Depreciation and amortization expense for the years ended December 31, 2020 and 2019 was $163 and $140, respectively. During the year ended December 31, 2020, assets with a cost of $640 were disposed of for $208 in proceeds, resulting in a gain on sale of $86. During the year ended December 31, 2019, assets with a cost of $749 were disposed of for no proceeds, resulting in a loss on disposal of $5.

6. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following:

	December 31, 2020	December 31, 2019
External research and development services	$ 896	$ 1,673
Payroll and payroll-related costs	922	1,281
Professional fees	135	635
Other	243	352
	$ 2,196	$ 3,941

7. Paycheck Protection Loan

On April 30, 2020, the Company received loan proceeds in the amount of approximately $384 under the Paycheck Protection Program (“PPP”). The PPP, established as part of the Coronavirus Aid, Relief and Economic Security Act (“CARES Act”), provides for loans to qualifying businesses for amounts up to 2.5 times of the average monthly payroll expenses of the qualifying business. The loan and accrued interest are forgivable after eight weeks if the borrower uses the loan proceeds for eligible purposes, including payroll, benefits, rent and utilities. The amount of loan forgiveness may be reduced if the borrower terminates employees or reduces salaries during the eight-week period. The unforgiven portion of the PPP loan is payable over two years at an interest rate of 1%, with a deferral of payments for the first six months. The Company used the proceeds for purposes consistent with the PPP.

The Company has determined to account for the PPP loan as debt under Accounting Standards Update (“ASC 470”), “Debt”, and has allocated and recorded the loan proceeds between current and non-current liabilities.

The Company further determined that loan forgiveness would become probable of occurring upon acceptance by the Small Business Association of the Company's forgiveness application. If and when the loan forgiveness becomes probable, the Company will recognize income for debt extinguishment pursuant to ASC 470-50-15-4. The Company submitted a loan forgiveness application in December 2020.

8. Preferred Stock

On July 5, 2017, in connection with the closing of the Company's IPO, the Company filed its amended and restated certificate of incorporation, which authorizes the Company to issue up to 5,000,000 shares of preferred stock, $0.001 par value per share. As of December 31, 2020 and 2019, the Company had no shares of preferred stock issued or outstanding.

9. Common Stock

On July 5, 2017, the Company filed the amended and restated certificate of incorporation which increased the authorized number of shares of common stock from 143,500,000 shares of $0.001 par value common stock to 150,000,000 shares of common stock.

Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders. Common stockholders are entitled to receive dividends, as may be declared by the Company's board of directors, if any, subject to the preferential dividend rights of the preferred stock. As of December 31, 2020 and 2019, no dividends had been declared.

As of December 31, 2020, the Company had reserved 5,098,505 shares for the exercise of outstanding stock options and grant of future awards under the Company's stock incentive plans (see Note 10).

10. Stock-Based Awards

2017 Stock Incentive Plan

The Company's 2017 Stock Incentive Plan (the "2017 Plan") was approved by the Company's stockholders on June 16, 2017 and became effective on June 28, 2017. Under the 2017 Plan, the Company may grant incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock awards, awards of restricted stock units and other stock-based awards. The Company's employees, officers, directors, consultants and advisors are eligible to receive awards under the 2017 Plan; however, incentive stock options may only be granted to employees. The 2017 Plan is administered by the board of directors or, at the discretion of the board of directors, by a committee of the board. The number of shares of common stock covered by options and the date those options become exercisable, type of options to be granted, exercise prices, vesting and other restrictions are determined at the discretion of the board of directors, or its committee if so delegated.

Stock options granted under the 2017 Plan with service-based vesting conditions generally vest over four years and may not have a duration in excess of ten years, although options have been granted with vesting terms of less than four years.

The total number of shares of common stock that may be issued under the 2017 Plan was 4,701,056 as of December 31, 2020, of which 382,919 shares remained available for grant. The Company initially reserved 1,244,816 shares of common stock plus the number of shares equal to the sum of the number of shares of common stock then available for issuance under the 2016 Plan, which was 424,601 shares, and the number of shares of common stock subject to outstanding awards under the 2006 Plan and the 2016 Plan that expire, terminate or are otherwise surrendered, canceled, forfeited or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right. The number of shares of common stock that may be issued under the 2017 Plan will automatically increase on January 1 of each year, beginning with the fiscal year ending December 31, 2018 and continuing for each fiscal year until, and including, the fiscal year ending December 31, 2027, equal to the least of (i) 1,244,816 shares of common stock, (ii) 4% of the outstanding shares of common stock on such date and (iii) an amount determined by the Company's board of directors. For the year ended December 31, 2020, the Company's compensation committee of the board of directors authorized an additional 1,112,414 shares that may be issued under the 2017 Plan.

During the year ended December 31, 2020, pursuant to the terms of the 2017 Plan, the Company granted options to employees and directors to purchase 1,821,000 shares of common stock at a weighted average exercise price of $0.76 per share.

Shares that are expired, terminated, surrendered or canceled without having been fully exercised will be available for future awards. In addition, shares of common stock that are tendered to the Company by a participant to exercise an award are added to the number of shares of common stock available for the grant of awards.

The exercise price for stock options granted may not be less than the fair market value of the common stock as of the date of grant.

2017 Employee Stock Purchase Plan

On June 16, 2017, the Company's stockholders approved the 2017 Employee Stock Purchase Plan (the "2017 ESPP"), which became effective on June 28, 2017. As of December 31, 2019, a total of 150,000 shares of common stock are reserved for issuance under the 2017 ESPP. The number of shares of common stock that may be issued under the 2017 ESPP automatically increase on each January 1 and continuing for each fiscal year until, and including, the fiscal year ending December 31, 2027, equal to the least of (i) 622,408 shares, (ii) 1% of the outstanding shares of common stock on such date and (iii) an amount determined by the Company's board of directors. The board of directors has not initiated any offerings under the ESPP.

2016 Stock Incentive Plan

The Company's 2016 Stock Incentive Plan (the "2016 Plan") provided for the Company to grant incentive stock options or nonqualified stock options, restricted stock, restricted stock units and other equity awards to employees, directors and consultants of the Company. The 2016 Plan was administered by the board of directors or, at the discretion of the board of directors, by a committee of the board. The exercise prices, vesting and other restrictions were determined at the discretion of the board of directors, or its committee if so delegated.

Stock options granted under the 2016 Plan with service-based vesting conditions vest over four years and expire after ten years.

After the effective date of the 2017 Plan, no stock options or other awards were made under the 2016 Plan. No shares remained available for future issuance as of December 31, 2017.

Shares that are expired, terminated, surrendered or canceled without having been fully exercised will be available for future awards under the 2017 Plan. In addition, shares of common stock that are tendered to the Company by a participant to exercise an award are added to the number of shares of common stock available for the grant of awards under the 2017 Plan.

2006 Stock Incentive Plan

The Company's 2006 Stock Incentive Plan, as amended, (the "2006 Plan") provided for the Company to grant incentive stock options or nonqualified stock options, restricted stock, restricted stock units and other equity awards to employees, directors and consultants of the Company. The 2006 Plan was administered by the board of directors or, at the discretion of the board of directors, by a committee of the board. The exercise prices, vesting and other restrictions were determined at the discretion of the board of directors, or its committee if so delegated.

Stock options granted under the 2006 Plan with service-based vesting conditions generally vest over four years and expire after ten years, although options have been granted with vesting terms of less than four years.

The 2006 Plan expired in 2016. No shares remained available for future issuance as of December 31, 2016.

Shares that are expired, terminated, surrendered or canceled without having been fully exercised will be available for future awards under the 2017 Plan. In addition, shares of common stock that are tendered to the

Company by a participant to exercise an award are added to the number of shares of common stock available for the grant of awards under the 2017 Plan.

Stock Option Valuation

The assumptions that the Company used to determine the grant-date fair value of the stock options granted to employees and directors during the year ended December 31, 2020 and 2019 were as follows, presented on a weighted average basis:

	Year Ended December 31,	
	2020	2019
Risk-free interest rate	1.17%	2.35%
Expected term (in years)	6.2	6.2
Expected volatility	76.0%	76.0%
Expected dividend yield	0%	0%

Stock Options

The following table summarizes the Company's stock option activity since January 1, 2020:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value
Outstanding at December 31, 2019	3,320,706	$ 3.87	7.4	$ —
Granted	1,821,000	0.76		
Exercised	—	0.00		
Canceled	(463,119)	6.59		
Forfeited	(13,001)	2.54		
Outstanding at December 31, 2020	4,665,586	$ 2.39	8.1	$ 622
Options exercisable at December 31, 2020	2,377,533	$ 3.28	7.6	$ 197
Options vested and expected to vest at December 31, 2020	4,592,729	$ 2.41	8.1	$ 606
Options exercisable at December 31, 2019	1,415,900	$ 5.56	5.2	$ —
Options vested and expected to vest at December 31, 2019	3,264,851	$ 3.89	7.4	$ —

The weighted average grant-date fair value of stock options granted during the year ended December 31, 2020 and 2019 was $0.51 and $1.11, respectively.

The aggregate fair value of stock options that vested during the year ended December 31, 2020 and 2019 was $2,099 and $2,236, respectively.

The aggregate intrinsic value of stock options is calculated as the difference between the exercise price of the stock options and the fair value of the Company's common stock for those stock options that had exercise prices lower than the fair value of the Company's common stock. The aggregate intrinsic value of stock options exercised during the year ended December 31, 2020 and 2019 was $0 and $109, respectively.

Restricted Stock Units

On April 15, 2019, the Company granted restricted stock units under the 2017 Stock Incentive Plan. The following table summarizes the Company's restricted stock unit activity during the year ended December 31, 2020:

	Units	Weighted-Average Grant Date per Unit
Outstanding, non-vested at December 31, 2019	50,000	$ 1.75
Issued	—	—
Vested	(50,000)	$ 1.75
Canceled/forfeited	—	—
Outstanding, non-vested at December 31, 2020	—	—

Stock-Based Compensation

The Company recorded stock-based compensation expense related to stock options in the following expense categories of its statements of operations and comprehensive loss:

	Year Ended December 31,	
	2020	2019
Research and development expenses	$ 572	$ 524
General and administrative expenses	1,321	1,592
	$ 1,893	$ 2,116

The Company used an estimated forfeiture rate of 2.43% to calculate its stock compensation expense for each of the years ended December 31, 2020 and 2019.

As of December 31, 2020, the Company had an aggregate of $2,144 of unrecognized stock-based compensation expense, which it expects to recognize over a weighted average period of 2.14 years.

11. Net Loss per Share

Basic and diluted net loss per share attributable to common stockholders was calculated as follows**:**

	Year Ended December 31,	
	2020	2019
Numerator:		
Net loss	$ (21,157)	$ (29,369)
Denominator:		
Weighted average common shares outstanding—basic and diluted	34,866,690	24,535,454
Net loss per share attributable to common stockholders—basic and diluted	$ (0.61)	$ (1.20)

The Company's potential dilutive securities, which include stock options as of December 31, 2020 and 2019, have been excluded from the computation of diluted net loss per share attributable to common stockholders whenever the effect of including them would be to reduce the net loss per share. In periods where there is a net loss, the weighted average number of shares of common stock outstanding used to calculate both basic and diluted net loss per share attributable to common stockholders is the same. The following potential shares of common stock, presented based on amounts

outstanding at each period end, were excluded from the calculation of diluted net loss per share attributable to common stockholders for the periods indicated because including them would have had an anti-dilutive effect:

	Year Ended December 31,	
	2020	2019
Warrants to purchase common stock	12,935,323	12,935,323
Stock options to purchase common stock	4,665,586	3,320,706
Restricted stock units to purchase common stock	—	50,000
Total	17,600,909	16,306,029

12. Commitments and Contingencies

Operating Leases

490 Arsenal Way

On April 4, 2018, the Company entered into a lease agreement for office and laboratory space located in a building (the "Building") at 490 Arsenal Way, Watertown, Massachusetts (the "490 Arsenal Way Lease"). Under the terms of the 490 Arsenal Way Lease, starting on August 21, 2018, the Company leases approximately 18,768 square feet of office and laboratory space at $52.55 per square foot per year, or $986 per year in base rent, which is subject to scheduled annual rent increases plus certain operating expenses and taxes. The Company currently maintains a $568 security deposit related to the 490 Arsenal Way Lease. Pursuant to the 490 Arsenal Way Lease, the landlord contributed an aggregate of $2,419 toward the cost of construction and tenant improvements for the Building.

The Company occupied the Building from August 21, 2018 through November 11, 2020 when the 490 Arsenal Way Lease was terminated. The Company accounted for this lease under ASC 842 using its initial eight-year term through August 31, 2026.

As part of its adoption of ASC 842, the Company de-recognized the building asset and corresponding financing obligation recorded on the Company's consolidated balance sheets as of January 1, 2019, in accordance with the ASC 842 transition guidance. In applying the ASC 842 transition guidance, the Company classified this lease as an operating lease and recorded a right-of-use asset of $6,697 and lease liability of $5,401 on the effective date. The Company recognizes rent expense on a straight-line basis throughout the remaining term of the lease.

On November 11, 2020, the Company entered into a lease termination agreement with respect to its former corporate headquarters at 490 Arsenal Way, Watertown, Massachusetts. In connection with the lease termination the right of use assets and operating lease liabilities associated with the lease were derecognized. The derecognition of these assets and liabilities resulted in a charge of $823.

Summary of all lease costs recognized under ASC 842

The following table contains a summary of the lease costs recognized under ASC 842 and other information pertaining to the Company's operating leases for the year ended December 31, 2020:

	Twelve Months Ended December 31, 2020
Lease cost (1)	
Operating lease cost	$ 1,095
Total lease cost	$ 1,095
Other Information	
Cash paid for amounts included in the measurement of lease liabilities	$ 884
Weighted average remaining lease term (in years)	—
Weighted average discount rate	—

(1) Short-term lease costs and variable lease costs incurred by the Company for the twelve months ended December 31, 2020 were not material.

As of December 31, 2020, there were no future minimum commitments under ASC 842 under the Company's operating leases.

Intellectual Property Licenses

Harvard and Dana-Farber Agreement

In August 2006, the Company entered into an exclusive license agreement with President and Fellows of Harvard College ("Harvard") and Dana-Farber Cancer Institute ("DFCI"). The agreement granted the Company an exclusive worldwide license, with the right to sublicense, under specified patents and patent applications to develop, obtain regulatory approval for and commercialize specified product candidates based on cell-permeating peptides. Under the agreement, the Company is obligated to use commercially reasonable efforts to develop and commercialize one or more licensed products and to achieve specified milestone events by specified dates. In connection with entering into the agreement, the Company paid an upfront license fee and issued to Harvard and DFCI shares of its common stock.

In February 2010, the agreement was amended and restated (the "Harvard/DFCI agreement") under which additional patent rights were added to the scope of the license agreement and the annual license maintenance fees were increased. Under the Harvard/DFCI agreement, the Company is obligated to make aggregate milestones payments of up to $7,700 per licensed therapeutic product upon the Company's achievement of specified clinical, regulatory and sales milestones with respect to such product and up to $700 per licensed diagnostic product upon the Company's achievement of specified regulatory and sales milestones with respect to such product. In addition, the Company is obligated to pay royalties of low single-digit percentages on annual net sales of licensed products sold by the Company, its affiliates or its sublicensees. The royalties are payable on a product-by-product and country-by-country basis and may be reduced in specified circumstances. In addition, the agreement obligates the Company to pay a percentage, up to the mid-twenties, of fees received by the Company in connection with its sublicense of the licensed products. In accordance with the terms of the agreement, the Company's sublicense payment obligations may be subject to specified reductions.

The Harvard/DFCI agreement requires the Company to pay annual license maintenance fees of $145 each year. Any payments made in connection with the annual license maintenance fees will be credited against any royalties due.

The Company incurred license fees of $145 during each of the years ended December 31, 2020 and 2019. In addition, the Company did not make any milestone payments during the years ended December 31, 2020 and 2019. During the years ended December 31, 2019, no milestones were achieved and no liabilities for milestone payments were recorded in the Company's financial statements. From 2010 through December 31, 2020 and December 31,

2019, the Company had made non-refundable cash payments, consisting of license and maintenance fees, milestone payments and sublicense fees, totaling $4,863 and $4,718, respectively.

As of December 31, 2020, the Company had not developed a commercial product using the licensed technologies and no royalties under the agreement had been paid or were due.

Under the Harvard/DFCI agreement, the Company is responsible for all patent expenses related to the prosecution and maintenance of the licensed patents and applications in-licensed under the agreement as well as cost reimbursement of amounts incurred for all documented patent-related expenses. The agreement will expire on a product-by-product and country-by-country basis upon the last to expire of any valid patent claim pertaining to licensed products covered under the agreement.

Umicore Agreement

In December 2006, the Company entered into a license agreement with Materia, Inc. ("Materia"), under which it was granted a non-exclusive worldwide license, with the right to sublicense, under specified patent and patent applications to utilize Materia's catalysts to develop, obtain regulatory approval for and commercialize specified peptides owned or controlled by Materia and the right to manufacture specified compositions owned or controlled by Materia. In February 2017, Materia assigned the license agreement (the "Umicore agreement") to Umicore Precious Metals Chemistry USA, LLC ("Umicore"), and Umicore agreed to continue to supply the Company under the agreement.

Under the Umicore agreement, the Company is obligated to make aggregate milestone payments to Umicore of up to $6,400 upon the Company's achievement of specified clinical, regulatory and sales milestones with respect to each licensed product. In addition, the Company is obligated to pay tiered royalties ranging in the low single-digit percentages on annual net sales of licensed products sold by the Company or its sublicensees. The royalties are payable on a product-by-product and country-by-country basis, and may be reduced in specified circumstances.

The Umicore agreement requires the Company to pay annual license fees of $50. The Company incurred license fees of $50 during each of the years ended December 31, 2020 and 2019. The Company did not make any milestone payments during the years ended December 31, 2020 or 2019. During the year ended December 31, 2020, no milestones were achieved and no liabilities for additional milestone payments were recorded in the Company's financial statements.

The agreement expires upon the expiration of the Company's obligation to pay royalties in each territory covered under the agreement.

Indemnification Agreements

In the ordinary course of business, the Company may provide indemnification of varying scope and terms to vendors, lessors, business partners and other parties with respect to certain matters including, but not limited to, losses arising out of breach of such agreements or from intellectual property infringement claims made by third parties. In addition, the Company has entered into indemnification agreements with members of its board of directors and officers that will require the Company, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors or officers. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is, in many cases, unlimited. To date, the Company has not incurred any material costs as a result of such indemnifications. The Company does not believe that the outcome of any claims under indemnification arrangements will have a material effect on its financial position, results of operations or cash flows, and it had not accrued any liabilities related to such obligations in its financial statements as of December 31, 2020 or December 31, 2019.

13. Income Taxes

There is no provision for income taxes because the Company has historically incurred operating losses and maintains a full valuation allowance against its net deferred tax assets. The reported amount of income tax expense

for the years differs from the amount that would result from applying domestic federal statutory tax rates to pretax losses primarily because of changes in valuation allowance.

On March 27, 2020, the previous U.S. President signed into law the Coronavirus Aid, Relief, and Economic Security Act (the CARES Act) in response to the U.S. COVID-19 pandemic, which, among other things, suspends the 80% limitation on the deduction for NOLs in taxable years beginning before January 1, 2021, permits a 5-year carryback of NOLs arising in taxable years beginning after December 31, 2017 and before January 1, 2021, and generally caps the limitation on the deduction for net interest expense at 50% of adjusted taxable income for taxable years beginning in 2019 and 2020. In addition, the CARES Act raises the corporate charitable deduction limit to 25% of taxable income and makes qualified improvement property generally eligible for 15-year cost-recovery and 100% bonus depreciation. The enactment of the CARES Act did not result in any material adjustments to the Company's income tax provision for the year ended December 31, 2020, or to its net deferred tax assets and related allowances as of December 31, 2020.

A reconciliation of the U.S. federal statutory income tax rate to the Company’s effective income tax rate is as follows:

	Year Ended December 31,	
	2020	2019
Federal statutory income tax rate	(21.0)%	(21.0)%
State taxes, net of federal benefit	(5.9)	(5.0)
Research and development tax credits	(2.6)	(3.0)
Other permanent items	0.6	0.6
Change in deferred tax asset valuation allowance	28.9	28.4
Effective income tax rate	—%	—%

Net deferred tax assets as of December 31, 2020 and 2019 consisted of the following:

	December 31,	
	2020	2019
Deferred tax assets:		
Net operating loss carryforwards	$ 55,229	$ 50,240
Research and development tax credit carryforwards	4,979	4,449
Capitalized research and development expenses	57	63
Accrued expenses and reserves	265	312
Depreciation and amortization	462	435
Lease Liability	—	1,368
Stock compensation	940	605
Total deferred tax assets	61,932	57,472
Valuation allowance	(61,932)	(55,825)
Net deferred tax assets	$ —	$ 1,647
Deferred Tax Liabilities:		
Right of Use Asset	$ —	$ (1,647)
Total Deferred Tax Liabilities	$ —	$ (1,647)
Net Deferred Tax Asset (Liability)	$ —	$ —

Since inception in 2001, the Company has not recorded any U.S. federal or state income tax benefits for the net losses the Company has incurred in any year or for its earned research and development tax credits, due to its uncertainty of realizing a benefit from those items. As of December 31, 2020, the Company had net operating loss carryforwards for federal and state purposes of $203,505 and $197,672, respectively. $129,596 of the U.S. federal tax operating loss carryforwards will begin to expire in 2029. Approximately $73,909 of the U.S. federal tax operating losses can be carried forward indefinitely. The state tax operating loss carryforwards expire beginning in 2030. As of December 31, 2020, the Company also had available research and development tax credit carryforwards for federal and state income tax purposes of $2,630 and $1,766, respectively, which begin to expire in 2025. As of December 31, 2020, the Company also had available orphan drug credit carryforwards of $954 for federal income tax purposes, which begin to expire in 2039.

Utilization of the net operating loss carryforwards and research and development tax credit carryforwards may be subject to a substantial annual limitation under Section 382 of the Internal Revenue Code of 1986 due to ownership changes that have occurred previously or that could occur in the future. These ownership changes may limit the amount of carryforwards that can be utilized annually to offset future taxable income. In general, an ownership change, as defined by Section 382, results from transactions increasing the ownership of certain shareholders or public groups in the stock of a corporation by more than 50% over a three-year period. The Company has not conducted a study to assess whether a change of control has occurred or whether there have been multiple changes of control since inception due to the significant complexity and cost associated with such a study. If the Company has experienced a change of control, as defined by Section 382, at any time since inception, utilization of the net operating loss carryforwards or research and development tax credit carryforwards would be subject to an annual limitation under Section 382, which is determined by first multiplying the value of the Company's stock at the time of the ownership change by the applicable long-term tax-exempt rate, and then could be subject to additional adjustments, as required. Any limitation may result in expiration of a portion of the net operating loss carryforwards or research and development tax credit carryforwards before utilization. Further, until a study is completed and any limitation is known, no amounts are being presented as an uncertain tax position.

The Company has evaluated the positive and negative evidence bearing upon its ability to realize the deferred tax assets. Management has considered the Company's cumulative net losses and its lack of commercialization of any products or generation of any revenue from product sales since inception and has concluded that it is more likely than not that the Company will not realize the benefits of the deferred tax assets. Accordingly, a full valuation allowance has been established against the net deferred tax assets as of December 31, 2020 and 2019. Management reevaluates the positive and negative evidence at each reporting period. The increase in the valuation allowance for deferred tax assets during the years ended December 31, 2020 and 2019 related primarily to the increase in net operating loss carryforwards. Changes in the valuation allowance were as follows:

	Year Ended December 31,	
	2020	2019
Valuation allowance at beginning of year	$ (55,825)	$ (47,399)
Increases recorded to income tax provision	(6,107)	(8,426)
Valuation allowance at end of year	$ (61,932)	$ (55,825)

The Company has not recorded any amounts for unrecognized tax benefits as of December 31, 2020 or 2019.

The Company files tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In the normal course of business, the Company is subject to examination by federal and state jurisdictions, where applicable. There are currently no pending tax examinations. The Company's tax years are still open under statute from 2017 to the present. Earlier years may be examined to the extent that tax credit or net operating loss carryforwards are used in future periods. The Company's policy is to record interest and penalties related to income taxes as part of its income tax provision. As of December 31, 2020 and 2019, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Company's statements of operations and comprehensive loss.

14. 401(k) Plan

The Company has a 401(k) plan available for participating employees who meet certain eligibility requirements. Eligible employees may defer a portion of their salary as defined by the plan. Company contributions to the plan may be made at the discretion of the Company's board of directors. The Company has not elected to make any employer contributions for the years ended December 31, 2020 or 2019.

15. Selected Quarterly Financial Data (unaudited)

The following table contains selected quarterly financial information for 2020 and 2019. The Company believes that the following information reflects all normal recurring adjustments necessary for a fair statement of the information for the periods presented. The operating results for any quarter are not necessarily indicative of results for any future period.

	Three Months Ended			
	March 31, 2020	June 30, 2020	September 30, 2020	December 31, 2020
Revenue	$ —	$ —	$ —	$ —
Operating expenses:				
Research and development	4,069	2,488	2,684	1,925
General and administrative	2,807	1,912	2,344	2,267
Total operating expenses	6,876	4,400	5,028	4,192
Loss from operations	(6,876)	(4,400)	(5,028)	(4,192)
Other income (expense), net	62	10	5	(738)
Net loss	(6,814)	(4,390)	(5,023)	(4,930)
Net loss per share—basic and diluted	$ (0.24)	$ (0.14)	$ (0.13)	$ (0.12)
Weighted average common shares outstanding—basic and diluted	27,810,358	31,221,139	39,321,177	40,997,759
Comprehensive loss:				
Net loss	$ (6,814)	$ (4,390)	$ (5,023)	$ (4,930)
Other comprehensive gain (loss):				
Unrealized gain (loss) on investments, net of tax of $0	(8)	(1)	1	(1)
Total other comprehensive gain (loss)	(8)	(1)	1	(1)
Total comprehensive loss	$ (6,822)	$ (4,391)	$ (5,022)	$ (4,931)

	Three Months Ended			
	March 31, 2019	June 30, 2019	September 30, 2019	December 31, 2019
Revenue	$ —	$ —	$ —	$ —
Operating expenses:				
Research and development	4,174	4,305	4,475	4,709
General and administrative	3,139	3,075	3,440	2,639
Total operating expenses	7,313	7,380	7,915	7,348
Loss from operations	(7,313)	(7,380)	(7,915)	(7,348)
Other income (expense), net	101	208	166	112
Net loss	(7,212)	(7,172)	(7,749)	(7,236)
Net loss per share attributable to common stockholders—basic and diluted	$ (0.49)	$ (0.26)	$ (0.28)	$ (0.26)
Weighted average common shares outstanding—basic and diluted	14,816,253	27,526,065	27,810,358	27,810,358
Comprehensive loss:				
Net loss	$ (7,212)	$ (7,172)	$ (7,749)	$ (7,236)
Other comprehensive loss:				
Unrealized loss on investments, net of tax of $0	5	24	(7)	(10)
Total other comprehensive loss	5	24	(7)	(10)
Total comprehensive loss	$ (7,207)	$ (7,148)	$ (7,756)	$ (7,246)

16. Subsequent Event

On January 6, 2021, the Company entered into a securities purchase agreement (the "2021 Purchase Agreement") with certain institutional investors, pursuant to which the Company issued and sold, in a registered direct offering (the "Offering"), an aggregate of 32,630,983 shares of common stock, $0.001 par value per share, at a purchase price per share of $1.10 (the "Shares"). The aggregate gross proceeds of the Offering were $35,894 million, before deducting fees payable to the placement agent and other estimated offering expenses payable by the Company. The shares were offered by the Company pursuant to a shelf registration statement on Form S-3 (File No. 333-226650) that was filed with the United States Securities and Exchange Commission ("SEC") on July 1, 2018, and declared effective by the SEC on July 15, 2019 (the "Registration Statement"), and a prospectus supplement thereunder. The Offering closed on January 8, 2021. In addition, between January 1, 2021 and January 28, 2021, the Company issued and sold an aggregate of 7,174,993 shares of its common stock pursuant to its ATM Sales Agreement with JonesTrading Institutional Services LLC, resulting in net proceeds of $9,368.

On January 29, 2021, the Company entered into a Capital on Demand™ Sales Agreement (the "ATM Sales Agreement") with JonesTrading Institutional Services LLC and William Blair & Company, L.L.C. (the "Agents"), pursuant to which the Company may offer and sell shares of its common stock having an aggregate offering price of up to $30,000 from time to time through or to the Agents (the "ATM Offering"). On January 29, 2021, the Company filed a prospectus supplement with the SEC in connection with the ATM Offering under its Registration Statement. Between January 29, 2021 and March 24, 2021, the Company issued and sold an aggregate of 5,225,406 shares of its common stock pursuant to the ATM Sales Agreement, resulting in net proceeds of $10,594.

Between January 1, 2021 and March 24, 2021, the Company issued and sold an aggregate of 1,375,000 shares of its common stock to LPC pursuant to the Purchase Agreement, resulting in gross proceeds of $2,614.

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-1 (No. 333-249319 and 333-231143), Form S-3 (Nos. 333-226650, 333-244367 and 333-252587) and Form S-8 (Nos. 333-219158, 333-224785, 333-230592 and 333-237480) of Aileron Therapeutics, Inc. of our report dated March 24, 2021 relating to the financial statements, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts
March 24, 2021

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Manuel C. Alves Aivado, M.D., Ph.D., certify that:

1. I have reviewed this Annual Report on Form 10-K of Aileron Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Aileron Therapeutics, Inc.

Date: March 24, 2021

/s/ Manuel C. Alves Aivado, M.D., Ph.D.

Manuel C. Alves Aivado, M.D., Ph.D.
President and Chief Executive Officer

Exhibit 31.2

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Donald V. Dougherty, certify that:

1. I have reviewed this Annual Report on Form 10-K of Aileron Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Aileron Therapeutics, Inc.

Date: March 24, 2021

/s/ Richard J. Wanstall

Richard J. Wanstall
Principal Financial Officer and Chief Financial Officer

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Aileron Therapeutics, Inc. (the "Company") for the period ending December 31, 2020 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 24, 2021

/s/ Manuel C. Alves Aivado, M.D., Ph.D.

Manuel C. Alves Aivado, M.D., Ph.D.
President and Chief Executive Officer

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Aileron Therapeutics, Inc. (the "Company") for the period ending December 31, 2020 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 24, 2021

/s/ Richard J. Wanstall

Richard J. Wanstall
Principal Financial Officer and Chief Financial Officer