UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2022

OR

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

Commission File Number 001-38130

Aileron Therapeutics, Inc.

(Exact name of Registrant as specified in its Charter)

Delaware	**13-4196017**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
738 Main Street #398 Waltham, MA	**02451**
(Address of principal executive offices)	**(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 ☒

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

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

As of June 30, 2022, 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 $19,137,097.

As of March 16, 2023, the Registrant has 4,541,167 shares of Common Stock, $0.001 par value per share, outstanding.

Portions of the Registrant's definitive proxy statement for its 2023 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, 2022, are incorporated by reference into Part III of this Annual Report on Form 10-K.

Table of Contents

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 assessment of strategic options and our ability to identify and implement any strategic transaction;
- anticipated cost savings in connection with our discontinuation of ALRN-6924 and our workforce reduction announced in February 2023;
- 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;
- our intellectual property position and strategy;
- 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, 2022. These risks include the following:

- We may not be successful in identifying and implementing any strategic transaction and any strategic transactions that we do enter into and consummate may not be successful, lead to increased stockholder

value or achieve the anticipated results. In addition, our efforts to identify and implement a strategic transaction will require the devotion of significant time and resources and may expose us to other operational and financial risks.

- Our decision to discontinue development of ALRN-6924 and the related reduction in our workforce may not result in the anticipated savings and could disrupt our business.
- If we are unable to identify and implement a strategic transaction and determine to pursue a dissolution and liquidation or seek protection under the bankruptcy laws, it is uncertain as to the amount of cash that would be available for distribution to our stockholders, if any, and our stockholders could lose all or a significant portion of their investment.
- We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern.
- If we continued to pursue product development, we would have needed substantial additional funding to continue such activities.
- We have incurred significant losses since inception and expect to incur losses for the foreseeable future.
- The approach we took to discover and develop novel drugs is unproven and may never lead to marketable products.
- Our business depended entirely on the successful development and commercialization of ALRN-6924. At the time we ceased clinical development of ALRN-6924, we still would have been required to conduct additional clinical trials, preclinical and manufacturing activities, obtain marketing approvals and developed the capacity either internally or with third parties to market any approved product, and such activities would have involved significant investment and risk.
- Our development of ALRN-6924 was focused on the development of ALRN-6924 as a chemoprotective agent in combination with approved chemotherapeutics. As a result, our development of ALRN-6924 would have been impacted by any events with respect to any such chemotherapeutics. For instance, if the U.S. Food and Drug Administration, or the FDA, revoked approval of any such therapeutic, or if safety, efficacy, manufacturing or supply issues arose with any therapeutic that we used in combination with ALRN-6924, we may have been unable to further develop and/or market ALRN-6924, or we may have experienced significant regulatory delays.
- 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.
- Clinical drug development is a lengthy and expensive process, with an uncertain outcome. For instance, the failure of ALRN-6924 to result in positive results in our most recent trial resulted in our determination to cease development of ALRN-6924.
- We conducted clinical trials of ALRN-6924 at sites outside the United States. The FDA may not accept data from clinical trials conducted in such locations.
- If serious adverse or unacceptable side effects were identified during the development of ALRN-6924, we may have needed to abandon or limit the development of ALRN-6924 for that reason.
- Any development of ALRN-6924 would face substantial competition from third parties developing other products for indications similar to the indications for which ALRN-6924 may be developed.
- Our development of ALRN-6924 relied on third parties for the manufacture of ALRN-6924. This reliance on third parties increased the risk that we would not have sufficient quantities of ALRN-6924 or such quantities at an acceptable cost.

- The value of ALRN-6924 is and has been dependent 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 the value of ALRN-6924 and our platform technology.
- Even if we or a third party completed the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may have prevented us, or any future collaborators, from obtaining approvals for the commercialization of ALRN-6924.
- Even if ALRN-6924 received marketing approval, it may have failed to achieve the degree of market acceptance by physicians, patients, healthcare payors and others in the medical community necessary for commercial success.

Presentation of our Common Stock

On November 10, 2022, we effected a 1-for-20 reverse stock split of our common stock. All references to shares of common stock outstanding and per share amounts in this Annual Report on Form 10-K give effect to the reverse stock split unless otherwise indicated.

PART I

Item 1. Business

Announcement of Exploration of Strategic Alternatives

In February 2023, we announced that a review of initial data from our Phase 1b chemoprotection trial of ALRN-6924 in patients with p53-mutated breast cancer showed that patients in the trial experienced severe neutropenia (Grade 4) and alopecia. The primary endpoint of the Phase 1b open-label trial, which was evaluating ALRN-6924 in patients with breast cancer receiving neoadjuvant or adjuvant treatment with docetaxel, doxorubicin, and cyclophosphamide, or TAC chemotherapy, was duration and incidence of severe neutropenia in cycle 1. Incidence of chemotherapy-induced alopecia (hair loss) was a secondary endpoint. Based on these findings, we have decided to terminate the Phase 1b breast cancer trial and further development of ALRN-6924.

We also announced that we are exploring a range of strategic alternatives to maximize shareholder value and have engaged Ladenburg Thalmann & Co., Inc. to act as an advisor for this process. Strategic alternatives that are being evaluated may include, but are not limited to, an acquisition, a merger, a business combination, a sale of assets or other transactions. There is no set timetable for this process and there can be no assurances that this process will result in us pursing a transaction or that any transaction, if pursued, will be completed on attractive terms. Due to the inherent uncertainty in the timing and cost of these potential strategic alternatives, including their impact on our cash consumption, we have concluded that as of the date of this Annual Report on Form 10-K there is substantial doubt about our ability to continue as a going concern.

In addition, we have determined to reduce our workforce to three full-time employees, which we expect to complete in the second quarter of 2023. We plan to retain the remaining employees to assist in executing the strategic alternatives review process.

Overview

ALRN-6924, is a MDM2/MDMX dual inhibitor that leverages our proprietary peptide drug technology.

When used as a chemoprotective agent, ALRN-6924 is designed to activate p53, which in turn upregulates p21, a known inhibitor of the cell replication cycle. ALRN-6924 was the only reported chemoprotective agent in clinical development to employ a biomarker strategy, in which we exclusively focused on treating patients with p53-mutated cancers. Prior to clinically evaluating ALRN-6924 as a chemoprotective agent in patients with p53-mutant cancer, we originally initiated clinical development of ALRN-6924 as an anti-cancer agent to restore p53-dependent tumor suppression in p53 wild-type tumors. When used as an anti-cancer agent, ALRN-6924 is designed to disrupt the interaction of p53 suppressors MDM2 and MDMX with tumor suppressor p53 to reactivate tumor suppression in non-mutant, or wild-type, p53 cancers.

Our clinical development program for ALRN-6924 as a selective chemoprotective agent in patients with p53-mutated cancer included the following clinical trials:

- A Phase 1b open-label clinical trial that evaluated ALRN-6924 as a chemoprotective agent in patients with p53-mutated small cell lung cancer, or SCLC, undergoing treatment with second-line topotecan;
- A Phase 1 pharmacology study of ALRN-6924 in healthy volunteers that evaluated the safety and tolerability of ALRN-6924, in addition to its cell cycle arrest mechanism of action, pharmacokinetic, and pharmacodynamic effects, including time to onset, magnitude and duration of cell cycle arrest;
- A Phase 1b randomized, double-blind, placebo-controlled clinical trial that evaluated ALRN-6924 as a chemoprotective agent in patients with p53-mutated non-small cell lung cancer, or NSCLC, undergoing first-line treatment with carboplatin plus pemetrexed with or without immune checkpoint inhibitors; and
- A Phase 1b open-label clinical trial that evaluated ALRN-6924 as a chemoprotective agent in patients with p53-mutated breast cancer undergoing either neoadjuvant or adjuvant treatment with TAC chemotherapy.

Our clinical development program for ALRN-6924 as an anti-cancer agent in patients with wild-type p53 included the following clinical trials:

- A single-agent Phase 1 clinical trial that evaluated ALRN-6924 for the treatment of patients with solid tumors and patients with lymphoma;

- A single-agent Phase 2a clinical trial that evaluated ALRN-6924 for the treatment of patients with peripheral T-cell lymphoma
- A single-agent and Ara-C-combination Phase 1/1b trial that evaluated ALRN-6924 for the treatment of patients with acute myeloid leukemia and myelodysplastic syndrome; and
- A combination trial that evaluated ALRN-6924 in combination with palbociclib for the treatment of patients with tumors harboring MDM2 amplifications.

Our Proprietary Peptide Drug Technology

We designed ALRN-6924 using our proprietary peptide drug technology. Using this technology, 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 proprietary technology 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.

We own worldwide commercial rights to ALRN-6924 and our peptide technology.

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

Cancer is a major public health problem in the United States and worldwide. The U.S. National Cancer Institute has 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 2.0 million new cancer cases will be diagnosed in the United States and more than 600,000 people will die from cancer in 2023.

Chemotherapy is a critical therapeutic pillar to treat cancer patients, but chemotherapy causes 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 proliferating 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 potentially 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 hematological toxicities most often present as neutropenia, thrombocytopenia and anemia, and represent key dose-limiting toxicities occurring in the course of treatment of cancer patients. In addition to the impact on patients' quality of life, 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 hematological toxicities 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 hematological toxicity remains a significant unmet medical need for millions 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, or EPO, 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.

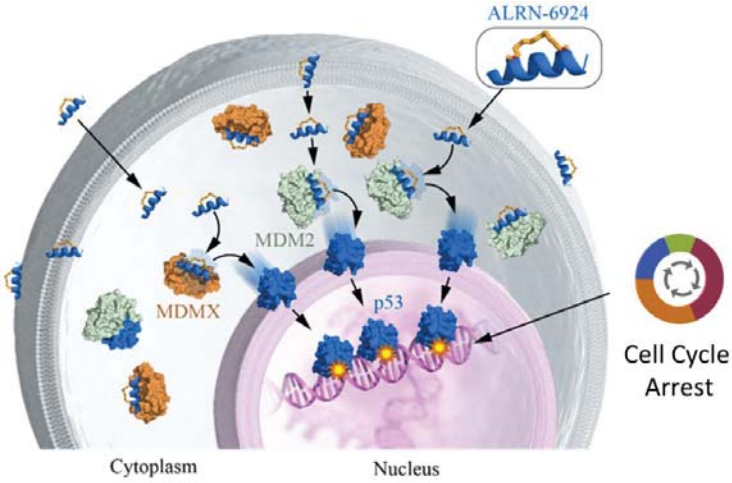
While growth factors are widely used in the medical management of cancer patients who experience cytopenias, their prescribing information indicates that those drugs may stimulate the growth and aggressiveness of cancer cells Another important consideration is that those supportive care measures are 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 a mechanism of action that selectively protect normal healthy cells from chemotherapy-related toxicities without protecting cancer cells from chemotherapeutic destruction, while leaving cancer cells fully vulnerable to chemotherapy. We were developing ALRN-6924 as a chemoprotective agent for patients with p53-mutated cancers, with its specific mechanism of p53 upregulation, to address both requirements. ALRN-6924 was designed to release functional p53 in normal healthy cells only, and, thus, was not expected to functionally affect p53-mutated cancer cells. Due to lack of effect in p53 mutated cancer cells, we believed 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.



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. 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, or WT, p53, including normal bone marrow cells, and ALRN-6924 has no activity against cancer cells with mutations in p53. We were developing ALRN-6924 to show that treatment of patients with ALRN-6924 may reduce the toxic effects of chemotherapy in the bone marrow, as well as other tissues, as well as a reduction of common chemotherapy-induced toxicities outside the bone marrow, including alopecia, stomatitis, and gastrointestinal illness, in each case without adversely impacting the anti-cancer activity of chemotherapy against p53-mutant tumor 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. We were developing ALRN-6924 to show that it may serve as a chemoprotective agent for 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

We have published extensive biochemical, cellular and in vivo data on ALRN-6924. 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. Our preclinical data show that ALRN-6924 can induce transient and reversible cell-cycle arrest in normal human bone marrow cells invitro, and ALRN-6924 protected bone marrow cells from chemotherapy induced DNA damage when administered in advance of topotecan, a chemotherapy used to treat SCLC and other cancers.

Clinical Development of ALRN-6924 as a Chemoprotective Agent

Phase 1b Clinical Trial in Patients with SCLC

In 2021, we completed a Phase 1b clinical trial that demonstrated proof-of-concept of ALRN-6924 as an investigational treatment to protect in patients with p53-mutated SCLC undergoing treatment with the chemotherapy topotecan from chemotherapy-induced toxicities. In this trial we evaluated multiple dose levels and dosing schedules

of ALRN-6924 when administered before topotecan. In September 2021, we presented final results from the trial at the European Society for Medical Oncology (ESMO) Congress. A total of 39 patients were enrolled in the trial, 38 of whom were evaluable per the trial protocol. In the trial, topotecan (1.5 mg/m^2) was administered to all patients on days 1 through 5 of every 21-day treatment cycle. Of these patients, 32 patients (31 evaluable) were treated with ALRN-6924 at 24 hours before each dose of topotecan at the following dose levels: 0.2 mg/kg (N=4), 0.3 mg/kg (N=16), 0.6 mg/kg (N=6; 5 evaluable) and 1.2 mg/kg (N=6). Seven patients were treated with 0.3 mg/kg of ALRN-6924 at 6 hours before each dose of topotecan.

In the trial, toxicities were evaluated using the National Cancer Institute's, or NCI, Common Terminology Criteria for Adverse Events, or CTCAE. Per protocol, patients were not permitted to receive prophylactic, or G-CSF, treatment in cycle 1.

Key findings from the final 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 and schedules, Grade 3/4 anemia, Grade 3/4 thrombocytopenia and Grade 4 neutropenia in cycle 1 were limited to 15%, 46% and 36% of patients, respectively.
- While chemoprotection effects were observed across all ALRN-6924 dose levels and schedules, 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 in cycle 1 limited to 19%, 44% and 31% of patients, respectively.
- None of the patients treated at 0.3 mg/kg dose level had hematological serious adverse events. One patient (6%) 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 and schedules, one patient (3%) experienced febrile neutropenia which is a life-threatening side effect commonly observed with topotecan treatment in this patient population.

The median number of completed topotecan treatment cycles across all cohorts was 3. In addition, 13% of patients required topotecan dose reduction. No patients reported National Cancer Institute Common Terminology Criteria Adverse Events, or NCI CTCAE, Grade 3 or greater events of nausea, vomiting or diarrhea; 5% of patients had Grade 3 fatigue.

While chemoprotective effects were observed across all ALRN-6924 dose levels studied in the Phase 1b SCLC trial, the 0.3 mg/kg ALRN 6924 dose level given 24 hours prior to topotecan demonstrated the most robust chemoprotection effect. None of the 16 of patients treated at the 0.3 mg/kg 24 hour ALRN-6924 dose level had a related serious adverse event. One patient (6%) at the 0.3 mg/kg 24 hour ALRN-6924 dose level required a red blood cell transfusion and a platelet transfusion.

Phase 1 Pharmacology Study in Healthy Volunteers

In October 2022, we presented additional results from our completed Phase 1 study of ALRN-6924 in healthy volunteers, which showed that ALRN-6924 induced p53-mediated cell cycle arrest in bone marrow stem cells and hair follicles. The data from the study support the potential of ALRN-6924 to prevent chemotherapy-induced neutropenia, thrombocytopenia and anemia, as well as chemotherapy-induced alopecia.

In this study, cell cycle arrest was directly measured in the bone marrow and hair follicles of an additional 41 females. ALRN-6924 was administered as a single one-hour IV infusion or three-minute bolus injection at 0.3, 0.6, or 0.9 mg/kg to cohorts of three to nine subjects and compared to placebo. Subjects were evaluated for safety and tolerability. Plasma and serum samples were obtained to determine pharmacokinetics and levels of macrophage

inhibitory cytokine-1, or MIC-1, a biomarker of p53 activation. Bone marrow was sampled 12 hours post-dose to directly measure cell cycle arrest by flow cytometry in CD34+, lineage-negative bone marrow stem cells. Occipital scalp skin was sampled by 2 mm punch biopsy for p21 immunohistochemistry in hair follicles.

ALRN-6924 continued to demonstrate a favorable safety and tolerability profile, with subjects experiencing only mild, transient adverse events, with nausea/vomiting as the most frequent related adverse events. The degree and duration of serum MIC-1 elevation was dose-dependent, indicating more durable p53 activation at higher ALRN-6924 doses. At 12 hours post-dose, the proportion of cycling bone marrow stem cells was significantly reduced at all dose levels. A blinded pathology review suggested that there was ALRN-6924-dependent p21 induction in anagen-phase hair follicles. Safety profiles, PK and PD were similar for both the three-minute bolus injection and one-hour IV infusion which, provided a rationale for development of ALRN-6924 bolus administration.

Phase 1b Clinical Trial in Patients with NSCLC

In the second quarter of 2021, we initiated a randomized, double-blind, placebo-controlled Phase 1b clinical trial of ALRN-6924 in patients with advanced NSCLC, undergoing chemotherapy. We planned to enroll 60 patients with advanced p53-mutated NSCLC undergoing treatment with first-line carboplatin plus pemetrexed with or without immune checkpoint inhibitors. Patients enrolled in the NSCLC trial were to be randomized 1:1 to receive carboplatin/pemetrexed plus 0.3 mg/kg ALRN-6924 or placebo for at least four 21-day treatment cycles. Components of the composite primary endpoint were the proportion of treatment cycles free of severe hematological and other toxicities, including Grade ≥ 3 neutropenia, Grade ≥ 3 thrombocytopenia, Grade ≥ 3 anemia, Grade 4 neutropenia and febrile neutropenia, as well as duration of Grade 4 neutropenia. An additional component of the primary endpoint was the proportion of completed treatment cycles without chemotherapy dose reduction or without the use of growth factors or transfusions. Other endpoints included the proportion of patients with NCI CTCAE Grade 3/4 treatment-emergent adverse events, quality of life, overall response rate, and progression-free survival.

In the first quarter of 2022, we conducted a blinded safety evaluation of the first ten patients enrolled in the trial who completed the first cycle of treatment with ALRN-6924 and chemotherapy. The evaluation did not identify any safety concern, consistent with ALRN-6924's previously demonstrated safety and tolerability profile. In the second quarter of 2022, we announced interim trial data from the first 20 patients in the NSCLC trial.

Key findings from the NSCLC trial interim analysis included:

- ALRN-6924-treated patients demonstrated 56% of cycles free from these Grade ≥3 hematologic toxicities and related events compared to 50% on placebo.
- ALRN-6924-treated patients were able to stay on chemotherapy treatment longer, completing 93% of the first 4 cycles of carboplatin/pemetrexed administered compared to 78% on placebo.
    - This imbalance of completed cycles between the treatment arms may have introduced a bias against ALRN-6924 on the composite primary endpoint.
    - The imbalance increased further when looking at percentages of patients completing 6 cycles of treatment (79% on ALRN-6924 versus 57% on placebo). This is reflected in the progression free survival, which was 4.6 months in the ALRN-6924 arm versus 3.2 months in the placebo arm.

The composite primary endpoint was designed to evaluate the first four cycles of chemotherapy, which is standard of care for patients receiving checkpoint inhibitors. Given that of the 20 patients in the interim analysis received a checkpoint inhibitor and therefore the interim analysis also included results for all 6 cycles of chemotherapy, which is the standard of care of patients not receiving a checkpoint inhibitor.

Based on this interim data, we decided to stop further enrollment in and terminate the NSCLC trial. Following this trial, we observed in our concurrently conducted Phase 1 pharmacology study in healthy volunteers that a higher dose level of ALRN-6924 could provide more durable cell cycle arrest and, thus more chemoprotection against certain chemotherapies, including carboplatin/pemetrexed. This observation was supported by earlier data generated from the healthy volunteer study in which serum MIC-1 levels were measured as an indicator of the duration of

effect of ALRN-6924, including the duration of cell cycle arrest. Increasing dose levels of ALRN-6924 elicited more durable p53 activation, which correlates with cell cycle arrest in the bone marrow.

Phase 1b clinical trial in patients with Breast Cancer

We initiated a Phase 1b clinical trial in the first half of 2022 to evaluate ALRN-6924 as a chemoprotective agent in patients with p53-mutated breast cancer undergoing either neoadjuvant or adjuvant treatment with TAC chemotherapy. We planned to enroll up to 24 patients in a parallel group design trial with a dose expansion cohort.

In August 2022, we announced modifications to the trial design based on key, collective learnings from our healthy volunteer study, as well as our NSCLC and SCLC clinical trials, that were intended to improve the opportunity to demonstrate protection against chemotherapy-induced severe neutropenia, alopecia and potentially other toxicities in patients with p53-mutated breast cancer. The primary endpoint of the Phase 1b open-label trial was duration and incidence of severe neutropenia in cycle 1. Incidence of chemotherapy-induced alopecia (hair loss) was a secondary endpoint.

In February 2023, we reviewed initial data from our Phase 1b chemoprotection trial of ALRN-6924 in patients with p53-mutated breast cancer, which showed that patients in the trial experienced severe neutropenia (Grade 4) and alopecia. Based on these findings, we decided to terminate the Phase 1b breast cancer trial and further development of ALRN-6924.

Clinical Trials of ALRN-6924 as an Anti-Cancer Agent

We originally initiated development of ALRN-6924 as an anti-cancer agent to restore p53-dependent tumor suppression in p53 wild-type tumors. We evaluated ALRN-6924 as an anti-cancer agent in 196 patients in multiple clinical trials. In these trials, ALRN-6924 was generally well-tolerated, with evidence of single-agent anti-tumor activity including complete and partial responses.

We have evaluated high dose therapy with ALRN-6924 (up to 5 mg/kg body weight) in 196 patients in earlier clinical trials evaluating ALRN-6924 as an anti-cancer agent including a single-agent Phase 1 trial in solid tumor and lymphoma patients; a Phase 2a trial for the treatment of peripheral T-cell lymphoma; 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.

In March 2020, we determined to cease further clinical development of ALRN-6924 as a direct anti-cancer agent in light of our available resources at that time, the data generated thus far, and our assessment of the commercial opportunities and competitive landscape in indications for which we were evaluating ALRN-6924.

Manufacturing

We contracted with third parties for the GMP manufacture of ALRN-6924 for certain materials, including raw materials and consumables necessary for their manufacture, for use in our completed preclinical studies and clinical trials. We have paused manufacture of ALRN-6924 as we engage in a process to evaluate strategic alternatives. As such, we do not intend to continue to contract for these materials for the foreseeable future. In addition, we do not own or operate GMP manufacturing facilities. Although we have relied upon contract manufacturers for the manufacture of ALRN-6924 for clinical trials, we had personnel with extensive manufacturing experience who oversaw our contract manufacturers.

The active pharmaceutical ingredient, or API, for ALRN-6924 was manufactured by a single contract manufacturer. We used 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 adequate alternative sources for the supply of materials for ALRN-6924 exist.

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 purchased 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. Under the license agreement, if Umicore is unable to meet requirements for such olefin metathesis catalyst compositions in terms of amount or delivery date, then we were permitted to procure such olefin metathesis catalyst compositions from a third party until such time that Umicore could meet our requirements. We have paused manufacturing of ALRN-6924 as we engage in a process to evaluate strategic alternatives.

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 relied upon commercially available third-party assays and employed 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 patients with p53-mutated cancer or cancer patients with wild-type p53.

If we had continued development of ALRN-6924 as a chemoprotective agent, we would have been required to have a companion in vitro diagnostic to identify patients with p53-mutated cancer, approved for use with ALRN-6924, because our clinical trials were designed to only include patients with p53-mutated cancers. We also would have needed to engage a third party to develop and supply a commercially available diagnostic to identify patients with p53-mutant cancer.

Similarly, if we had continued development of ALRN-6924 an anti-cancer agent, we would have been required to have a companion in vitro diagnostic, to identify cancer patients with wild-type 53, approved for use with ALRN-6924. We also would have needed to engage a third party to develop and supply a commercially available diagnostic to identify cancer patients with wild-type p53.

Competition

The biopharmaceutical industry 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. The development of ALRN-6924 faced and would have continued to 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, and with respect to existing chemoprotective agents and other supportive care products and new therapies that may become available in the future.

There are a large number of companies developing or marketing treatments for cancer. Many of these companies have significant 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 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 have been necessary for, our programs.

Our competitors could develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than ALRN-6924. 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.

We designed ALRN-6924 to act as a reactivator of p53. We are aware of product candidates that are in clinical development by third parties 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 as anti-cancer agents 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, including a Phase 3 clinical trial in patients with triple-negative breast cancer, a Phase 2 trial in combination with an antibody-drug conjugate in patients with triple-negative breast cancer, a Phase 2 trial in patients with neoadjuvant triple-negative breast cancer and a Phase 2 clinical trial in patients with bladder cancer. BeyondSpring Inc. is developing plinabulin in combination with G-CSF for the treatment of chemotherapy-induced neutropenia. In December 2021, BeyondSpring Inc. received a complete response letter from the FDA after submitting an NDA to the FDA for approval. BeyondSpring is conducted clinical trials evaluating plinabulin for the prevention of docetaxel-induced neutropenia in patients with NSCLC and breast cancer.

Intellectual Property

We sought to protect the proprietary technologies that we believed are important to our business, including seeking and maintaining patent protection intended to cover the composition of matter of ALRN-6924, its 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.

We protected our intellectual property estate by filing patent applications directed to dosage forms, methods of treatment, diagnostics, and additional compounds and their derivatives. Specifically, we sought and may 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 ALRN-6924 will be protectable or remain protected by enforceable patents. We cannot predict whether the patent applications we filed 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. No earlier than June 1, 2023, European applications will soon have the option, upon grant of a patent, of becoming a Unitary Patent which will be subject to the jurisdiction of the Unitary Patent Court, or UPC. This will be a significant change in European patent practice. As the UPC is a new court system, there is no precedent for the court, increasing the uncertainty of any litigation. 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.

Geo-political actions in the United States and in foreign countries could increase the uncertainties and costs surrounding the prosecution or maintenance of our patent applications or those of any current or future licensors and the maintenance, enforcement or defense of our issued patents or those of any current or future licensors. For example, the United States and foreign government actions related to Russia's invasion of Ukraine may limit or prevent filing, prosecution and maintenance of patent applications in Russia. Government actions may also prevent maintenance of issued patents in Russia. These actions could result in abandonment or lapse of our patents or patent applications, resulting in partial or complete loss of patent rights in Russia. If such an event were to occur, it could have a material adverse effect on our business. In addition, a decree was adopted by the Russian government in March 2022, allowing Russian companies and individuals to exploit inventions owned by patentees from the United States without consent or compensation. Consequently, we would not be able to prevent third parties from practicing our inventions in Russia or from selling or importing products made using our inventions in and into Russia.

Patent Portfolio

We have rights in patents and patent applications directed to the composition of matter and/or use of 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, 2023, we owned or had an exclusive license to 38 U.S. patents, 7 pending U.S. provisional or non-provisional patent applications, 123 foreign patents and 27 pending foreign applications. The claims of these owned or in-licensed patents and patent applications are directed toward various aspects of ALRN-6924. 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 2024 through 2041, without taking into account any possible patent term adjustments or extensions. Within our patent portfolio, as of March 1, 2023, we owned or had an exclusive license to 25 U.S. patents, 6 pending U.S. provisional or non-provisional patent applications, 52 foreign patents and 18 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 2024 through 2041, with the owned patents and patent applications, if issued, expiring on various dates from 2029 to 2041, in each case without taking into account any possible patent term adjustment or extensions. Without taking into account any possible patent term adjustments or extensions, such owned and in-licensed patents claiming compositions of matter covering ALRN-6924 are expected to expire on various dates from 2024 through 2033, with the owned patents and patent applications, if issued, expiring on various dates from 2029 to 2033. Lastly, within our patent portfolio, as of March 1, 2023, 8 U.S. patents, 27 foreign patents are licensed to us by the 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 2024 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 Umicore 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 ALRN-6924 receives FDA approval, we expect to apply for patent term extensions on patents covering such product candidate. 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 Dana-Farber Cancer Institute, or 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, 2022, 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 $110,000, 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, 2022, 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. The agreement obligates us 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 product under the FDCA. Accordingly, based on this FDA guidance, we believe that products based on our stapled peptide technology 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.

A company, institution, or organization which takes responsibility for the initiation and management of a clinical development program for drug products, and for their regulatory approval, is typically referred to as a sponsor. A sponsor 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;
- design of a clinical protocol and submission to the FDA of an IND, which must take effect before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or 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 filing and approval by the FDA 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 a sponsor 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. These studies are generally referred to as IND-enabling studies. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations and standards and the United States Department of Agriculture's Animal Welfare Act, if applicable. 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, sponsors must submit a protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the filing of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research subjects 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.

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.

There is no obligation for a sponsor to make its investigational products available for expanded access; however, as required by amendments to the FDCA included in the 21st Century Cures Act, or the Cures Act, passed in 2016, if a sponsor has a policy regarding how it responds to expanded access requests with respect to product candidates in development to treat serious diseases or conditions, it must make that policy publicly available. 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.

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

In December 2022, with the passage of Food and Drug Omnibus Reform Act, or FDORA, Congress required sponsors to develop and submit a diversity action plan for each phase 3 clinical trial or any other "pivotal study" of a new drug or biological product. These plans are meant to encourage the enrollment of more diverse patient populations in late-stage clinical trials of FDA-regulated products. Specifically, actions plans must include the sponsor's goals for enrollment, the underlying rationale for those goals, and an explanation of how the sponsor intends to meet them. In addition to these requirements, the legislation directs the FDA to issue new guidance on diversity action plans.

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.

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

Finally, sponsors of clinical trials are required to register and disclose certain clinical trial information on a public registry (clinicaltrials.gov) maintained by the U.S. National Institutes of Health, or NIH. In particular,

information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. The NIH's Final Rule on registration and reporting requirements for clinical trials became effective in 2017, and both the NIH and the FDA have recently signaled the government's willingness to begin enforcing those requirements against non-compliant clinical trial sponsors. The failure to submit clinical trial information to clinicaltrials.gov, as required, is a prohibited act under the FDCA with violations subject to potential civil monetary penalties of up to $10,000 for each day the violation continues. Although the FDA has historically not enforced these reporting requirements due to HHS's long delay in issuing final implementing regulations, those regulations have now been issued and the FDA has issued several Notices of Noncompliance to manufacturers since April 2021.

Manufacturing and Other Regulatory Requirements

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.

Specifically, the FDA's regulations require that pharmaceutical products be manufactured in specific approved facilities and in accordance with cGMPs. The cGMP regulations include requirements relating to organization of personnel, buildings and facilities, equipment, control of components and product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports and returned or salvaged products. Manufacturers and other entities involved in the manufacture and distribution of approved pharmaceuticals are required to register their establishments with the FDA and some state agencies, and they are subject to periodic unannounced inspections by the FDA for compliance with cGMPs and other requirements. Inspections must follow a "risk-based schedule" that may result in certain establishments being inspected more frequently. Manufacturers may also have to provide, on request, electronic or physical records regarding their establishments. Delaying, denying, limiting, or refusing inspection by the FDA may lead to a product being deemed to be adulterated. Changes to the manufacturing process, specifications or container closure system for an approved product are strictly regulated and often require prior FDA approval before being implemented. The FDA's regulations also require, among other things, the investigation and correction of any deviations from cGMP and the imposition of reporting and documentation requirements upon the sponsor and any third-party manufacturers involved in producing the approved product.

The PREVENT Pandemics Act, which was enacted in December 2022, clarifies that foreign drug manufacturing establishments are subject to registration and listing requirements even if a drug or biologic undergoes further manufacture, preparation, propagation, compounding, or processing at a separate establishment outside the United States prior to being imported or offered for import into the United States.

Pediatric Studies

Under the Pediatric Research Equity Act, or PREA, 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 (if required under PREA), before the date on which the sponsor submits the required assessments or investigation and no later than either 60 calendar days after the date of the end-of-phase 2 meeting or such other time as agreed upon between FDA and the sponsor. Those plans must contain an outline of the proposed pediatric study or studies the sponsor plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The sponsor, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the sponsor may request an amendment to the plan at any time.

For drugs intended to treat a serious or life-threatening disease or condition, the FDA must, upon the request of a sponsor, meet to discuss preparation of the initial pediatric study plan or to discuss deferral or waiver of pediatric assessments.

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 the FDA determines to be substantially relevant to the growth or progression of a pediatric cancer. The investigation must be designed to yield clinically meaningful pediatric study data regarding the dosing, safety and preliminary efficacy to inform pediatric labeling for the product.

The FDA may, on its own initiative or at the request of the sponsor, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. A deferral may be granted for several reasons, including a finding that the product or therapeutic candidate is ready for approval for use in adults before pediatric trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric trials begin. Pursuant to the Food and Drug Administration Safety and Innovation Act of 2012, or FDASIA, the FDA must send a PREA Non-Compliance letter to sponsors who have failed to submit their pediatric assessments required under PREA, have failed to seek or obtain a deferral or deferral extension or have failed to request approval for a required pediatric formulation. FDASIA further requires the FDA to publicly post the PREA Non-Compliance letter and sponsor's response.

Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation, although the FDA has recently taken steps to limit what it considers abuse of this statutory exemption in PREA by announcing that it does not intend to grant any additional orphan drug designations for rare pediatric subpopulations of what is otherwise a common disease. The FDA also maintains a list of diseases that are exempt from PREA requirements due to low prevalence of disease in the pediatric population.

Submission and Filing of an NDA

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 2023 is $3,242,026, 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 federal fiscal year 2023 is $393,933 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 that time or before whether the application is sufficiently complete to permit substantive review. In the event that the FDA determines an application does not satisfy this standard, it will issue a Refuse to File determination to the sponsor. 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, or PDUFA, goal date may be extended by the FDA for three additional months to consider new information or clarification provided by the sponsor to address an outstanding deficiency identified by the FDA following the original submission. Despite these review goals, it is not uncommon for FDA review of an application to extend beyond PDUFA goal date.

In connection with its review of 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 and the integrity of the data relied upon in the NDA. 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. With passage of FDORA, Congress clarified FDA's authority to conduct inspections by expressly permitting inspection of facilities involved in the preparation, conduct, or analysis of clinical and non-clinical studies submitted to FDA as well as other persons holding study records or involved in the study process.

In addition, as a condition of approval, the FDA may require a sponsor 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.

Finally, 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.

Expedited Review Programs

The FDA is authorized to expedite the review of applications in several ways. None of these expedited programs changes the standards for approval but each may help expedite the development or approval process governing product candidates

- *Fast Track designation*. The sponsor of a product candidate may request the FDA to designate the product for a specific indication as a Fast Track product concurrent with or after the filing of the IND. Candidate products are eligible for Fast Track designation if *they* are intended to treat a serious or life-threatening condition and demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to the combination of the product candidate and the specific indication for which it is being studied. In addition to other benefits, such as the ability to have greater interactions with the FDA, the FDA may initiate review of sections of a Fast Track application before the application is complete, a process known as rolling review.
- *Breakthrough therapy designation.* To qualify for the breakthrough therapy program, product candidates must be intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence must indicate that such product candidates may demonstrate substantial improvement on one or more clinically significant endpoints over existing therapies. The FDA will seek to ensure the sponsor of a breakthrough therapy product candidate receives intensive guidance on an efficient development program, intensive involvement of senior managers and experienced staff on a proactive, collaborative and cross-disciplinary review and rolling review.
- *Priority review.* A product candidate is eligible for priority review if it treats a serious condition and, if approved, it would be a significant improvement in the safety or effectiveness of the treatment, diagnosis or prevention compared to marketed products. The FDA aims to complete its review of priority review applications within six months as opposed to 10 months for standard review.

- *Accelerated approval.* Drug products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval. Accelerated approval means that a product candidate may be approved on the basis of adequate and well controlled clinical trials establishing that the product candidate has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity and prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a drug product candidate receiving accelerated approval perform adequate and well controlled post-marketing clinical trials. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials. With passage of the Food and Drug Omnibus Reform Act, or FDORA, in December 2022, Congress modified certain provisions governing accelerated approval of drug and biologic products. Specifically, the new legislation authorized the FDA to: require a sponsor to have its confirmatory clinical trial underway before accelerated approval is awarded, require a sponsor of a product granted accelerated approval to submit progress reports on its post-approval studies to FDA every six months (until the study is completed; and use expedited procedures to withdraw accelerated approval of an NDA or BLA after the confirmatory trial fails to verify the product's clinical benefit. Further, FDORA requires the agency to publish on its website "the rationale for why a post-approval study is not appropriate or necessary" whenever it decides not to require such a study upon granting accelerated approval.
- *Regenerative advanced therapy.* With passage of 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 candidate 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 the 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.

The FDA's Decision on an NDA

The FDA reviews an NDA to determine, among other things, whether the candidate product is safe and whether it is effective for its intended use(s), with the latter determination being made on the basis of substantial evidence. The FDA has interpreted this evidentiary standard to require at least two adequate and well-controlled clinical investigations to establish effectiveness of a new product. Under certain circumstances, however, the FDA has indicated that a single trial with certain characteristics and additional information may satisfy this standard. Ultimately, the FDA will determine whether the expected benefits of the drug product outweigh its potential risks to patients. 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 will issue either a complete response letter, or CRL, or an approval letter.

A CRL 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 a CRL is issued, the sponsor will have one year to respond to the deficiencies identified by the FDA, at which time the FDA can deem the application withdrawn or, in its discretion, grant the sponsor an additional six month extension to respond. For those seeking to challenge FDA's CRL decision, the agency has indicated that sponsors may request a formal hearing on the CRL or they may file a request for reconsideration or a request for a formal dispute resolution.

An approval letter, on the other hand, authorizes commercial marketing of the product with specific prescribing information for specific indications. The FDA 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 September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug product.

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. Moreover, with passage of the Pre-Approval Information Exchange Act, or PIE Act, in December 2022, sponsors of products that have not been approved may proactively communicate to payors certain information about products in development to help expedite patient access upon product approval. Previously, such communications were permitted under FDA guidance but the new legislation explicitly provides protection to sponsors who convey certain information about products in development to payors, including unapproved uses of approved products.

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 regulatory 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. This interpretation of the FDCA by the FDA was confirmed with enactment of the Ensuring Innovation Act in April 2021. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, an ANDA or 505(b)(2) application 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 regulatory 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 and 505(b)(2) applications 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.

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. The FDA's regulations governing patent listings were largely codified into law with enactment of the Orange Book Modernization Act, or the Orange Book, in January 2021. 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 exclusivity in the United States and, if granted, provides for the attachment of an additional six months of regulatory exclusivity to the term of any existing unexpired patent or regulatory exclusivity, including orphan drug 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 about the active moiety in the product. 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 receive 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. 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.

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. Under Omnibus legislation signed by President Trump on December 27, 2020, the requirement for a product to show clinical superiority applies to drug products that received orphan drug designation before enactment of amendments to the FDCA in 2017 but have not yet been approved by the FDA.

In September 2021, the Court of Appeals for the 11th Circuit held that, for the purpose of determining the scope of market exclusivity, the term "same disease or condition" in the statute means the designated "rare disease or condition" and could not be interpreted by the FDA to mean the "indication or use." Thus, the court concluded, orphan drug exclusivity applies to the entire designated disease or condition rather than the "indication or use." Although there have been legislative proposals to overrule this decision, they have not been enacted into law. On January 23, 2023, FDA announced that, in matters beyond the scope of that court order, FDA will continue to apply its existing regulations tying orphan-drug exclusivity to the uses or indications for which the orphan drug was approved.

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 clearing the clinical investigations 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

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. In April 2020, the FDA issued additional guidance which describes considerations for the development and labeling of companion diagnostic devices to support the indicated uses of multiple drug or biological oncology products, when appropriate.

The 2014 guidance also explains that a companion diagnostic device used to make treatment decisions in clinical trials of a biologic product candidate generally will be considered an investigational device, unless it is employed for an intended use for which the device is already approved or cleared. If used to make critical treatment decisions, such as patient selection, the diagnostic device generally will be considered a significant risk device under the FDA's Investigational Device Exemption, or IDE, regulations. Thus, the sponsor of the diagnostic device will be required to comply with the IDE regulations. According to the guidance, if a diagnostic device and a product are to be studied together to support their respective approvals, both products can be studied in the same investigational study, if the study meets both the requirements of the IDE regulations and the IND regulations. The guidance provides that depending on the details of the study plan and subjects, a sponsor may seek to submit an IND application alone, or both an IND- and IDE-application.

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 would 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 sponsor 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 2023, the standard fee for review of a PMA is $441,547 and the small business fee is $110,387.

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 sponsor'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 sponsor. 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.

Federal and State Data Privacy Laws

There are multiple privacy and data security laws that may impact our business activities in the United States and in other countries where we conduct trials or where we may do business in the future. These laws are evolving and may increase both our obligations and our regulatory risks in the future. In the health care industry generally, under the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, the U.S. Department of Health and Human Services, or HHS, has issued regulations to protect the privacy and security of protected health information used or disclosed by covered entities including certain healthcare providers, health plans and healthcare clearinghouses. HIPAA also regulates standardization of data content, codes and formats used in healthcare transactions and standardization of identifiers for health plans and providers. HIPAA also imposes certain obligations on the business associates of covered entities that obtain protected health information in providing services to or on behalf of covered entities. HIPAA may apply to us in certain circumstances and may also apply to our business partners in ways that may impact our relationships with them. Our clinical trials are regulated by the Common Rule, which also includes specific privacy-related provisions. In addition to federal privacy regulations, there are a number of state laws governing confidentiality and security of health information that may be applicable to our business. In addition to possible federal civil and criminal penalties for HIPAA violations, state attorneys general are authorized to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state attorneys general (along with private plaintiffs) have brought civil actions seeking injunctions and damages resulting from alleged violations of HIPAA's privacy and security rules. State attorneys general also have authority to enforce state privacy and security laws. New laws and regulations governing privacy and security may be adopted in the future as well.

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 authorization 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

On January 31, 2022, the new Clinical Trials Regulation (EU) No 536/2014 became effective in the European Union and replaced the prior Clinical Trials Directive 2001/20/EC. The new regulation aims at simplifying and streamlining the authorization, conduct and transparency of clinical trials in the European Union. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial to be conducted in more than one Member State of the European Union, or EU Member State, will only be required to submit a single application for approval. The submission will be made through the Clinical Trials Information System, a new clinical trials portal overseen by the European Medicines Agency, or EMA, and available to clinical trial sponsors, competent authorities of the EU Member States and the public.

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.

The new regulation did not change the preexisting requirement that a sponsor must obtain prior approval from the competent national authority of the EU Member State in which the clinical trial is to be conducted. If the clinical trial is conducted in different EU Member States, the competent authorities in each of these EU Member States must provide their approval for the conduct of the clinical trial. Furthermore, the sponsor may only start a clinical trial at a specific study site after the applicable ethics committee has issued a favorable opinion.

Parties conducting certain clinical trials must, as in the United States, post clinical trial information in the European Union at the EudraCT website: https://eudract.ema.europa.eu.

PRIME Designation in the EU

In March 2016, the 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, a sponsor 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 a sponsor 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, sponsors 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 sponsor 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 sponsor 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 Union, medical devices such as companion diagnostics must comply with the General Safety and Performance Requirements, or SPRs, detailed in Annex I of the EU Medical Devices Regulation (Regulation (EU) 2017/745), or MDR which came into force on May 26, 2021 and replaced the previously applicable EU Medical Devices Directive (Council Directive 93/42/EEC). Compliance with SPRs and additional requirements applicable to companion medical devices is a prerequisite to be able to affix the CE Mark of Conformity to medical devices, without which they cannot be marketed or sold. To demonstrate compliance with the SPRs, a manufacturer must undergo a conformity assessment procedure, which varies according to the type of medical device and its classification. The MDR is meant to establish a uniform, transparent, predictable, and sustainable regulatory framework across the European Union for medical devices.

Separately, the regulatory authorities in the European Union also adopted a new *In Vitro Diagnostic Regulation, or IVDR, (EU) 2017/746*, which became effective in May 2022. The new regulation replaced the In Vitro Diagnostics Directive (IVDD) 98/79/EC. Manufacturers wishing to apply to a notified body for a conformity assessment of their in vitro diagnostic medical device had until May 2022 to update their Technical Documentation to meet the requirements and comply with the new, more stringent Regulation. The regulation 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; set up a central database to provide patients, healthcare professionals and the public with comprehensive information on products available in the European Union; and strengthen rules for the assessment of certain high-risk devices, such as implants, which may have to undergo an additional check by experts before they are placed on the market.

Brexit and the Regulatory Framework in the United Kingdom

The United Kingdom's withdrawal from the European Union took place on January 31, 2020. The European Union and the United Kingdom. reached an agreement on their new partnership in the Trade and Cooperation Agreement, or the Agreement, which was applied provisionally beginning on January 1, 2021 and which entered into force on May 1, 2021. The Agreement focuses primarily on free trade by ensuring no tariffs or quotas on trade in goods, including healthcare products such as medicinal products. Thereafter, the European Union and the United Kingdom will form two separate markets governed by two distinct regulatory and legal regimes. As such, the Agreement seeks to minimize barriers to trade in goods while accepting that border checks will become inevitable as a consequence that the United Kingdom is no longer part of the single market. As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or the MHRA, became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law whereas Northern Ireland continues to be subject to European Union rules under the Northern Ireland Protocol. The MHRA will rely on the Human Medicines Regulations 2012 (SI 2012/1916) (as amended), or the HMR, as the basis for regulating medicines. The HMR has incorporated into the domestic law the body of EU law instruments governing medicinal products that pre-existed prior to the U.K.'s withdrawal from the EU. The MHRA may rely on a decision taken by the European Commission on the approval of a new marketing authorization via the centralized procedure until December 31, 2023.

General Data Protection Regulation

Many countries outside of the United States maintain rigorous laws governing the privacy and security of personal information. The collection, use, disclosure, transfer, or other processing of personal data, including personal health data, regarding individuals who are located in the European Economic Area, or EEA, and the processing of personal data that takes place in the EEA, is subject to the General Data Protection Regulation, or GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, and it imposes heightened requirements on companies that process health and other sensitive data, such as requiring in many situations that a company obtain the consent of the individuals to whom the sensitive personal data relate before processing such data. Examples of obligations imposed by the GDPR on companies processing personal data that fall within the scope of the GDPR include providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, appointing a data protection officer, providing notification of data breaches and taking certain measures when engaging third-party processors.

The GDPR also imposes strict rules on the transfer of personal data to countries outside the EEA, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR 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. Compliance with the GDPR is a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance. In July 2020, the Court of Justice of the European Union, or the CJEU, invalidated the EU-U.S. Privacy Shield framework, one of the mechanisms used to legitimize the transfer of personal data from the EEA to the United States. The CJEU decision also drew into

question the long-term viability of an alternative means of data transfer, the standard contractual clauses, for transfers of personal data from the EEA to the United States. Following the withdrawal of the United Kingdom from the European Union, the U.K. Data Protection Act 2018 applies to the processing of personal data that takes place in the United Kingdom and includes parallel obligations to those set forth by GDPR.

Additionally, in October 2022, President Biden signed an executive order to implement the EU-U.S. Data Privacy Framework, which would serve as a replacement to the EU-US Privacy Shield. The EC initiated the process to adopt an adequacy decision for the EU-US Data Privacy Framework in December 2022. It is unclear if and when the framework will be finalized and whether it will be challenged in court. The uncertainty around this issue may further impact our business operations in the EU.

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, other healthcare providers 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

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.

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.

Healthcare Reform

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 2031 pursuant to the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act. These Medicare sequester reductions were suspended and reduced through the end of June 2022 , with the full 2% cut resuming thereafter. 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 ALRN-6924 for which we may obtain regulatory approval or the frequency with which such product candidate is prescribed or used. Indeed, under current legislation, the actual reductions in Medicare payments may vary up to 4%.

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.

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. There has also been litigation with respect to the ACA. For instance, in June 2021 the Supreme Court rejected a challenge to the ACA. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

Pharmaceutical Prices

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. There have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid.

On August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law by President Biden. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of Health and Human Services (HHS) to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least 9 years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law also caps Medicare out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at 2,000 a year.

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. A number of states, for example, require drug manufacturers and other entities in the drug supply chain, including health carriers, pharmacy benefit managers, wholesale distributors, to disclose information about pricing of pharmaceuticals. In addition, regional healthcare organizations and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription pharmaceutical and other healthcare 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 March 16, 2023 we had six full-time employees, including a total of three employees with M.D. or Ph.D. degrees, all 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.

In connection with our decision to terminate our Phase 1b breast cancer trial and further development of ALRN-6924, and our related decision to explore a range of strategic alternatives, we have determined to reduce our remaining workforce from nine to three full-time employees in the first and second quarters of 2023. We plan to retain the remaining employees to assist in executing the strategic alternatives review process.

We estimate that the severance and termination-related costs for the six former employees will be approximately $1.0 to $1.1 million and expect to record these costs in the first quarter of 2023. We expect that payment of these costs will be made through the second quarter of 2023. Our estimate of costs and the expected timing for recording and paying those costs are subject to a number of assumptions and actual results may differ. We may also incur other costs not currently contemplated due to events that may occur as a result of, or associated with, the workforce reduction.

We are dedicated to fostering a workplace environment that keeps our employees inspired, including providing a comprehensive benefits program that supports the health care, family, and financial needs of our employees. All of our full-time employees are eligible for cash bonuses and equity awards in addition to other benefits including comprehensive health insurance, life and disability insurance, and 401(k) matching.

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 738 Main Street #398, Waltham, MA 02451, 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 Strategic Alternative Process and Potential Strategic Transaction

We may not be successful in identifying and implementing any strategic transaction and any strategic transaction that we may consummate may not be successful.

In February 2023, we made the decision to discontinue further development of ALRN-6924. In connection with this decision, we announced that we would be reducing our remaining workforce from nine to three full-time employees, designed to substantially reduce our operating expenses while we undertake a comprehensive assessment of strategic options to maximize stockholder value. These strategic options may include a merger, reverse merger, sale, wind-down, liquidation and dissolution or other strategic transaction. However, there can be no assurance that we will be able to successfully consummate any particular strategic transaction. The process of continuing to evaluate these strategic options may be very costly, time-consuming and complex and we may incur significant costs related to this continued evaluation. We may also incur additional unanticipated expenses in connection with this process. A considerable portion of these costs will be incurred regardless of whether any such course of action is implemented or transaction is completed. Any such expenses will decrease the remaining cash available for use in our business and may eliminate, diminish or delay any future distributions to our stockholders.

In addition, there can be no assurances that any particular course of action, business arrangement or transaction, or series of transactions, will be pursued, successfully consummated, lead to increased stockholder value, or achieve the anticipated results. Any failure of such potential transaction to achieve the anticipated results could significantly impair our ability to enter into any future strategic transactions and may significantly reduce or delay any future distributions to our stockholders.

We may not realize any additional value in a strategic transaction.

The market capitalization of our company is below the value of our current cash, cash equivalents and investments. Potential counterparties in a strategic transaction involving our company may place minimal or no value on our assets, including ALRN-6924. Further, the development and any potential commercialization of ALRN-6924 would require substantial additional cash to fund the costs associated with conducting the necessary clinical testing and obtaining regulatory approval. Consequently, any potential counterparty in a strategic transaction involving our company may choose not to spend the additional resources necessary to continue developing ALRN-6924 and may attribute little or no value, in such a transaction, to it or our platform technology.

If we are successful in completing a strategic transaction, we may be exposed to other operational and financial risks.

Although there can be no assurances that a strategic transaction will result from the process we have undertaken to identify and evaluate strategic alternatives, the negotiation and consummation of any such transaction will require significant time on the part of our management.

The negotiation and consummation of any such transaction may also require more time or greater cash resources than we anticipate and expose us to other operational and financial risks, including:

- increased near-term and long-term expenditures;
- exposure to unknown liabilities;
- higher than expected acquisition or integration costs;
- write-downs of assets or incurrence of non-recurring, impairment or other charges;
- increased amortization expenses;
- difficulty and cost in combining the operations and personnel of any combined business with our operations and personnel;
- impairment of relationships with key suppliers or customers of any combined business due to changes in management and ownership;
- inability to retain key employees of our company or any combined business; and
- possibility of future litigation.

Any of the foregoing risks could have a material adverse effect on our business, financial condition and prospects.

Our decision to discontinue further development of ALRN-6924 and the related reduction in our workforce may not result in the anticipated savings and could disrupt our business.

In February 2023, we made the decision to discontinue further development of ALRN-6924 and we decided to reduce our workforce to substantially reduce our operating expenses while we undertake a comprehensive assessment of strategic options to maximize stockholder value. We may not realize, in full or in part, the anticipated benefits and savings in operating expenses from these decisions due to unforeseen difficulties, delays or unexpected costs. This may include higher than expected costs associated with winding down our Phase 1b breast cancer trial. If we are unable to realize the expected cost savings, our financial condition would be adversely affected and it may be more difficult to complete a potential strategic transaction. Furthermore, the reduction in our workforce may result in weaknesses in our infrastructure and operations and may increase the risk that we become unable to comply with legal and regulatory requirements.

Our board of directors may decide to pursue a dissolution and liquidation or seek protection under the bankruptcy laws. In such an event, the amount of cash available for distribution to our stockholders will depend

heavily on the timing of such liquidation as well as the amount of cash that will need to be reserved for commitments and contingent liabilities.

There can be no assurance that a strategic transaction will be completed and our board of directors may decide to pursue a dissolution and liquidation. In such an event, the amount of cash available for distribution to our stockholders will depend heavily on the timing of such decision and, as with the passage of time the amount of cash available for distribution will be reduced as we continue to fund our operations. In addition, if our board of directors were to approve and recommend, and our stockholders were to approve, a dissolution and liquidation, we would be required under Delaware corporate law to pay our outstanding obligations, as well as to make reasonable provision for contingent and unknown obligations, prior to making any distributions in liquidation to our stockholders. As a result of this requirement, a portion of our assets may need to be reserved pending the resolution of such obligations and the timing of any such resolution is uncertain. In addition, we may be subject to litigation or other claims related to a dissolution and liquidation. If a dissolution and liquidation were pursued, our board of directors, in consultation with our advisors, would need to evaluate these matters and make a determination about a reasonable amount to reserve. It is unclear whether and to what extent any resources would be available for distribution to our stockholders and when such distributions could be made, and holders of our common stock could lose all or a significant portion of their investment in the event of a liquidation, dissolution or winding up.

We also may consider seeking protection under the bankruptcy laws in order to continue to pursue potential transactions and conduct a wind-down of our company. If we decide to seek protection under the bankruptcy laws, we would expect that we would file for bankruptcy at a time that is significantly earlier than when we would otherwise exhaust our cash resources. If we decide to seek protection under the bankruptcy laws, it is unclear to what extent we will be able to pay our obligations, and, accordingly, it is further unclear whether, to what extent and when any resources would be available for distributions to stockholders and holders of our common stock could lose all or a significant portion of their investment.

Our ability to consummate a strategic transaction depends on our ability to retain our employees required to consummate such transaction.

Our ability to consummate a strategic transaction depends upon our ability to retain our employees required to consummate such a transaction, and the loss of such employees' services may adversely impact the ability to consummate such transaction. In February 2023, we announced a reduction in our workforce intended to substantially reduce our operating expenses while we undertake a comprehensive assessment of strategic options to maximize stockholder value. Our cash conservation activities may yield unintended consequences, such as attrition beyond our planned reduction in workforce and reduced employee morale, which may cause remaining employees to seek alternative employment. Our ability to successfully complete a strategic transaction depends in large part on our ability to retain our remaining personnel. If we are unable to successfully retain our remaining personnel, we are at risk of a disruption to our exploration and consummation of strategic options as well as business operations.

We may become involved in securities class action litigation that could divert management's attention and harm the company's business, and insurance coverage may not be sufficient to cover all costs and damages.

In the past, securities class action litigation has often followed certain significant business transactions, such as the sale of a company or announcement of any other strategic transaction, or the announcement of negative events, such as negative results from clinical trials. These events may also result in or be concurrent with investigations by the SEC. We may be exposed to such litigation or investigation even if no wrongdoing occurred. Litigation and investigations are usually expensive and divert management's attention and resources, which could adversely affect our business and cash resources and our ability to consummate a potential strategic transaction or the ultimate value our stockholders receive in any such transaction.

We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern.

Due to the inherent uncertainty in the timing and cost of potential strategic alternatives, including their impact on our cash consumption, we believe there is substantial doubt about our ability to continue as a going concern as of the date of this Annual Report on Form 10-K. See Note 1 to our financial statements appearing elsewhere in this Annual Report on Form 10-K for additional information on our assessment. If we are unable to obtain additional capital and continue as a going concern, we might have to liquidate our assets and the values we receive for our assets in liquidation or dissolution could be significantly lower than the values reflected in our financial statements.

Our lack of cash resources and our conclusion that we may be unable to continue as a going concern may materially adversely affect our share price and our ability to raise new capital or to enter into critical contractual relations with third parties.

Risks Related to Our Financial Position

If we continued to pursue product development, we would have needed substantial additional funding to continue such activities.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a time-consuming, expensive and uncertain process that takes years to complete. Although we are not currently developing any product candidates, if we continued pursuing development of ALRN-6924, we would have been required to expend significant funds in order to advance the development of, conduct clinical trials of, and seek marketing approval for ALRN-6924. If we were able to obtain marketing approval for ALRN-6924, we would have incurred significant commercialization expenses related to drug sales, marketing, manufacturing and distribution to the extent that such sales, marketing, manufacturing and distribution were not then the responsibility of any collaborator.

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

- whether we realize the anticipated cost savings in connection with our February 2023 workforce reduction;
- our ability to consummate a strategic transaction and the nature and type of such transaction;
- the time and cost necessary to close out our Phase 1b breast cancer trial; and
- the costs associated with operating as a public company.

If we had continued to pursue development of ALRN-6924 our capital requirements would have depended on many factors, including:

- the scope, progress, results and costs of our preclinical studies, CMC, and clinical trials of ALRN-6924;
- the costs, timing and outcome of regulatory review of ALRN-6924;
- our ability to establish and maintain collaborations with third parties on favorable terms, if at all, and the extent to which any third party collaborator would have assumed the costs of development and commercialization activities;
- the success of any collaborations that we may have entered into with third parties;
- the extent to which we acquired or invested in businesses, products and technologies, including entering into licensing or collaboration arrangements for ALRN-6924, although we currently have no commitments or agreements to complete any such transactions;
- the costs and timing of commercialization activities, including drug sales, marketing, manufacturing and distribution, for any product candidate for which we receive marketing approval; and
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims.

Subject to the outcome of our exploration of strategic alternatives, we believe that, based on our current operating plan, our cash, cash equivalents and investments as of December 31, 2022 will enable us to fund our operating expenses for at least twelve months following the date of this Annual Report on Form 10-K. However, due to the inherent uncertainty in the timing and cost of these potential strategic alternatives, including their impact on our cash consumption, we have concluded that as of the date of this Annual Report on Form 10-K there is substantial doubt about our ability to continue as a going concern. 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. While we have implemented certain cash preservation measures, we cannot be certain that such measures will result in the savings anticipated.

We have incurred significant losses since inception. We expect to incur losses for the foreseeable future and do not expect to achieve or maintain profitability.

Since our inception, we have incurred significant losses on an aggregate basis. Our net loss was $27.3 million and $26.2 million for the years ended December 31, 2022 and December 31, 2021, 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. In February 2023, we discontinued development of ALRN-6924 in order to substantially reduce our operating expenses while we undertake a comprehensive assessment of our strategic options. Notwithstanding these events, we expect to continue to incur operating losses for the foreseeable future. In addition, our losses from operations may fluctuate significantly from quarter to quarter.

While we recently made the decision to discontinue development of ALRN-6924 and are not currently developing product candidates, to become and remain profitable, we would have needed to develop, obtain approval for and eventually commercialize a product or products with significant market potential. This would have required us to be successful in a range of challenging activities, including completing preclinical studies and clinical trials of ALRN-6924, obtaining marketing approval for ALRN-6924, manufacturing, marketing and selling ALRN-6924 following any marketing approval we may have obtained and establishing and managing any collaborations for the development, marketing and/or commercialization of ALRN-6924. We may never have succeeded in these activities and, even if we did, may never have generated revenues that would have been significant or large enough to achieve profitability.

We hold a portion of our cash and cash equivalents that we use to meet our working capital and operating expense needs in deposit accounts that could be adversely affected if the financial institutions holding such funds fail.

We hold a portion of cash and cash equivalents that we use to meet our working capital and operating expense needs in deposit accounts. The balance held in these accounts may exceed the Federal Deposit Insurance Corporation, or FDIC, standard deposit insurance limit of $250,000. If a financial institution in which we hold such funds fails or is subject to significant adverse conditions in the financial or credit markets, we could be subject to a risk of loss of all or a portion of such uninsured funds or be subject to a delay in accessing all or a portion of such uninsured funds. Any such loss or lack of access to these funds could adversely impact our short-term liquidity and ability to meet our operating expense obligations.

For example, on March 10, 2023, Silicon Valley Bank, or SVB, and Signature Bank, were closed by state regulators and the FDIC was appointed receiver for each bank. The FDIC created successor bridge banks and all deposits of SVB and Signature Bank were transferred to the bridge banks under a systemic risk exception approved by the United States Department of the Treasury, the Federal Reserve and the FDIC. If financial institutions in which we hold funds for working capital and operating expenses were to fail, we cannot provide any assurances that such governmental agencies would take action to protect our uninsured deposits in a similar manner.

We also maintain investment accounts in which we hold our investments and, if access to the funds we use for working capital and operating expenses is impaired, we may not be able to open new operating accounts or to sell investments or transfer funds from our investment accounts to new operating accounts on a timely basis sufficient to meet our operating expense obligations.

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

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

We concentrated our efforts and therapeutic product research on stabilized cell-permeating alpha-helical peptide technology. Neither we nor any other company has received marketing approval to market therapeutics utilizing stabilized cell-permeating peptides. The scientific discoveries that formed 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 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. In addition, 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.

Moreover, we believe 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 was the first and only product candidate in clinical development that could 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 were 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 and healthy normal cells outside of the bone marrow is a novel approach and we believe that we were the only company 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 limited. Even though ALRN-6924 has demonstrated positive results in some preclinical studies and clinical trials, if we had continued product development of ALRN-6924, we may not have succeeded 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 would have the expected effect on patients receiving chemotherapy in any cancer indications and whether ALRN-6924 could or would demonstrate the safety and efficacy needed to advance in clinical development and obtain marketing approval.

We were dependent on the success of ALRN-6924 and there was no guarantee that our clinical trials of ALRN-6924 would have been successful.

We invested a substantial portion of our efforts and financial resources in the research and development of ALRN-6924 as a chemoprotective agent, and our business depended entirely on the successful development and commercialization of ALRN-6924.

If we had decided to continue the development of ALRN-6924, instead of ceasing clinical development of ALRN-6924, we would have been required to conduct additional clinical development, preclinical and manufacturing activities, obtained marketing approval in multiple jurisdictions and established commercial capabilities before we could have generated any revenues from product sales. We were not permitted to market or promote ALRN-6924 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 have received such marketing approvals.

The success of ALRN-6924 would have been dependent on several factors, including the following:

- successful and timely patient enrollment and completion of preclinical studies and clinical trials of ALRN-6924;
- 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 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
- the ability to compete with other therapies.

We were pursuing the development of ALRN-6924 in combination with other approved chemotherapeutics. If the FDA revoked approval of any such therapeutic, or if safety, efficacy, manufacturing or supply issues arose with any therapeutic that we used in combination with ALRN-6924, we would have been unable to further develop and/or market ALRN-6924, or we may have experienced significant regulatory delays.

We were pursuing the development of ALRN-6924 in combination with approved chemotherapeutics. We did not develop or obtain regulatory approval for, and we do not manufacture or sell, any of these approved chemotherapeutics. If the FDA revoked its approval of any of these therapeutics, we would not have been able to continue clinical development of or market ALRN-6924 in combination with such revoked therapeutic. If safety or efficacy issues arose with these or any other therapeutics that we sought to combine with ALRN-6924, we would have experienced significant regulatory delays, and the FDA may have required 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 pursued approval, such approval could have impacted the feasibility and design of any subsequent clinical trials that we may have sought to conduct evaluating ALRN-6924 in combination with such therapeutic. If manufacturing, cost or other issues resulted in a supply shortage of these therapeutics or any other combination therapeutics, we may not have been able to complete clinical development of ALRN-6924.

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

Even if ALRN-6924 received regulatory approval and was commercialized for use in combination with an approved chemotherapeutic, we would have continued 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 have resulted in ALRN-6924, 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 clinical trials may not satisfy the requirements of the FDA or comparable foreign regulatory authorities.

Clinical trials may produce negative or inconclusive results, such as the initial results of our most recent Phase 1b trial of ALRN-6924. 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,

such as the results of our Phase 1b trial of ALRN-6924 in patients with small cell lung cancer, may not be predictive of the success of later-stage clinical trials in the same or different indications, including in patients with non-small cell lung cancer and breast cancer.

Interim or preliminary data from clinical trials may not be indicative of the final results of the trial and there is a 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. 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.

In the event that an adverse safety issue, clinical hold or other adverse finding occurred in one or more of our clinical trials of ALRN-6924, such event could have adversely affected our 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 have adversely affected our clinical trials of ALRN-6924.

Further, ALRN-6924 may not have been approved even if it achieved its primary endpoints in Phase 3 clinical trials or registration trials. The FDA or non-U.S. regulatory authorities may have disagreed with our trial design, including the lack of a concurrent control arm or the use of historical controls, and our interpretation of data from preclinical studies and clinical trials.

In addition, any of these regulatory authorities may have also approved ALRN-6924 for fewer or more limited indications than we requested or may have granted approval contingent on the performance of costly post-marketing clinical trials. In addition, the FDA or other non-U.S. regulatory authorities may not have approved the labeling claims that we believed would be necessary or desirable for the successful commercialization of ALRN-6924.

Before obtaining marketing approvals for the commercial sale of any product candidate for a target indication, we would have been required to demonstrate with substantial evidence gathered in preclinical studies and well-controlled clinical trials, 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 would consider any clinical trials to be sufficient to serve as the basis for approval of ALRN-6924 for any indication. The FDA and non-U.S. regulatory authorities retain broad discretion in evaluating the results of clinical trials and in determining whether the results demonstrate that a product candidate is safe and effective.

Clinical drug development is a lengthy and expensive process, with an uncertain outcome.

Before obtaining marketing approval from regulatory authorities for the sale of ALRN-6924, we would have needed to complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of ALRN-6924. 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. For example, in February 2023, we discontinued further development of ALRN-6924 based on initial results from our Phase 1b breast cancer trial. 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.

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

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

Clinical trials are subject to numerous unforeseen events that could delay or prevent the ability to receive marketing approval or commercialize products, including:

- feedback from regulatory authorities that requires modifications to the design of clinical trials;
- clinical trials may produce negative or inconclusive results, and we or third party collaborators 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 may be larger than anticipated, enrollment may be slower than anticipated or participants may drop out of clinical trials at a higher rate than anticipated;
- third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations in a timely manner, or at all;
- clinical investigators might have to suspend or terminate clinical trials for various reasons, including non-compliance with regulatory requirements, a finding of 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 may be greater than anticipated;
- the supply or quality of a product candidate or other materials necessary to conduct clinical trials may be insufficient or inadequate; and
- regulators may revise the requirements for approving a product candidate, or such requirements may not be as anticipated.

We conducted clinical trials of ALRN-6924 at sites outside the United States. The FDA may not accept data from clinical trials conducted in such locations.

We conducted clinical trials of ALRN-6924 at clinical 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 did not accept

the data from any trial that we conducted outside the United States, there could be a need for additional clinical trials, which would be costly and time-consuming.

Other risks inherent in conducting international clinical trials or using international trial sites include:

- foreign regulatory requirements that could restrict or limit the ability to conduct clinical trials;
- the administrative burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatment;
- the failure of enrolled patients to adhere to clinical protocols or inadequate collection and assessment of clinical data as a result of differences in healthcare services or cultural customs;
- foreign exchange fluctuations and potentially high inflation rates;
- diminished or loss of protection of intellectual property in the relevant jurisdiction; and
- political, economic, environmental, and health risks relevant to specific foreign countries, including risks related to natural disasters or disease outbreaks, including the current the COVID-19 pandemic.

Delays or difficulties in the enrollment of patients in clinical trials, could delay or prevent receipt of necessary marketing approvals

The ability to initiate or continue clinical trials dependent upon the ability 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. In particular, because our chemoprotection clinical trials were targeted at a subset of patients in indications with p53-mutated cancers and our anti-cancer clinical trials were targeted at a subset of patients in indications with wild-type 53, our ability to enroll eligible patients was limited.

In addition, physicians were often not willing to advise patients to enroll in our clinical trials of ALRN-6924 in the absence of placebo-controlled data showing that treating patients with ALRN-6924 in combination with chemotherapy does not adversely affect the effectiveness of the chemotherapy. As a result of the unwillingness of physicians to enroll patients in our trials in these circumstances, we had opened fewer clinical trial sites in the United States than initially planned.

Patient enrollment may be affected if competitors have ongoing clinical trials for product candidates that are under development for the same indications, and patients who would have otherwise been eligible for clinical trials instead enrolled in clinical trials of 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.

If serious adverse or unacceptable side effects were identified during the development of ALRN-6924 or we observed limited efficacy of ALRN-6924, we may have needed to abandon or limit the development of ALRN-6924 for those reasons.

Adverse events or undesirable side effects caused by, or other unexpected properties of, ALRN-6924 could have caused us, an institutional review board, or IRB, or regulatory authorities to interrupt, delay or halt clinical trials and could have resulted 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 included cancer patients who were very sick and whose health was deteriorating, and we expect that additional clinical trials of ALRN-6924, if conducted, would have included similar patients with deteriorating health. It is possible that some of these patients might have died prior to their completion of the 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. Even if the deaths were not related to ALRN-6924, the deaths could affect perceptions regarding the safety of ALRN-6924.

If ALRN-6924 or any product candidate 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, trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order further development to cease or deny approval for any or all targeted indications. In addition, development of ALRN-6924 or such product candidate could be limited 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.

The FDA or comparable foreign regulatory authorities may, under certain circumstances, require that a companion diagnostic be approved for use with ALRN-6924. If approval of a companion diagnostic were required, and a diagnostic could not be successfully developed and approval could not be obtained or there were significant delays in doing so, marketing approval for ALRN-6924 may not be obtained in a timely manner, or at all.

We expect that the FDA and comparable foreign regulator authorities would, under certain circumstances, require a companion in vitro diagnostic to identify cancer patients with mutated p53 or wild-type p53 approved for use with ALRN-6924. We relied upon commercially available third-party assays and employed 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.

The process of obtaining or creating such diagnostic is time consuming and costly. Companion diagnostics, which provide information that is essential for the safe and effective use of a corresponding therapeutic product, are subject to regulation by the FDA, EMA and other comparable foreign regulatory authorities as medical devices and require separate regulatory approval from therapeutic approval prior to commercialization. The FDA previously has required in vitro companion diagnostics intended to select the patients who will respond to a product candidate to obtain pre-market approval, or PMA, simultaneously with approval of the therapeutic candidate. The PMA process, including the gathering of preclinical studies and clinical trial data and the submission and review by the FDA, can take several years or longer. It involves a rigorous pre-market 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. After a device is placed on the market, it remains subject to significant regulatory requirements, including requirements governing development, testing, manufacturing, distribution, marketing, promotion, labeling, import, export, record-keeping, and adverse event reporting.

Given our limited experience in developing and commercializing diagnostics, we did not engage in efforts to develop companion diagnostics internally and thus would have been dependent on the sustained cooperation and effort of third-party collaborators in developing and obtaining approval for these companion diagnostics. We and any future collaborator could encounter difficulties in developing and obtaining approval for companion diagnostics, including issues relating to selectivity/specificity, analytical validation, reproducibility, or clinical validation. In

addition, we or third parties may have encountered production difficulties that could constrain the supply of the companion diagnostics, and both they and we have had difficulties gaining acceptance of the use of the companion diagnostics by physicians.

We believe that adoption of screening and treatment into clinical practice guidelines is important for payer access, reimbursement, utilization in medical practice and commercial success, but both our collaborators and we may have had difficulty gaining acceptance of the companion diagnostic into clinical practice guidelines. If such companion diagnostics failed to gain market acceptance, it would have had an adverse effect on our ability to derive revenues from sales, if any, of any of our product candidates that were approved for commercial sale. In addition, any third party with whom we contracted may have decided not to commercialize or to discontinue selling or manufacturing the companion diagnostic that we anticipated using in connection with development and commercialization of ALRN-6924, or our relationship with such third party may otherwise have terminated. We may not have been able to enter into arrangements with another provider to obtain supplies of an alternative diagnostic test for use in connection with the development and commercialization of ALRN-6924 or do so on commercially reasonable terms, which could have adversely affected and/or delayed the development or commercialization of ALRN-6924.

Accordingly, 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.

If ALRN-6924 received marketing approval and we, or others, later discovered that the drug was less effective than previously believed or caused undesirable side effects that were not previously identified, the ability to market the drug could have been compromised.

Clinical trials must be conducted in carefully defined subsets of patients who have agreed to enter into clinical trials. Consequently, it is possible that clinical trials 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 ALRN-6924 had received marketing approval and we, or others, discovered that the drug was less effective than previously believed or caused undesirable side effects that were not previously identified, a number of potentially significant negative consequences could have resulted, including:

- regulatory authorities may have withdrawn their approval of the drug or seize the drug;
- we or any future collaborators may have been required to recall the drug, change the way the drug is administered or conduct additional clinical trials;
- additional restrictions may have been imposed on the marketing of, or the manufacturing processes for, the particular drug;
- we may have been subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may have required the addition of labeling statements, such as a “black box” warning or a contraindication;
- we, or any future collaborators, may have been 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 have been sued and held liable for harm caused to patients;
- the drug may have become less competitive; and
- our reputation may have suffered.

Even if ALRN-6924 received marketing approval, it may have failed 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 received marketing approval, it may have nonetheless failed 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 not be willing to utilize chemoprotective agents in combination with effective anti-cancer therapies.

The degree of market acceptance of ALRN-6924, if approved for commercial sale, would have depended 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.

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 targeted at treating and reducing chemotherapy-induced toxicity specifically, are highly competitive and characterized by rapidly advancing technologies, evolving understanding of disease etiology and a strong emphasis on proprietary drugs. ALRN-6924 faced competition 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 and for prevention of chemotherapy-induced toxicities. 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 and chemotherapy-induced toxicities,. Many of the companies that we competed against had 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 did. Small or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also may have competed with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or that may be necessary for, our programs.

The commercial opportunity of ALRN-6924 could be reduced or eliminated if competitors develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive. Competitors also may obtain FDA or other regulatory approval for their drugs more rapidly t. The key competitive factors affecting the success of ALRN-6924, if approved, were 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.

We are aware of another company that is actively developing agents to reduce chemotherapy-induced toxicities, G1 Therapeutics, Inc. In addition, ALRN-6924 may compete with multiple approved drugs or drugs that may be approved in the future, such as plinabulin which is being developed by BeyondSpring Inc. for the treatment of chemotherapy-induced neutropenia.

If the FDA or comparable foreign regulatory authorities approved generic versions of any of our drugs that received marketing approval, or such authorities did not grant our drugs appropriate periods of data or market exclusivity before approving generic versions of our drugs, the sales of our drugs could have been 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 have faced from generic versions of our drugs could have materially and adversely impacted our future revenue, profitability and cash flows and substantially limited our ability to obtain a return on the investments we made in those drug candidates. Our future revenues, profitability and cash flows could also have been materially and adversely affected and our ability to obtain a return on the investments we made in those drug candidates may have been substantially limited if our drugs, if and when approved, were not afforded the appropriate periods of non-patent exclusivity.

Even if we were able to commercialize any product candidate, such product candidate may have 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 have obtained marketing approval for a product in a particular country, but then be subject to price regulations that delayed our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we were able to generate from the sale of the product in that country. Adverse pricing limitations may have hindered our ability to recoup our investment in ALRN-6924, even if ALRN-6924 obtained marketing approval.

Our ability to commercialize any products successfully also would have depended in part on the extent to which reimbursement and coverage for these products and related treatments would have been available from government authorities, private health insurers and other organizations, and if reimbursement and coverage was 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 could not be sure that reimbursement would be available for any drug that we commercialized and, if reimbursement was available, we could not be sure as to the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product candidate for which we may have obtained marketing approval. If reimbursement was not available or was available only to limited levels, we may not have been able to successfully commercialize any product candidate for which we obtained 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 may have developed and for which we obtained marketing approval could have had 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 liability claims 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 ALRN-6924 in clinical trials. If we cannot successfully defend ourselves against claims that ALRN-6924 caused injuries, we will incur substantial liability claims. 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 clinical 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 liability claims that we may incur. 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 claims that may arise.

Governments outside of the United States tend to impose strict price controls, which may have adversely affected 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 have been required to conduct a clinical trial or other studies that compare the cost-effectiveness of ALRN-6924 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 have been materially harmed.

Risks Related to Our Dependence on Third Parties

We contracted with third parties for the manufacture of ALRN-6924. This reliance on third parties increased the risk that we would not have sufficient quantities of ALRN-6924 or access to such quantities at an acceptable cost.

We do not have any manufacturing facilities or personnel. We relied on third-party manufacturers for the manufacture of ALRN-6924 for clinical trials under the guidance of members of our organization. We obtained the active pharmaceutical ingredient, or API, of ALRN-6924 from one third-party manufacturer. We 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 purchased our required drug supplies on a purchase order basis.

We expected to rely on third-party manufacturers or third-party collaborators for the manufacture of the commercial supply of ALRN-6924 if it obtained marketing approval. Even if we established agreements with third-party manufacturers, reliance on third-party manufacturers entailed additional risks, including:

- the possible failure of the third party to manufacture ALRN-6924 according to our schedule, or at all, including if our third-party contractors gave greater priority to the supply of other products over ALRN-6924 or otherwise did 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 ALRN-6924 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 drugs must be approved by the FDA pursuant to inspections that will be conducted after we submit an NDA to the FDA. We would not have had complete control over all aspects of the manufacturing process of, and would have been 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 could not successfully manufacture material that conformed to our specifications and the strict regulatory requirements of the FDA or others, they would not have been able to secure and/or maintain marketing approval for their manufacturing facilities. In addition, we would not have had 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 did not approve these facilities for the manufacture of ALRN-6924 or if it withdrew any such approval, we would have needed to find alternative manufacturing facilities, which would have significantly impacted our ability to develop, obtain marketing approval for or market ALRN-6924, if approved. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could have resulted 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.

ALRN-6924 would have competed 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.

Risks Related to Our Intellectual Property

The value of our business and platform technology 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.

The value of ALRN-6924 and our platform technology will depend in large part on obtaining and maintaining patent, trademark and trade secret protection of our proprietary technologies and ALRN-6924, its components, formulations, methods used to manufacture it 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. 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.

Prior to our February 2023 decision to discontinue development of ALRN-6924, the growth of our business depended in part on our ability to acquire or in-license additional proprietary rights. Our product candidates may also have required specific formulations to work effectively and efficiently. These formulations may have been covered by intellectual property rights held by others. We may have developed products containing our compounds and pre-existing pharmaceutical compounds. These pharmaceutical compounds may have been covered by intellectual property rights held by others. We may have been 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 have been unable to acquire or in-license any relevant third-party intellectual property rights that we identified as necessary or important to our business operations. We may have failed to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all, which would have harmed our business. We may have needed to cease use of the compositions or methods covered by such third-party intellectual property rights, and may have needed to seek to develop alternative approaches that did not infringe on such intellectual property rights which may have entailed additional costs and development delays, even if we were able to develop such alternatives, which may not have been feasible. Even if we were able to obtain a license under such intellectual property rights, any such license may not have been non-exclusive, which may have allowed our competitors access to the same technologies licensed to us.

Additionally, we had collaborated with academic institutions to accelerate our preclinical research or development under written agreements with these institutions. In certain cases, these institutions provided 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 have been unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we were unable to do so, the institution may have offered the intellectual property rights to others, potentially blocking our ability to pursue our program. If we were unable to successfully obtain rights to required third-party intellectual property or to maintain the existing intellectual property rights we have, we may have had to abandon development of such program and our business and financial condition could have 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 have considered 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.

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. 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 ALRN-6924 but that are not covered by the claims of our patents;
- the active pharmaceutical ingredients in ALRN-6924 may 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 ALRN-6924;
- 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 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 ALRN-6924 are expected to expire on various dates from 2024 through 2033, including a composition of matter patent that we own covering 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 2024 through 2040, 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 ALRN-6924. 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 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 prior development of ALRN-6924 or our other ongoing programs at that time. 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 depended upon our ability to develop, manufacture, market and sell ALRN-6924 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 ALRN-6924. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that others may assert ALRN-6924 infringes 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 candidate, 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 ALRN-6924 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 ALRN-6924, 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 ALRN-6924 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 ALRN-6924 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 ALRN-6924 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 ALRN-6924 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.

Our internal information technology systems may fail or suffer security breaches, loss of data and other disruptions, which could result in a material disruption of our programs, compromise sensitive information related to our business or prevent us from accessing critical information, trigger contractual and legal

obligations, potentially exposing us to liability, reputational harm or otherwise adversely affecting our business and financial results.

We are dependent upon information technology systems, infrastructure and data to operate our business. In the ordinary course of business, we collect, store and transmit confidential information, including but not limited to intellectual property, proprietary business information and personal information. It is critical that we, our vendors, contractors and consultants, do so in a secure manner to maintain the availability, security, confidentiality, privacy and integrity of such confidential information.

Despite the implementation of security measures, our internal information technology systems and those of any vendors, contractors or consultants are vulnerable to damage or interruption from computer viruses, computer hackers, malicious code, employee error, theft or misuse, denial-of-service attacks, sophisticated nation-state and nation-state-supported actors, unauthorized access, natural disasters, terrorism, wars or other armed conflict, telecommunication and electrical failures or other compromise. There could be an increase in cybersecurity attacks generally as a result of the ongoing conflict between Russia and Ukraine and the resulting sanctions imposed by the United States and European governments, together with any additional future sanctions or other actions by them.

Cyber-attacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyber-attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, unauthorized access to or deletion of files, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. Cyber-attacks also could include phishing attempts or e-mail fraud to cause payments or information to be transmitted to an unintended recipient. We may not be able to anticipate all types of security threats, and we may not be able to implement preventive measures effective against all such security threats. The techniques used by cyber criminals change frequently, may not be recognized until launched, and can originate from a wide variety of sources, including outside groups such as external service providers, organized crime affiliates, terrorist organizations or hostile foreign governments or agencies. We cannot guarantee that the measures we have taken to date, and actions we may take in the future, will be sufficient to prevent any future breaches.

To the extent we experience a material system failure, accident, cyber-attack or security breach, it could result in a material disruption of our business operations, whether due to a loss of our trade secrets or other proprietary or confidential information or other disruptions. If we do not allocate and effectively manage the resources necessary to build and sustain the proper technology and cybersecurity infrastructure, we could suffer significant business disruption, including transaction errors, supply chain or manufacturing interruptions, processing inefficiencies, data loss or the loss of or damage to intellectual property or other proprietary information.

To the extent that any disruption or security breach were to result in a loss of, or damage to, our or our vendors', contractors' or consultants' data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, including litigation exposure, penalties and fines, we could become the subject of regulatory action or investigation, and our competitive position and reputation could be harmed. As a result of such an event, we may be in breach of our contractual obligations. Furthermore, any such event that leads to unauthorized access, use, or disclosure of personal information, including personal information regarding our customers or employees, could harm our reputation, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information, which could result in significant legal and financial exposure and reputational damages. Any of the above could have a material adverse effect on our business, financial condition, results of operations or prospects.

The financial exposure from the events referenced above could either not be insured against or not be fully covered through any insurance that we maintain and could have a material adverse effect on our business, financial condition, results of operations or prospects. In addition, we cannot be sure that our existing insurance coverage will continue to be available on acceptable terms or that our insurers will not deny coverage as to any future claim. There can be no assurance that the limitations of liability in our contracts would be enforceable or adequate or would otherwise protect us from liabilities or damages as a result of the events referenced above.

Risks Related to Marketing Approval and Other Legal Compliance Matters

Even if we completed the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may have prevented us from obtaining approvals for the commercialization of ALRN-6924.

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 are not permitted to market ALRN-6924 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. We have not submitted an application for or received marketing approval for ALRN-6924 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 ALRN-6924 is not safe and effective, only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that would have precluded our obtaining marketing approval or prevented or limited commercial use. Any marketing approval we ultimately may have obtained may have been limited or subject to restrictions or post-approval commitments that rendered the approved product not commercially viable.

ALRN-6924 could have failed to receive marketing approval for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may have disagreed with the design or implementation of our clinical trials;
- we may have been unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate was safe and effective for its proposed indication;
- the results of clinical trials may not have met the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may have been unable to demonstrate that a product candidate's clinical and other benefits outweighed its safety risks;
- the FDA or comparable foreign regulatory authorities may have disagreed with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of ALRN-6924 may not have been 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 have failed to approve the manufacturing processes or facilities of third-party manufacturers with which we contracted for clinical and commercial supplies;
- the FDA or comparable foreign regulatory authorities may have failed to approve any companion diagnostics that may have been 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 have significantly changed in a manner rendering our clinical data insufficient for approval.

This lengthy approval process as well as the unpredictability of clinical trial results may have resulted in our failing to obtain marketing approval to market ALRN-6924, which would have significantly harmed 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 have refused to accept any application or decided 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 for ALRN-6924 may have been limited or subject to restrictions or post-approval commitments that render the approved drug not commercially viable.

Failure to obtain marketing approval in foreign jurisdictions would have prevented ALRN-6924 from being marketed abroad. Any approval we may have been granted for ALRN-6924 in the United States would not have assured approval of ALRN-6924 in foreign jurisdictions.

In order to market and sell products in the European Union and many other foreign jurisdictions, separate marketing approvals must be obtained and numerous and varying regulatory requirements must be complied with. 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 third-party collaborators may not have obtained 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 have been able to file for marketing approvals and may not have received necessary approvals to commercialize our products candidates in any market.

Additionally, we could have faced heightened risks with respect to seeking marketing approval in the United Kingdom as a result of the withdrawal of the United Kingdom from the European Union, commonly referred to as Brexit. The United Kingdom is no longer part of the European Single Market and European Union Customs Union. As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or the MHRA, became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law, whereas Northern Ireland will continue to be subject to European Union rules under the Northern Ireland Protocol. The MHRA will rely on the Human Medicines Regulations 2012 (SI 2012/1916) (as amended), or the HMR, as the basis for regulating medicines. The HMR has incorporated into the domestic law of the body of European Union law instruments governing medicinal products that pre-existed prior to the United Kingdom’s withdrawal from the European Union.

Since a significant proportion of the regulatory framework for pharmaceutical products in the U.K. covering the quality, safety, and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales, and distribution of pharmaceutical products is derived from EU directives and regulations, Brexit may have a material impact upon the regulatory regime with respect to the development, manufacture, importation, approval and commercialization of product candidates in the U.K. For example, the U.K. is no longer covered by the centralized procedures for obtaining EU-wide marketing authorization from the EMA, and a separate marketing authorization will be required to market product candidates in the U.K. Until December 31, 2023, it is possible for the MHRA to rely on a decision taken by the European Commission on the approval of a new marketing authorization via the centralized procedure.

Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may have forced us to restrict or delay efforts to seek regulatory approval in the United Kingdom for our product candidates, which would have significantly and materially harmed our business.

Even if we obtained marketing approvals for ALRN-6924, the terms of approvals and ongoing regulation of our drugs could have required substantial expenditure of resources and may have limited how we manufactured and marketed our drugs, which would have materially impaired 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. Requirements concerning advertising and promotion must also be complied with. 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. In September 2021, the FDA published final regulations which describe the types of evidence that the FDA will consider in determining the intended us of a drug product.

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 and any contract manufacturers could have been subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMPs.

Accordingly, if we received marketing approval for one or more of our product candidates, we and any contract manufacturers would have continued to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control.

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

Inadequate funding for the FDA, the SEC and other government agencies, including from government shut downs, or other disruptions to these agencies' operations, could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business relied, which could have negatively impacted our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would have adversely affected our business. In addition, government funding of the SEC and other government agencies on which our operations may relied, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would have adversely affected our business. For example, over the last several years the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have had a material adverse effect on our business. Further, future government shutdowns could have impacted our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Separately, in response to the COVID-19 pandemic, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. As of early 2022, the FDA has resumed inspections of domestic and foreign facilities to ensure timely reviews of applications for medical products. However, the FDA may not be able to continue its current pace and review timelines could be extended, including where a pre-approval inspection or an inspection of clinical sites is required. Moreover, on January 30, 2023, the Biden administration announced that it will end the public health emergency declarations related to COVID-19 on May 11, 2023. On January 31, 2023, the FDA indicated that it would soon issue a Federal Register notice describing how the termination of the public health emergency will impact the agency's COVID-19 related guidance. Regulatory authorities outside the U.S. have adopted or may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities

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

If ALRN-6924 received marketing approval, it would have been subject to substantial penalties if weor any future collaborator failed to comply with regulatory requirements or experienced unanticipated problems following approval.

If ALRN-6924had received marketing approval, ALRN-6924 would have been 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 ALRN-6924 was not marketed for the indications for which it received marketing approval , we or any future collaborator may have been 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 have yielded 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 submitted;
- recall of drugs;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- 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.

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

Recently enacted and future legislation may have increased the difficulty and cost to obtain marketing approval of and commercialize ALRN-6924 and affected the prices at which of ALRN-6924 may have been sold.

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 have prevented or delayed marketing approval of ALRN-6924, restricted or regulated post-approval activities and affected the ability to profitably sell ALRN-6924. 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 have received for any approved products. If reimbursement of our products was unavailable or limited in scope, our business could have been 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 2031 under the CARES Act. These Medicare sequester reductions were suspended through the end of June 2022, with the full 2% cut resuming thereafter. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise have affected the prices we may have obtained for ALRN-6924 for which we may have obtained regulatory approval or the frequency with which any such product candidate is prescribed or used. Indeed, under current legislation, the actual reductions in Medicare payments may vary up to 4%.

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 to a case challenging the ACA. On February 10, 2021, the Biden Administration withdrew the federal government's support for overturning the ACA. On June

17, 2021, the Supreme Court rejected this challenge to the ACA. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The Trump Administration also took executive actions to undermine or delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. 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.

We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we may have received for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might have brought to market. Reductions in reimbursement levels may negatively impact the prices we may have received or the frequency with which our products would have been prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. Accordingly, such reforms, if enacted, could have had an adverse effect on anticipated revenue from product candidates that we may have successfully developed and for which we may have obtained marketing approval and may have affected our overall financial condition and ability to develop or commercialize product candidates.

The prices of prescription pharmaceuticals in the United States and foreign jurisdictions are subject to considerable legislative and executive actions and could impact the prices we may have obtained for products, if and when licensed.

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

In addition, in October 2020, HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program, or SIP, to import certain prescription drugs from Canada into the United States. The final rule is currently the subject of ongoing litigation, but at least six states (Vermont, Colorado, Florida, Maine, New Mexico, and New Hampshire) have passed laws allowing for the importation of drugs from Canada with the intent of developing SIPs for review and approval by the FDA. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The final rule would eliminate the current safe harbor for Medicare drug rebates and create new safe harbors for beneficiary point-of-sale discounts and pharmacy benefit manager ("PBM") service fees. It originally was set to go into effect on January 1, 2022, but with passage of the Inflation Reduction Act has been delayed by Congress to January 1, 2032.

On July 9, 2021, President Biden signed Executive Order 14063, which focuses on, among other things, the price of pharmaceuticals. The Order directs the Department of Health and Human Services, or HHS, to create a plan within 45 days to combat "excessive pricing of prescription pharmaceuticals and enhance domestic pharmaceutical

supply chains, to reduce the prices paid by the federal government for such pharmaceuticals, and to address the recurrent problem of price gouging." On September 9, 2021, HHS released its plan to reduce pharmaceutical prices. The key features of that plan are to: (a) make pharmaceutical prices more affordable and equitable for all consumers and throughout the health care system by supporting pharmaceutical price negotiations with manufacturers; (b) improve and promote competition throughout the prescription pharmaceutical industry by supporting market changes that strengthen supply chains, promote biosimilars and generic drugs, and increase transparency; and (c) foster scientific innovation to promote better healthcare and improve health by supporting public and private research and making sure that market incentives promote discovery of valuable and accessible new treatments.

More recently, on August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law by President Biden. The new legislation has implications for Medicare Part D, which is a program available to individuals who are entitled to Medicare Part A or enrolled in Medicare Part B to give them the option of paying a monthly premium for outpatient prescription drug coverage. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of Health and Human Services (HHS) to implement many of these provisions through guidance, as opposed to regulation, for the initial years.

Specifically, with respect to price negotiations, Congress authorized Medicare to negotiate lower prices for certain costly single-source drug and biologic products that do not have competing generics or biosimilars and are reimbursed under Medicare Part B and Part D. CMS may negotiate prices for ten high-cost drugs paid for by Medicare Part D starting in 2026, followed by 15 Part D drugs in 2027, 15 Part B or Part D drugs in 2028, and 20 Part B or Part D drugs in 2029 and beyond. This provision applies to drug products that have been approved for at least 9 years and biologics that have been licensed for 13 years, but it does not apply to drugs and biologics that have been approved for a single rare disease or condition. Nonetheless, since CMS may establish a maximum price for these products in price negotiations, we would have been fully at risk of government action if our products were the subject of Medicare price negotiations. Moreover, given the risk that could be the case, these provisions of the IRA may also have further heightened the risk that we would not have been able to achieve the expected return on our drug products or full value of our patents protecting our products if prices are set after such products had been on the market for nine years.

Further, the legislation subjects drug manufacturers to civil monetary penalties and a potential excise tax for failing to comply with the legislation by offering a price that is not equal to or less than the negotiated "maximum fair price" under the law or for taking price increases that exceed inflation. The legislation also requires manufacturers to pay rebates for drugs in Medicare Part D whose price increases exceed inflation. The new law also caps Medicare out-of-pocket drug costs at an estimated $4,000 a year in 2024 and, thereafter beginning in 2025, at 2,000 a year. In addition, the IRA potentially raises legal risks with respect to individuals participating in a Medicare Part D prescription drug plan who may experience a gap in coverage if they required coverage above their initial annual coverage limit before they reached the higher threshold, or "catastrophic period" of the plan. Individuals requiring services exceeding the initial annual coverage limit and below the catastrophic period, must pay 100% of the cost of their prescriptions until they reach the catastrophic period. Among other things, the IRA contains many provisions aimed at reducing this financial burden on individuals by reducing the co-insurance and co-payment costs, expanding eligibility for lower income subsidy plans, and price caps on annual out-of-pocket expenses, each of which could have potential pricing and reporting implications

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 healthcare organizations and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. These measures could have reduced 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 have resulted in reduced demand for our product candidates or additional pricing pressures.

In the E.U., similar political, economic and regulatory developments may have affected our ability to profitably commercialize our product candidates, if approved. In markets outside of the U.S. and the E.U., reimbursement and healthcare payment systems vary significantly by country and many countries have instituted price ceilings on specific products and therapies. In many countries, including those of the E.U., the pricing of prescription pharmaceuticals is subject to governmental control and access. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we or our collaborators may have been required to conduct a clinical trial that compares the cost-effectiveness of our product to other available therapies. If reimbursement of our products was unavailable or limited in scope or amount or if pricing was set at unsatisfactory levels, our business could have been materially harmed.

We may have needed to seek to obtain certain regulatory designations for ALRN-6924. We may not have received such designations, and even if we did, such designation may not have led to a faster development or regulatory review or approval process.

We may have needed to 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 have approved any application that we submitted. 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.

If we had continued development of ALRN-6924, our relationships with healthcare providers, physicians and third-party payors would have been subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could have exposed us to penalties, including criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

If we had continued development of ALRN-6924, our relationships with healthcare providers, physicians and third-party payors would have been subject to additional healthcare statutory and regulatory requirements and enforcement by the federal government and the states and foreign governments. Arrangements with healthcare providers, physicians and third-party payors and patients may have exposed us to broadly applicable fraud and abuse and other healthcare laws and regulations that may have constrained the business or financial arrangements and relationships through which we would have marketed, sold and distributed our products. 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, other healthcare providers 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 would comply with applicable healthcare laws and regulations would involve substantial costs. It is possible that governmental authorities would 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 were found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may have been 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 would cause us to incur significant legal expenses and would divert our management's attention from the operation of our business, even if our defense was successful. If any of the physicians or other healthcare providers or entities with whom we expect to do business was found to be not in compliance with applicable laws, it may have been costly to us in terms of money, time and resources, and they may have been 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 may have involved the use of hazardous and flammable materials, including chemicals and biological materials. Our operations may also have produced hazardous waste products. We generally contracted 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 have been held liable for any resulting damages, and any liability could have exceeded our resources. We also could have incurred 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 have provided 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 could have impaired our research, development or commercialization efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

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). In November 2020 California voters passed a ballot initiative for the California Privacy Rights Act, or the CPRA, which went into effect on January 1, 2023, and significantly expanded the CCPA to incorporate additional GDPR-like provisions including requiring that the use, retention, and sharing of personal information of California residents be reasonably necessary and proportionate to the purposes of collection or processing, granting additional protections for sensitive personal information, and requiring greater disclosures related to notice to residents regarding retention of information. The CPRA also created a new enforcement agency – the California Privacy Protection Agency – whose sole responsibility is to enforce the CPRA, which will further increase compliance risk. The provisions in the CPRA may apply to some of our business activities. In addition, other states, including Virginia, Colorado, Utah, and Connecticut, already have passed state privacy laws. Virginia's privacy law also went into effect on January 1, 2023, and the laws in the other three states will go into effect later in the year. Other states will be considering these laws in the future, and Congress has also been debating passing a federal privacy law. If we decide to pursue further product development efforts, these laws may impact our business activities, including our identification of research subjects, relationships with business partners and ultimately the marketing and distribution of any products we may develop.

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 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.

Our stock price has in the past and may in the future fail to meet minimum requirements for continued listing on the Nasdaq Capital Market. Our ability to publicly or privately sell equity securities and the liquidity of our common stock could be adversely affected if we are delisted from the Nasdaq Capital Market or if we are unable to transfer our listing to another stock market.

In the past we have received written notification from the Nasdaq Stock Market, or Nasdaq, informing us that we were not in compliance with certain continued listing requirements of the Nasdaq Capital Market. As previously disclosed, on December 16, 2021, we received a deficiency letter from the Listing Qualifications Department of Nasdaq 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 Capital Market pursuant to Nasdaq Listing Rule 5550(a)(2), or the Bid Price Rule. On June 7, 2022, we received notification from Nasdaq notifying us that we were provided an additional 180 calendar day period or until December 5, 2022 to regain compliance with the Bid Price Rule.

We completed a 1-for-20 reverse stock split on our common stock on November 10, 2022. We regained compliance with the Bid Price Rule after the closing bid price of our common stock was above $1.00 per share for 10 consecutive business days from November 11, 2022 to November 25, 2022. On November 28, 2022, we received a letter from Nasdaq notifying us that we had regained compliance with the Bid Price Rule and have remained in compliance.

There can be no assurance that we will continue to maintain compliance with the requirements for listing our common stock on Nasdaq. Any potential delisting of our common stock from the Nasdaq Capital Market would likely result in decreased liquidity and increased volatility for our common stock and would adversely affect our ability to raise additional capital or to enter into strategic transactions. Any potential delisting of our common stock from the Nasdaq Capital Market would also make it more difficult for our stockholders to sell our common stock in the public market

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 16, 2023, the closing price of our common stock ranged from a high of $298.20 per share to a low of $1.30 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 success of any strategic transaction we may consummate;
- the timing and results of clinical trials of ALRN-6924;
- regulatory actions with respect to ALRN-6924 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;
- 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 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, including potential high inflation rates; 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 a "smaller reporting company" and the reduced disclosure requirements applicable to smaller reporting companies may make our common stock less attractive to investors.

We are 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. Smaller reporting companies are able to provide simplified executive compensation disclosure, are exempt from the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002 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 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. . The TCJA, as amended by the CARES Act, 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% and, the limitation of the deduction for net operating losses to 80% of current year taxable income and the elimination of loss carrybacks for losses arising in taxable years

beginning after December 31, 2017 (though any such net operating losses may be carried forward indefinitely. The CARES Act delayed the 80% net operating loss limitation and allowed losses to be carried back five years for net operating losses generated in years beginning after December 31, 2017 and before December 1, 2021. In addition, beginning in 2022, the TCJA eliminates the option to deduct research and development expenditures currently and requires corporations to capitalize and amortize them over five years.

In addition to the CARES Act, as part of Congress' response to the COVID-19 pandemic, economic relief legislation has been enacted in 2020 and 2021 containing tax provisions. The Inflation Reduction Act, or IRA, was also signed into law in August 2022. The IRA introduced new tax provisions, including a 1% excise tax imposed on certain stock repurchases by publicly traded corporations. The 1% excise tax generally applies to any acquisition by the publicly traded corporation (or certain of its affiliates) of stock of the publicly traded corporation in exchange for money or other property (other than stock of the corporation itself), subject to a de minimis exception. Thus, the excise tax could apply to certain transactions that are not traditional stock repurchases.

Regulatory guidance under the TCJA, the IRA, and such additional legislation is and continues to be forthcoming, and such guidance could ultimately increase or lessen impact of these laws on our business and financial condition. In addition, it is uncertain if and to what extent various states will conform to the TCJA, the IRA, and additional tax legislation.

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, 2022, we had federal net operating loss carryforwards of $239.6 million, of which $129.6 million will, if not utilized, begin to expire in 2029. As of December 31, 2022, we had state net operating carryforwards of $231.6 million, which will, if not utilized, begin to expire in 2030. Our federal and state research and development tax credit carryforwards of $2.7 million and $1.9 million, respectively, will, if not utilized, begin to expire in 2025 and 2026, respectively. We also have federal orphan drug tax credit carryforwards of $2.4 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, as described above in "Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition," the TCJA, as amended by the CARES Act, includes changes to U.S. federal tax rates and the rules governing net operating loss carryforwards that may significantly impact our ability to utilize our net operating losses to offset taxable income in the future.

Furthermore, 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 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. We may have experienced such ownership changes in the past and may experience such ownership changes in the future as a result of any strategic transaction. If we have experienced, or do experience, a change of control, as defined by Section 382, at any time since inception, 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 16, 2023, we had 4,541,167 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 635,000 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.

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.

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.

We lease approximately 3,365 square feet of office space at our corporate headquarters in Boston, Massachusetts. The lease commenced April 2021, and has an initial term of two years. We do not plan to renew the lease following its expiration on March 31, 2023 and plan to operate virtually.

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 16, 2023, there were approximately 29 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. [Reserved]

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

The following discussion and analysis is meant to provide material information relevant to an assessment of the financial condition and results of operations of our company, including an evaluation of the amounts and certainty of cash flows from operations and from outside sources, so as to allow investors to better view our company from management's perspective. 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. Unless otherwise indicated, all information in this Annual Report on Form 10-K gives effect to a 1-for-20 reverse stock split of our common stock that became effective on November 10, 2022, and all references to shares of common stock outstanding and per share amounts give effect to the reverse stock split.

Announcement of Exploration of Strategic Alternatives

In February 2023, we announced a review of initial data from our Phase 1b chemoprotection trial of ALRN-6924 in patients with p53-mutated breast cancer showed that patients in the trial experienced severe neutropenia (Grade 4) and alopecia. The primary endpoint of the Phase 1b open-label trial, which was evaluating ALRN-6924 in patients with breast cancer receiving neoadjuvant or adjuvant treatment with docetaxel, doxorubicin, and cyclophosphamide, or TAC chemotherapy, was duration and incidence of severe neutropenia in cycle 1. Incidence of chemotherapy-induced alopecia (hair loss) was a secondary endpoint. Based on these findings, we have decided to terminate the Phase 1b breast cancer trial and further development of ALRN-6924.

We also announced that we are exploring a range of strategic alternatives to maximize shareholder value. We have engaged Ladenburg Thalmann & Co., Inc. to act as a strategic advisor for this process. Strategic alternatives that are being evaluated may include, but are not limited to, an acquisition, a merger, a business combination, a sale of assets or other transactions. There is no set timetable for this process and there can be no assurances that this process will result in us pursing a transaction or that any transaction, if pursued, will be completed on attractive terms. Due to the inherent uncertainty in the timing and cost of these potential strategic alternatives, including their impact on our cash consumption, we have concluded that as of the date of this Annual Report on Form 10-K there is substantial doubt about our ability to continue as a going concern.

In addition, we have determined to reduce our workforce from nine to three full-time employees, which we expect to complete in the second quarter of 2023. We plan to retain the remaining employees to assist in executing the strategic alternative review process.

Overview

ALRN-6924 is a MDM2/MDMX dual inhibitor that leverages our proprietary peptide drug technology.

When used as a chemoprotective agent, ALRN-6924 is designed to activate p53, which in turn upregulates p21, a known inhibitor of the cell replication cycle. ALRN-6924 was the only reported chemoprotective agent in clinical development to employ a biomarker strategy, in which we exclusively focused on treating patients with p53-mutated cancers. We originally initiated development of ALRN-6924 as an anti-cancer agent to restore p53-dependent tumor suppression in p53 wild-type tumors. When used as an anti-cancer agent, ALRN-6924 is designed to disrupt the interaction of p53 suppressors MDM2 and MDMX with tumor suppressor p53 to reactivate tumor suppression in non-mutant, or wild-type, p53 cancers.

Our clinical development program for ALRN-6924 as a selective chemoprotective agent in patients with p53-mutated cancer included the following clinical trials:

- A Phase 1b open-label clinical trial that evaluated ALRN-6924 as a chemoprotective agent in patients with p53-mutated breast cancer undergoing either neoadjuvant or adjuvant treatment with TAC chemotherapy;

- A Phase 1b open-label clinical trial that evaluated ALRN-6924 as a chemoprotective agent in patients with p53-mutated small cell lung cancer, or SCLC, undergoing treatment with second-line topotecan;
- A Phase 1 pharmacology study of ALRN-6924 in healthy volunteers that evaluated the safety and tolerability of ALRN-6924, in addition to its cell cycle arrest mechanism of action, pharmacokinetic, and pharmacodynamic effects, including time to onset, magnitude and duration of cell cycle arrest; and
- A Phase 1b randomized, double-blind, placebo-controlled clinical trial that evaluated ALRN-6924 as a chemoprotective agent in patients with p53-mutated non-small cell lung cancer, or NSCLC, undergoing first-line treatment with carboplatin plus pemetrexed with or without immune checkpoint inhibitors.

Our clinical development program for ALRN-6924 as an anti-cancer agent in patients with wild-type p53 included the following clinical trials:

- A single-agent Phase 1 clinical trial that evaluated ALRN-6924 for the treatment of patients with solid tumors and patients with lymphoma;
- A single-agent Phase 2a clinical trial that evaluated ALRN-6924 for the treatment of patients with peripheral T-cell lymphoma
- A single-agent and Ara-C-combination Phase 1/1b trial that evaluated ALRN-6924 for the treatment of patients with acute myeloid leukemia and myelodysplastic syndrome; and
- A combination trial that evaluated ALRN-6924 in combination with palbociclib for the treatment of patients with tumors harboring MDM2 amplifications.

Since our inception, we have devoted a substantial portion 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 operations primarily through $145.5 million in net proceeds from sales of common stock, $131.2 million from sales of preferred stock prior to our IPO, and $34.9 million from a collaboration agreement in 2010.

Since our inception, we have incurred significant losses on an aggregate basis. Our net losses were $27.3 million and $26.2 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of $272.8 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. In February 2023, we discontinued development of ALRN-6924 to substantially reduce our operating expenses while we undertake a comprehensive assessment of our strategic options. Notwithstanding these events, we expect to continue to incur operating losses for the foreseeable future.

Subject to the outcome of our exploration of strategic alternatives, we believe that, based on our current operating plan, our cash, cash equivalents and investments of $21.2 million as of December 31, 2022, will enable us to fund our operating expenses for at least twelve months following the date of this Annual Report on Form 10-K. Due to the inherent uncertainty in the timing and cost of these potential strategic alternatives, including their impact on our cash consumption, we have concluded that as of the date of this Annual Report on Form 10-K there is substantial doubt about our ability to continue as a going concern. 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, see “Liquidity and Capital Resources.” Our future viability is dependent on our ability to consummate a successful acquisition, merger, business combination, or a sale of assets or other transaction. If we do not, our board of directors may decide to explore other strategic alternatives, including, without limitation, a dissolution of our company.

Reverse Stock Split

On November 10, 2022, we completed a reverse stock split of our outstanding shares of common stock at a ratio of one-for-twenty. The reverse stock split was approved by our stockholders at our Annual Meeting of Stockholders on June 15, 2022. All share and per share amounts of the common stock included in this Annual Report on Form 10-K, including in the accompanying financial statements, have been retrospectively adjusted to give effect to the reverse stock split for all periods presented, including reclassifying an amount equal to the reduction in par value to additional paid-in capital.

Components of our Results of Operations

Revenue

We have not generated any revenue from product sales and, as we do not have any product candidates under development, we do not expect to generate any revenue from the sale of products in the future.

Operating Expenses

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

Research and Development Expenses

For the periods presented in this Annual Report on Form 10-K, research and development expenses consist primarily of costs incurred for our research activities, including our discovery efforts, and the development of ALRN-6924, and include:

- expenses incurred under agreements with third parties, including contract research organizations, or CROs, that conduct research, preclinical studies and clinical trials on our behalf as well as contract manufacturing organizations, or CMOs, that manufacture ALRN-6924 for use in our preclinical studies 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.

For the periods presented in this Annual Report on Form 10-K, our employee and infrastructure resources are primarily devoted to the development of ALRN-6924. 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.

In addition, 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.

Research and development activities were central to our business model. We expect our research and development expenses to decrease beginning in the first half of 2023 as our result of our February 2023 decision to discontinue development of ALRN-6924 and our related reduction in workforce.

If we had continued development of ALRN-6924, we could not determine with certainty the duration and costs of any clinical trials of ALRN-6924 or if, when, or to what extent we would generate revenue from the commercialization and sale of any of our product candidate for which we obtained marketing approval. We may never have been successful in obtaining marketing approval for any product candidate. If we had continued development of ALRN-6924, the duration, costs and timing of clinical trials and development of ALRN-6924 would depend on a variety of factors, including:

- the scope, rate of progress, expense and results of clinical trials of ALRN-6924, or other product candidates that we may have developed and other research and development activities that we may have conducted;
- 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 FDA, or another regulatory authority were to have required us to conduct clinical trials beyond those that we anticipated would be required for the completion of clinical development of a product candidate, or if we experienced significant trial delays due to patient enrollment or other reasons, we would have been 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.

We anticipate that our general and administrative expenses will decrease beginning in the first half of 2023 following our February 2023 decision to discontinue development of ALRN-6924 and the related reduction in workforce. Our future general and administrative expenses will be significantly dependent on the outcome of our strategic process

Interest Income

Interest income consists of interest income earned on our cash, cash equivalents and investments. Historically, our interest income had not been significant due to low investment balances and low interest earned on those balances. We anticipate that our interest income will fluctuate in the future in response to our cash, cash equivalents and investments, and the interest rate environment.

Other Income, net

Other income, net consists of gains or losses recognized from non-routine items such as debt forgiveness under the Paycheck Protection Program and gains or losses recognized from the disposal of fixed assets.

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, 2022, we had federal and state net operating loss carryforwards of $239.6 million and $231.6 million, respectively, which begin to expire in 2029 and 2030, respectively. As of December 31, 2022, we also had federal and state research and development tax credit carryforwards of $2.7 million and $1.9 million, respectively, which begin to expire in 2025 and 2026, respectively. We also have federal orphan drug tax credit carryforwards of $2.4 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 and similar state statutes 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. We may have experienced such ownership changes in the past and may experience such ownership changes in the future as a result of any strategic transaction. If we have experienced, or do experience, a change of control, as defined by Section 382 and similar state statutes, 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 and similar state statutes, 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.

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.

Results of Operations

Comparison of the Years Ended December 31, 2022 and 2021

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

	Year Ended December 31,		Increase (Decrease)
	2022	2021	
Revenue	$ —	$ —	$ —
Operating expenses:			
Research and development	17,967	17,008	959
General and administrative	9,680	9,597	83
Total operating expenses	27,647	26,605	1,042
Loss from operations	(27,647)	(26,605)	(1,042)
Other income (expense), net	318	441	(123)
Net loss	$ (27,329)	$ (26,164)	$ (1,165)

Research and Development Expenses

Research and development expenses for the year ended December 31, 2022 were $18.0 million, compared to $17.0 million for the year ended December 31, 2021. The increase of $1.0 million was primarily due to $3.5 million of increased spending for our terminated Phase 1b breast cancer trial, offset by reduced spending of $1.3 million for our completed healthy volunteer study, $1.0 million for our completed small cell lung cancer trial, and $0.3 million for our completed Phase 1b non-small cell lung cancer trial.

General and Administrative Expenses

General and administrative expenses were $9.7 million for the year ended December 31, 2022, compared to $9.6 million for the year ended December 31, 2021. The increase of $0.1 million in general and administrative expense was primarily a result of travel related expenses.

Other Income (Expense), net

Other income, net of $0.3 million for the year ended December 31, 2022 consisted solely of interest income.

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, and, as we do not have any product candidates under development, we do not expect to generate revenue from sales of any products. 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, sales of common stock under our equity line with Lincoln Park Capital LLC, or LPC, sales of preferred stock prior to our initial public offering and payments received under a collaboration agreement. As of December 31, 2022, we had cash, cash equivalents and investments of $21.2 million.

Public Offerings

On April 2, 2019, we issued and sold in a private placement an aggregate of (i) 591,922 units, consisting of 591,922 shares of our common stock and associated warrants, or the common warrants, to purchase an aggregate of 591,922 shares of common stock, for a combined price of $40.20 per unit and (ii) 54,837 units, consisting of (a) pre-funded warrants to purchase 54,837 shares of our common stock and (b) associated common warrants to purchase 54,837 shares of common stock, for a combined price of $40.20 per unit. The pre-funded warrants had an exercise price of $0.20 per share and had no expiration. The common warrants are exercisable at an exercise price of $40.00

per share and expire in April 2024. 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 54,837 shares of common stock.

In January 2021, we issued and sold an aggregate of 1,631,549 shares of common stock in a registered direct offering at a purchase price per share of $22.00. 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 $2.9 million.

At-the-Market Offering

In July 2019, we entered into a Sales Agreement with JonesTrading Institutional Services LLC, or JonesTrading, under which we were able to issue and sell shares of common stock, having an aggregate offering price of up to $15.0 million, or the Prior Sales Agreement. During the year ended December 31, 2020, we issued and sold an aggregate of 208,044 shares of common stock pursuant to the Prior 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 358,749 shares of common stock pursuant to the Prior Sales Agreement for gross proceeds of $9.7 million, before deducting commissions and fees. We terminated the Prior Sales Agreement in January 2021.

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 of 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. During the year ended December 31, 2021, we issued and sold an aggregate of 261,270 shares of common stock pursuant to the ATM Sales Agreement for proceeds of $10.6 million, after deducting commissions and fees, and approximately $19.4 million remained available for sale under the ATM Sales Agreement as of December 31, 2022. Pursuant to a prospectus relating to the ATM Sales Agreement we filed with the SEC on June 21, 2022, we may offer and sell shares of our common stock having an aggregate offering price of up to $14.0 million under the ATM Sales Agreement. There were no sales under the ATM Sales Agreement during the year ended December 31, 2022.

Equity Line Financing

On September 21, 2020, we entered into a purchase agreement, or the Purchase Agreement, with 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 purchase 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 18,382 shares of common stock, or the Initial Purchase Shares, to LPC at a price per share of $27.20, 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 of 11,029 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) 12,500 shares of common stock if the closing sale price of our common stock is not below $30.00 per share on Nasdaq, (ii) 10,000 shares of common stock if the closing sale price of our common stock is not below $20.00 per share on Nasdaq or (iii) 7,500 shares of common stock if the closing sale price of our common stock is below $20.00 per share on Nasdaq. In any case, LPC’s commitment in any single Regular Purchase may not exceed $1.0 million. The foregoing share amounts and per share prices will be adjusted for any reorganization, recapitalization, non-cash dividend, stock split, reverse stock split or other similar transaction.

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 $6.00 per share, which will be adjusted for any reorganization, recapitalization, non-cash dividend, stock split or other similar transaction. As of the date of this Annual Report on Form 10-K, the closing sale price of our common stock on Nasdaq is less than the floor price of $6.00 per share under the Purchase Agreement. As a result, we cannot issue and sell shares of our common stock to LPC under the Purchase Agreement, and we do not expect to be able to do so for the foreseeable future.

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, LPC 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. In the year ended December 31, 2020, we issued and sold an aggregate of 70,882 shares of common stock to LPC for gross proceeds of $1.8 million. In the year ended December 31, 2021, we issued and sold an aggregate of 68,750 shares of common stock to LPC for gross proceeds of $2.6 million. There were no sales under the Purchase Agreement during the year ended December 31, 2022.

Cash Flows

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

	Year Ended December 31,	
	2022	2021
	(in thousands)	
Cash used in operating activities	$ (24,865)	$ (23,754)
Cash (used in) provided by investing activities	26,459	(35,917)
Cash provided by financing activities	—	55,657
Net increase (decrease) in cash, cash equivalents and restricted cash	$ 1,594	$ (4,014)

Operating Activities.

During the year ended December 31, 2022, operating activities used $24.9 million of cash, primarily resulting from our net loss of $27.3 million and cash provided by the change in operating assets and liabilities of $0.4 million offset by non-cash charges of $2.0 million. Non-cash charges resulted primarily from stock-based compensation expense. Changes in our operating assets and liabilities during the year ended December 31, 2022 consisted primarily of a decrease of $1.6 million in accrued expenses and other current liabilities, a decrease of $1.6 million in prepaid expense and other assets, and an increase of $0.5 million in accounts payable.

During the year ended December 31, 2021, operating activities used $23.8 million of cash, primarily resulting from our net loss of $26.2 million and cash provided by the change in operating assets and liabilities of $0.2 million offset by non-cash charges of $2.2 million. Non-cash charges resulted primarily from stock-based compensation

expense. Changes in our operating assets and liabilities during the year ended December 31, 2021 consisted primarily of an increase of $1.0 million in accrued expenses and other current liabilities and a decrease of $0.3 million in prepaid expense and other assets, and $0.4 million in accounts payable

Investing Activities.

During the year ended December 31, 2022, investing activities provided $26.5 million of cash. We received $48.3 million of proceeds from the sale of investments, offset by $21.9 million of purchases of investments.

During the year ended December 31, 2021, investing activities used $35.9 million of cash. We received $37.8 million of proceeds from the sale of investments and $0.1 million from the sale of property and equipment offset by $73.6 million of purchases of investments.

Financing Activities.

During the year ended December 31, 2022, net cash provided by financing activities was $0 million.

During the year ended December 31, 2021, net cash provided by financing activities was $55.7 million due to the proceeds received from the sale of common stock in the first quarter of 2021.

Funding Requirements

We expect our operating expenses to decrease significantly beginning in the first half of 2023 following our February 2023 decision to discontinue development of ALRN-6924 and implement a reduction in workforce. However, we may not realize, in full or in part, the anticipated benefits and savings in operating expenses from these decisions due to unforeseen difficulties, delays or unexpected costs.

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

- whether we realize the anticipated cost savings in connection with our February 2023 workforce reduction;
- our ability to consummate a strategic transaction and the nature and type of such transaction;
- the time and costs necessary to close out our Phase 1b breast cancer trial; and
- the costs associated with operating as a public company.

If we continued to pursue development of ALRN-6924, our capital requirements would have depended on many factors, including:

- the scope, progress, results and costs of our preclinical studies, CMC, and clinical trials and ALRN-6924;
- the costs, timing and outcome of regulatory review of ALRN-6924;
- our ability to establish and maintain collaborations with third parties on favorable terms, if at all;
- the success of any collaborations that we may have entered into with third parties;
- the extent to which we acquired or invested in businesses, products and technologies, including entering into licensing or collaboration arrangements for ALRN-6924, although we currently have no commitments or agreements to complete any such transactions;
- the costs and timing of commercialization activities, including drug sales, marketing, manufacturing and distribution, for any product candidates for which we receive marketing approval; and

- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims.

Until such time, if ever, as we can generate substantial revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, or other third-party funding. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of existing stockholders. Debt financing, if available, may involve agreements that include liens or other restrictive covenants limiting our ability to take specific actions, such as incurring additional debt, making capital expenditures, or declaring dividends.

There can be no assurance that a strategic transaction will be completed and our board of directors may decide to pursue a dissolution and liquidation. In such an event, the amount of cash available for distribution to our stockholders will depend heavily on the timing of such decision and, as with the passage of time the amount of cash available for distribution will be reduced as we continue to fund our operations. In addition, if our board of directors were to approve and recommend, and our stockholders were to approve, a dissolution and liquidation, we would be required under Delaware corporate law to pay our outstanding obligations, as well as to make reasonable provision for contingent and unknown obligations, prior to making any distributions in liquidation to our stockholders. As a result of this requirement, a portion of our assets may need to be reserved pending the resolution of such obligations and the timing of any such resolution is uncertain. In addition, we may be subject to litigation or other claims related to a dissolution and liquidation. If a dissolution and liquidation were pursued, our board of directors, in consultation with our advisors, would need to evaluate these matters and make a determination about a reasonable amount to reserve. Accordingly, holders of our common stock could lose all or a significant portion of their investment in the event of a liquidation, dissolution or winding up. Due to the inherent uncertainty in the timing and cost of these potential strategic alternatives, including their impact on our cash consumption, we have concluded that as of the date of this Annual Report on Form 10-K there is substantial doubt about our ability to continue as a going concern.

If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce or terminate our strategic process and we may consider seeking protection under the bankruptcy laws in order to continue to pursue potential strategic alternatives. If we decide to seek protection under the bankruptcy laws, we would expect that we would file for bankruptcy at a time that is significantly earlier than when we would otherwise exhaust our cash resources. If we decide to dissolve and liquidate our assets or to seek protection under the bankruptcy laws, it is unclear to what extent we will be able to pay our obligations, and, it is further unclear whether and to what extent any resources will be available for distributions to stockholders.

Contractual Obligations

We lease 3,365 square feet of office space at our corporate headquarters in Boston, Massachusetts. Our remaining contractual rent commitment under this lease was less than $0.1 million as of December 31, 2022. The lease expires March 31, 2023 and we do not plan on renewing the lease. Following expiration of the lease, we plan to operate virtually. For a description of our lease obligations, refer to Note 12 to our consolidated financial statements appearing in this Annual Report on Form 10-K.

Emerging Growth Company Status

Prior to December 31, 2022, we qualified as an “emerging growth company” as defined in Section 101 of The Jumpstart Our Business Startups Act of 2012, or the JOBS Act. We ceased to qualify as an emerging growth company as of December 31, 2022, and are now subject to Section 14A(a) and (b) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, beginning with our fiscal year starting January 1, 2023. However, notwithstanding the loss of our status as an emerging growth company, we will continue to be exempt from Section 404(b) of the Sarbanes-Oxley Act of 2002 for so long as we are neither a “large accelerated filer” nor an “accelerated filer” as those terms are defined in Rule 12b-2 under the Exchange Act.

We are a “smaller reporting company” as defined in Rule 12b-2 under the Exchange Act. We may continue to be a smaller reporting company if either (i) the market value of our shares held by non-affiliates is less than $250 million or (ii) our annual revenue was less than $100 million during the most recently completed fiscal year and the

market value of our shares held by non-affiliates is less than $700 million. For so long as we continue to be a smaller reporting company, we may continue to rely on exemptions from certain disclosure requirements that are available to smaller reporting companies.

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 Interim Chief Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2022.

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, 2022. 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, 2022, 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, 2022 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

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

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 2023 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, 2022 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 2023 Annual Meeting of Stockholders and is, other than the information required by Item 402(v) of Regulation S-K, 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 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this Item 13 will be included, 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 2023 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 2023 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 on pages F2-F25 attached hereto and are filed as part of this Annual Report on Form 10-K:

Item 16. Form 10-K Summary.

None.

INDEX TO FINANCIAL STATEMENTS

(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, as amended	10-Q	8/11/2021	3.1	
3.2	Certificate of Amendment of Restated Certificate of Incorporation of the Registrant	8-K	11/10/2022	3.2	
3.3	Amended and Restated By-laws of the Registrant	8-K	7/5/2017	3.3	
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*	2021 Stock Incentive Plan	8-K	6/17/2021	99.1	
10.12*	Form of Stock Option Agreement under 2021 Stock Incentive Plan				X
10.13*	Form of Restricted Stock Unit Agreement under 2021 Stock Incentive Plan				X
10.14	Form of Director and Officer Indemnification Agreement	S-1^	6/19/2017	10.12	
10.15	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	
10.16+	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	
10.17*	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	
10.18*	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	
10.19*	Offer Letter, dated as of November 15, 2007, between the Registrant and D. Allen Annis, Ph.D.	10-K	3/29/2019	10.21	
10.20*	Severance Agreement, dated as of November 5, 2018, between the Registrant and D. Allen Annis, Ph.D.	10-K	3/29/2019	10.22	
10.21	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	
10.27	Sublease Agreement, dated March 26, 2021, by and among the Company, Vittoria Industries North America, Inc. and Waterfront Equity Partners, LLC	10-Q	5/11/2021	10.1	
10.28*	Separation and Release of Claims Agreement, dated July 8, 2022, by and between the Company and Vojislav Vukovic, M.D., Ph.D.	10-Q	8/15/2022	10.1	
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	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.				
101.SCH	Inline XBRL Taxonomy Extension Schema Document				
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document				
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document				

101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

* 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 20, 2023

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 20, 2023
/s/ Susan L. Drexler **Susan L. Drexler**	Interim Chief Financial Officer (principal financial officer and principal accounting officer)	March 20, 2023
/s/ Jeffrey A. Bailey **Jeffrey A. Bailey**	Chairman of the Board of Directors	March 20, 2023
/s/ Reinhard J. Ambros, Ph.D. **Reinhard J. Ambros, Ph.D.**	Director	March 20, 2023
/s/ William T. McKee **William T. McKee**	Director	March 20, 2023
/s/ Jodie P. Morrison **Jodie P. Morrison**	Director	March 20, 2023
/s/ Nolan Sigal, M.D., Ph.D. **Nolan Sigal, M.D., Ph.D.**	Director	March 20, 2023
/s/ Joseph H. Von Rickenbach **Joseph H. Von Rickenbach**	Director	March 20, 2023

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, 2022 and 2021, and the related statements of operations and comprehensive loss, of stockholders' equity 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, 2022 and 2021, 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.

Substantial Doubt about the Company's Ability to Continue as a Going Concern

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has incurred losses and negative cash flows from operations and had an accumulated deficit that raise substantial doubt about its ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

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

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

Critical Audit Matters

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that (i) relates to accounts or disclosures that are material to the financial statements and (ii) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates

Research Contract Costs and Accruals

As described in Notes 2 and 6 to the financial statements, research and development expenses were $18.0 million for the year ended December 31, 2022. 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, with $0.5 million recorded as of December 31, 2022 within accrued expenses and other current liabilities. 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.

The principal considerations for our determination that performing procedures relating to research contract costs and accruals is a critical audit matter are the significant judgment by management when recording accruals for estimated ongoing research costs and a high degree of auditor effort in performing procedures related to the Company's research contract costs and accruals.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the financial statements. These procedures included, among others (i) evaluating, on a sample basis, accruals for estimated ongoing research costs, by (a) testing the completeness and accuracy of costs incurred for services that have been performed and for which the Company has been invoiced by comparing amounts to third-party vendor contracts and invoices and (b) evaluating the reasonableness of the cost incurred for the services for which the Company has not yet been invoiced by comparing estimated amounts to information received from third-party vendors and (ii) testing, on a sample basis, classification of research and development expenses.

/s/ PricewaterhouseCoopers LLP
Boston, Massachusetts
March 20, 2023
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, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 5,194	$ 3,600
Investments	16,048	42,333
Prepaid expenses and other current assets	606	2,219
Restricted cash	25	25
Total current assets	21,873	48,177
Operating lease, right-of-use asset	40	152
Other non-current assets	24	24
Property and equipment, net	70	128
Total assets	$ 22,007	$ 48,481
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 1,720	$ 1,210
Accrued expenses and other current liabilities	1,631	3,205
Operating lease liabilities, current portion	33	93
Total current liabilities	3,384	4,508
Operating lease liabilities, net of current portion	—	69
Total liabilities	3,384	4,577
Commitments and contingencies (Note 12)		
Stockholders' equity:		
Preferred stock, $0.001 par value; 5,000,000 shares authorized at December 31, 2022 and December 31, 2021; no shares issued and outstanding at December 31, 2022 and December 31, 2021	—	—
Common stock, $0.001 par value; 45,000,000 and 15,000,000 shares authorized at December 31, 2022 and December 31, 2021; respectively; 4,541,167 and 4,528,667 shares issued and outstanding at December 31, 2022 and December 31, 2021, respectively	91	91
Additional paid-in capital	291,365	289,282
Accumulated other comprehensive (loss)	(48)	(13)
Accumulated deficit	(272,785)	(245,456)
Total stockholders' equity	18,623	43,904
Total liabilities and stockholders' equity	$ 22,007	$ 48,481

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,	
	2022	2021
Revenue	$ —	$ —
Operating expenses:		
Research and development	17,967	17,008
General and administrative	9,680	9,597
Total operating expenses	27,647	26,605
Loss from operations	(27,647)	(26,605)
Other income (expense), net	318	441
Net loss	$ (27,329)	$ (26,164)
Net loss per share—basic and diluted	$ (6.02)	$ (5.89)
Weighted average common shares outstanding—basic and diluted	4,539,318	4,440,338
Comprehensive loss:		
Net loss	$ (27,329)	$ (26,164)
Other comprehensive gain (loss):		
Unrealized (loss) on investments, net of tax of $0	(35)	(11)
Total other comprehensive (loss)	(35)	(11)
Total comprehensive loss	$ (27,364)	$ (26,175)

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

AILERON THERAPEUTICS, INC.
STATEMENT OF STOCKHOLDERS' EQUITY

(In thousands, except share data)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Par Value				
Balances at December 31, 2020	2,190,208	$ 44	$ 231,412	$ (2)	$ (219,292)	$ 12,162
Issuance of common stock	2,320,313	46	59,042	—	—	59,088
Issuance costs	—	—	(3,506)	—	—	(3,506)
RSUs vested, net of shares repurchased for tax	12,500	—	—	—	—	0
Exercise of stock options	5,646	1	74	—	—	75
Stock-based compensation expense	—	—	2,260	—	—	2,260
Unrealized loss on investments	—	—	—	(11)	—	(11)
Net loss	—	—	—	—	(26,164)	(26,164)
Balances at December 31, 2021	4,528,667	$ 91	$ 289,282	$ (13)	$ (245,456)	$ 43,904
RSUs vested, net of shares repurchased for tax	12,500	—	—	—	—	—
Stock-based compensation expense	—	—	2,083	—	—	2,083
Unrealized loss on investments	—	—	—	(35)	—	(35)
Net loss	—	—	—	—	(27,329)	(27,329)
Balances at December 31, 2022	4,541,167	$ 91	$ 291,365	$ (48)	$ (272,785)	$ 18,623

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

AILERON THERAPEUTICS, INC.
STATEMENTS OF CASH FLOWS

(In thousands)

	Year Ended December 31,	
	2022	**2021**
Cash flows from operating activities:		
Net loss	$ (27,329)	$ (26,164)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization expense	169	121
Net amortization of premiums and discounts on investments	(208)	240
Stock-based compensation expense	2,083	2,260
Forgiveness of Paycheck Protection Program loan	—	(387)
(Gain) on disposition of property and equipment	—	(66)
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	1,613	(291)
Other assets	—	(24)
Accounts payable	510	(386)
Operating lease liabilities	(129)	(66)
Accrued expenses and other current liabilities	(1,574)	1,009
Net cash used in operating activities	(24,865)	(23,754)
Cash flows from investing activities:		
Purchases of investments	(21,850)	(73,577)
Proceeds from sales or maturities of investments	48,309	37,751
Purchases of property and equipment	—	(157)
Proceeds from sale of fixed asset	—	66
Net cash (used in) provided by investing activities	26,459	(35,917)
Cash flows from financing activities:		
Proceeds from issuance of common stock, common warrants and pre-funded warrants, net of issuance costs	—	55,583
Proceeds from exercise of stock options	—	74
Net cash provided by financing activities	—	55,657
Net Increase (decrease) in cash, cash equivalents and restricted cash	1,594	(4,014)
Cash, cash equivalents and restricted cash at beginning of period	3,625	7,639
Cash, cash equivalents and restricted cash at end of period	$ 5,219	$ 3,625
Cash and cash equivalents, end of year	$ 5,194	$ 3,600
Restricted cash, end of year	25	25
Cash and cash equivalents and restricted cash, end of year	$ 5,219	$ 3,625

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 chemoprotection oncology company. Our product candidate, ALRN-6924, is a MDM2/MDMX dual inhibitor that leverages our proprietary peptide drug technology.

When used as a chemoprotective agent, ALRN-6924 is designed to activate p53, which in turn upregulates p21, a known inhibitor of the cell replication cycle. ALRN-6924 was the only reported chemoprotective agent in clinical development to employ a biomarker strategy, in which we exclusively focused on treating patients with p53-mutated cancers. We originally initiated development of ALRN-6924 as an anti-cancer agent to restore p53-dependent tumor suppression in p53 wild-type tumors. When used as an anti-cancer agent, ALRN-6924 is designed to disrupt the interaction of p53 suppressors MDM2 and MDMX with tumor suppressor p53 to reactivate tumor suppression in non-mutant, or wild-type, p53 cancers.

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.

In February 2023, the Company decided to terminate further development of ALRN-6924 and to reduce its workforce from nine to three full-time employees.

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

On November 10, 2022, the Company effected a one-for-twenty reverse stock split on its common stock (the “Reverse Stock Split”). The Reverse Stock Split was reflected on the Nasdaq Capital Market beginning with the opening of trading on November 11, 2022. Pursuant to the Reverse Stock Split, every 20 shares of the Company's issued and outstanding shares of common stock were automatically combined into one issued and outstanding share of common stock, without any change in the par value per share of the common stock. The Reverse Stock Split reduced the authorized number of shares of common stock from 300,000,000 to 15,000,000 and, pursuant to the certificate of amendment, such reduced authorized number of shares of common stock was subsequently multiplied by three, such that following the Reverse Stock Split the Company has 45,000,000 shares of common stock authorized. The Reverse Stock Split affected all issued and outstanding shares of the Company's common stock, and the respective numbers of shares of common stock underlying the Company’s outstanding stock options, outstanding warrants and the Company's equity incentive plans were proportionately adjusted. All share and per share amounts of the common stock included in the accompanying consolidated financial statements have been retrospectively adjusted to give effect to the Reverse Stock Split for all periods presented.

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, 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, 2022, the Company has financed operations primarily through $145,467 in net proceeds from sales of common stock and warrants, $131,211 from sales of preferred stock prior to its IPO, and $34,910 from a collaboration agreement in 2010.

As of December 31, 2022, the Company had cash, cash equivalents and investments of $21,242. The Company has incurred losses and negative cash flows from operations and had an accumulated deficit of $272,785 as of December 31, 2022. The Company expects to continue to generate losses for the foreseeable future.

On February 21, 2023, the Company has decided to terminate the Phase 1b breast cancer trial and further development of ALRN-6924. The Company determined to reduce the Company's remaining workforce from nine to three employees. The Company also announced that it is exploring a range of strategic alternatives to maximize stockholder value. The Company has engaged a third party to act as a strategic advisor for this process. Strategic alternatives that are being evaluated may include, but are not limited to, an acquisition, a merger, a business combination, a sale of assets or other transaction. There is no set timetable for this process and there can be no assurance that this process will result in the Company pursuing a transaction or that any transaction, if pursued, will be completed.

While the Company has cash, cash equivalents and investments of $21,242 as of December 31, 2022, due to the inherent uncertainty in the timing and cost of potential strategic alternatives, including their impact on its cash consumption, the Company has concluded that as of the date of this Annual Report on Form 10-K there is substantial doubt about its ability to continue as a going concern for a period of twelve months from the issuance of these financial statements.

The Company will need substantial funding to support its continuing operations. Until such time as the Company can generate significant revenue, if ever, it expects to finance its operations through the sale of common stock in public offerings and/or private placements, debt financings or other capital sources, including third-party funding. The Company may not be able to obtain financing when needed, on acceptable terms or at all. The terms of any financing may adversely affect the holdings or the rights of the Company's stockholders. There can be no assurance that a strategic transaction will be completed and our board of directors may decide to pursue a dissolution and liquidation. If the Company is unable to raise additional funds when needed or enter into a transaction, the Company may be required to delay, limit, reduce or terminate its strategic process and it may consider seeking protection under the bankruptcy laws. If the Company decides to seek protection under the bankruptcy laws, the Company would expect that it would file for bankruptcy at a time that is significantly earlier than when it would otherwise exhaust its cash resources. If the Company decides to dissolve and liquidate its assets or to seek protection under the bankruptcy laws, it is unclear to what extent the Company will be able to pay its obligations, and, it is further unclear whether and to what extent any resources will be available for distributions to its stockholders. 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 and commercial paper, are stated at fair value.

Restricted Cash

As of December 31, 2022 and December 31, 2021, restricted cash of $25 consisted of cash deposited in a separate restricted bank account as a security deposit for the Company's corporate credit cards.

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.

Prior to the February 2023 decision to discontinue development of ALRN-6924, the Company was 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 relied 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 have been 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.

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:

Computer equipment and software	3 to 5 years
Furniture and fixtures	7 years

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.

Leases

The Company has an operating lease of office space, which has a remaining lease term of less than 1 year and includes one or more options to renew or terminate early. The Company determines if an arrangement contains a lease at inception. Operating lease right-of-use assets and lease liabilities are recognized based on the present value of the future minimum lease payments over the lease term at commencement date. Certain adjustments to the right-of-use asset may be required for items such as prepaid or accrued lease payments, initial direct costs paid or incentives received. The Company's leases do not contain an implicit rate, and therefore the Company uses an estimated incremental borrowing rate based on the information available at the lease commencement date in determining the present value of lease payments. Options to extend or terminate the lease are reflected in the calculation when it is reasonably certain that the option will be exercised. The Company has elected to account for lease and non-lease components as a single lease component, however non-lease components that are variable, such as common area maintenance and utilities, are generally paid separately from rent based on actual costs incurred and therefore are not included in the right-of-use asset and operating lease liability and are reflected as an expense in the period incurred. Leases with an initial term of 12 months or less are not recorded on the balance sheet.

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.

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. Changes in valuation allowances from period to period are included in the Company's tax provision in the period of change. 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

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 are considered potential dilutive common shares.

Recently Issued 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 was effective for the Company in the first quarter of fiscal 2021. Adoption of ASU2019-12 did not have a material effect on the Company's consolidated financial statements or disclosures.

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments-Credit Losses* (ASU 2016-13 or Topic 326): Measurement of Credit Losses on Financial Instruments, which requires the measurement and recognition of expected credit losses for financial assets held at amortized cost. ASU 2016-13 replaces the existing incurred loss impairment model with an expected loss methodology, which will result in more timely recognition of credit losses. The ASU will be effective for the Company's fiscal year beginning January 1, 2023. The Company is currently evaluating the impact of the adoption of ASU 2016-13 and does not expect adoption to have a material effect on the Company's consolidated financial statements or disclosures.

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, 2022 using:			
	Level 1	Level 2	Level 3	Total
Cash equivalents:				
Money market funds	$ 1,661	$ —	$ —	$ 1,661
Investments:				
Commercial paper	—	12,814	—	12,814
Treasury bills	—	3,234	—	3,234
	$ 1,661	$ 16,048	$ —	$ 17,709

	Fair Value Measurements as of December 31, 2021 using:			
	Level 1	Level 2	Level 3	Total
Cash equivalents:				
Money market funds	2,438	—	—	2,438
Investments:				
Commercial paper	—	33,969	—	33,969
Corporate notes	—	6,366	—	6,366
Treasury bills	—	1,998	—	1,998
	$ 2,438	$ 42,333	$ —	$ 44,771

As of December 31, 2022 and 2021, 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, commercial paper, and treasury bills 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, 2022 and 2021, there were no transfers in or out of Level 3.

4. Investments

As of December 31, 2022 and 2021, the fair value of available-for-sale investments by type of security was as follows:

	December 31, 2022			
	Amortized Cost	Gross Unrealized Gain	Gross Unrealized Loss	Fair Value
Investments:				
Commercial paper	$ 12,846	$ —	$ (32)	$ 12,814
Treasury bills	3,250	—	(16)	3,234
	$ 16,096	$ —	$ (48)	$ 16,048

	December 31, 2021			
	Amortized Cost	Gross Unrealized Gain	Gross Unrealized Loss	Fair Value
Investments:				
Commercial paper	$ 33,976	$ —	$ (7)	$ 33,969
Corporate notes	6,368	—	(2)	6,366
Treasury bills	2,002	—	(4)	1,998
	$ 42,346	$ —	$ (13)	$ 42,333

5. Property and Equipment, Net

Property and equipment, net consisted of the following:

	December 31,	
	2022	2021
Computer equipment and software	$ 340	$ 340
	340	340
Less: Accumulated depreciation and amortization	(270)	(212)
	$ 70	$ 128

Depreciation and amortization expense for the years ended December 31, 2022 and 2021 was $169 and $121, respectively. During the year ended December 31, 2021, the Company received payment for disposed, fully depreciated assets, resulting in a gain on sale of $66.

6. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following:

	December 31, 2022	December 31, 2021
External research and development services	$ 533	$ 1,575
Payroll and payroll-related costs	425	1,182
Professional fees	492	388
Other	181	60
	$ 1,631	$ 3,205

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

On May 20, 2021 the Small Business Administration notified the Company that the PPP loan had been forgiven in full. During the year ended December 31, 2021 the Company recognized income for debt extinguishment pursuant to ASC 470-50-15-4 as other income.

8. Preferred Stock

On July 5, 2017, in connection with the closing of the Company's IPO, the Company filed its 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, 2022 and 2021, the Company had no shares of preferred stock issued or outstanding.

9. Common Stock

On June 16, 2021, the Company filed a certificate of amendment to its restated certificate of incorporation which increased the authorized number of shares of common stock from 7,500,000 shares of $0.001 par value common stock to 15,000,000 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, 2022 and 2021, no dividends had been declared.

Reverse Stock Split

The Company's stockholders approved a reverse stock split of the Company's common stock on June 15, 2022. The Company effected the Reverse Stock Split on November 10, 2022. Pursuant to the Reverse Stock Split, every 20 shares of the Company's issued and outstanding shares of common stock were automatically combined into one issued and outstanding share of common stock, without any change in the par value per share of the common stock. The Reverse Stock Split reduced the authorized number of shares of common stock from 300,000,000 to 15,000,000 and, pursuant to the certificate of amendment, such reduced authorized number of shares of common

stock was subsequently multiplied by three, such that following the Reverse Stock Split the Company has 45,000,000 shares of common stock authorized. The Reverse Stock Split affected all issued and outstanding shares of the Company's common stock, and the respective numbers of shares of common stock underlying the Company's outstanding stock options, outstanding warrants and the Company's equity incentive plans were proportionately adjusted. All share and per share amounts disclosed give effect to the Reverse Stock Split on a retroactive basis.

Sales of Common Stock

On January 6, 2021, the Company entered into a securities purchase agreement with certain institutional investors, pursuant to which the Company issued and sold, in a registered direct offering (the "Offering"), an aggregate of 1,631,549 shares of common stock, $0.001 par value per share, at a purchase price per share of $22.00 (the "Shares"). The aggregate gross proceeds of the Offering were $35,894, before deducting $2,887 of fees payable to the placement agent and other offering expenses payable by the Company. The Offering closed on January 8, 2021.

Between January 1, 2021 and January 28, 2021, the Company issued and sold an aggregate 358,749 shares of its common stock pursuant to its sales agreement with JonesTrading Institutional Services LLC ("JonesTrading"), resulting in gross proceeds of $9,658, before deducting expenses of $290. The Company terminated its sales agreement with Jones Trading in January 2021.

On January 29, 2021, the Company entered into a Capital on Demand™ Sales Agreement (the "ATM Sales Agreement") with JonesTrading and William Blair & Company, L.L.C. ("William Blair" and, collectively with JonesTrading, 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"). During the year ended December 31, 2021, the Company issued and sold an aggregate of 261,270 shares of its common stock pursuant to the ATM Sales Agreement, resulting in gross proceeds of $10,922 before deducting expenses of $329. Pursuant to a prospectus relating to the ATM Sales Agreement filed by the Company with the SEC on June 21, 2022, the Company may from time to time offer and sell shares of its common stock having an aggregate offering price of up to $14,024 under the ATM Sales Agreement. There were no sales under the ATM Sales Agreement during the twelve months ended December 31, 2022.

During the year ended December 31, 2021, the Company issued and sold an aggregate of 68,750 shares of its common stock to Lincoln Park Capital, LLC pursuant to a purchase agreement entered into between Lincoln Park Capital, LLC and the Company in September 2020, resulting in gross proceeds of $2,614. During the year ended December 31, 2020, the Company issued and sold 29,411 shares to LPC under the purchase agreement for proceeds of $500. There were no sales under the purchase agreement during the twelve months ended December 31, 2022. Under the purchase agreement, the Company may not effect any sales of shares of common stock on any purchase date that the closing sale price of its common stock on Nasdaq is less than the floor price of $6.00 per share, which will be adjusted for any reorganization, recapitalization, non-cash dividend, stock split or other similar transaction

In June 2020, the Company issued and sold in an underwritten public offering an aggregate of 508,102 shares of common stock, including an additional 53,557 shares of common stock upon the partial exercise of an option of the underwriter to purchase additional shares, for a purchase price to the public of $22.00 per share. The Company received aggregate gross proceeds from the public offering of approximately $11,178, before deducting underwriting discounts and commissions and offering expenses of $932.

On April 2, 2019, the Company issued and sold in a private placement an aggregate of (i) 591,922 units, consisting of 591,922 shares of its common stock and associated warrants, or the common warrants, to purchase an aggregate of 591,922 shares of common stock, for a combined price of $40.20 per unit and (ii) 54,837 units, consisting of (a) pre-funded warrants to purchase 54,837 shares of our common stock and (b) associated common warrants to purchase 54,837 shares of common stock, for a combined price of $40.20 per unit. The pre-funded warrants had an exercise price of $0.20 per share and had no expiration. In July 2019, all outstanding pre-funded warrants were exercised for 54,837 shares of common stock. At December 31, 2021 there were 646,759 common warrants outstanding with an exercise price of $40.00 per share.

The Company has assessed the warrants for appropriate equity or liability classification and determined the warrants are freestanding instruments that do not meet the definition of a liability pursuant to ASC 480 and do not meet the definition of a derivative pursuant to ASC 815. The warrants are indexed to the Company's common stock and meet all other conditions for equity classification under ASC 480 and ASC 815. Accordingly, the warrants are classified as equity and accounted for as a component of additional paid-in capital at the time of issuance.

As of December 31, 2022, the Company had reserved 612,269 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

2021 Stock Incentive Plan

The Company's 2021 Stock Incentive Plan (the "2021 Plan") was approved by the Company's stockholders on June 15, 2021 and became effective on June 16, 2021. Under the 2021 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 2021 Plan; however, incentive stock options may only be granted to employees. The 2021 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 2021 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 2021 Plan was 728,685 as of December 31, 2022, of which 315,948 shares remained available for grant. The Company initially reserved 625,000 shares of common stock, plus the number of shares of common stock subject to outstanding awards under the Company's 2017 Stock Incentive Plan (the "2017 Plan"), and the Company's 2016 Stock Incentive Plan ("the 2016 Plan") and the Company's 2006 Stock Incentive Plan, as amended (the "2006 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 up to 314,006 shares.

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 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 could 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 were eligible to receive awards under the 2017 Plan; however, incentive stock options could 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 granted, 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 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 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.

As of the effective date of the 2021 Plan, the board of directors determined to grant no further awards under the 2017 Plan.

Shares that are expired, terminated, surrendered or canceled without having been fully exercised will be available for future awards under the 2021 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 2021 Plan.

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. A total of 375 shares of common stock were initially reserved for issuance under this plan. Under the 2017 ESPP, the number of shares of common stock that may be issued under the 2017 ESPP will automatically increase on each January 1, 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) 1,556 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 compensation committee of the board of directors determined that the number of shares of common stock that may be issued under the 2017 ESPP would not be increased on January 1, 2022 or January 1, 2023. The Company has not issued any shares under the 2017 ESPP.

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, 2022 and 2021 were as follows, presented on a weighted average basis:

	Year Ended December 31,	
	2022	2021
Risk-free interest rate	2.50%	0.96%
Expected term (in years)	6.1	6.2
Expected volatility	94.2%	91.0%
Expected dividend yield	0%	0%

Stock Options

The following table summarizes the Company's stock option activity since January 1, 2022:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value
Outstanding at December 31, 2021	468,799	$ 35.78	8.5	$ 4
Granted	157,789	9.27		
Exercised	—	0.00		
Canceled	—	0.00		
Forfeited	(73,653)	20.31		
Expired	(15,823)	47.25		
Outstanding at December 31, 2022	537,112	$ 29.77	7.9	$ —
Options exercisable at December 31, 2022	288,821	$ 40.15	7.1	$ —
Options vested and expected to vest at December 31, 2022	529,549	$ 29.95	7.8	$ —
Options exercisable at December 31, 2021	2,944,622	$ 2.89	6.9	$ 4
Options vested and expected to vest at December 31, 2021	9,164,726	$ 1.80	8.4	$ 4

The weighted average grant-date fair value of stock options granted during the year ended December 31, 2022 and 2021 was $7.32 and $19.40, respectively.

The aggregate fair value of stock options that vested during the year ended December 31, 2022 and 2021 was $2,808 and $1,106, 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, 2022 and 2021 was $0 and $68, respectively.

Restricted Stock Units

The following table summarizes the Company's restricted stock unit activity since December 31, 2021:

	Units	Weighted-Average Grant Date per Unit
Outstanding, non-vested at December 31, 2021	—	$ —
Issued	12,500	7.80
Vested	(12,500)	7.80
Canceled/forfeited	—	—
Outstanding, non-vested at December 31, 2022	—	—

Stock-Based Compensation

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

	Year Ended December 31,	
	2022	2021
Research and development expenses	$ 600	$ 531
General and administrative expenses	1,483	1,729
	$ 2,083	$ 2,260

As of December 31, 2022, the Company had an aggregate of $3,187 of unrecognized stock-based compensation expense, which it expects to recognize over a weighted average period of 2.49 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,	
	2022	2021
Numerator:		
Net loss	$ (27,329)	$ (26,164)
Denominator:		
Weighted average common shares outstanding—basic and diluted	4,539,318	4,440,338
Net loss per share attributable to common stockholders—basic and diluted	$ (6.02)	$ (5.89)

The Company's potential dilutive securities, which include stock options as of December 31, 2022 and 2021, 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,	
	2022	2021
Warrants to purchase common stock	646,759	646,759
Stock options to purchase common stock	537,112	468,799
Total	1,183,871	1,115,558

12. Commitments and Contingencies

Operating Leases

285 Summer Street

On March 26, 2021, the Company entered into a lease agreement for office space located at 285 Summer Street, Boston, Massachusetts (the "285 Summer Street Lease"). Under the terms of the 285 Summer Street Lease, starting on April 1, 2021, and has a two year term, the Company leases approximately 3,365 square feet of office space at $42.00 per square foot per year, or $141 per year in base rent, which is subject to scheduled annual rent increases plus certain operating expenses and taxes. The lease expires March 31, 2023 and we do not plan to renew the lease. Following expiration of the lease, we plan to operate virtually.

The Company accounted for this lease under ASC 842 using its initial two-year term through March 31, 2023. The Company classified this lease as an operating lease and recorded a right-of-use asset of $228 and lease liability of $228 on the effective date. The Company recognizes rent expense on a straight-line basis throughout the remaining term of the lease.

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, 2022 and 2021:

	Twelve Months Ended December 31, 2022	Twelve Months Ended December 31, 2021
Lease cost (1)		
Operating lease cost	$ 125	$ 93
Total lease cost	$ 125	$ 93
Other Information		
Cash paid for amounts included in the measurement of lease liabilities	$ 143	$ 82
Weighted average remaining lease term (in years)	0.3	1.3
Weighted average discount rate	12%	12%

(1) Short-term lease costs and variable lease costs incurred by the Company for the twelve months ended December 31, 2022 and 2021 were not material.

As of December 31, 2022, future minimum commitments under ASC 842 under the Company's operating leases were as follows:

	2022
2023	35
2024 and thereafter	-
Total lease payments	35
Less: imputed interest	(2)
Total operating lease liabilities	$ 33

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 $110 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 $110 and $145 during each of the years ended December 31, 2022 and 2021, respectively. In addition, the Company did not make any milestone payments during the years ended December 31, 2022 and 2021. During the years ended December 31, 2022 and 2021, no milestones were achieved and no liabilities for milestone payments were recorded in the Company's financial statements. From 2010 through December 31, 2022 and December 31, 2021, the Company had made non-refundable cash payments, consisting of license and maintenance fees, milestone payments and sublicense fees, totaling $5,118 and $5,008, respectively.

As of December 31, 2022, 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, 2022 and 2021. The Company did not make any milestone payments during the years ended December 31, 2022 and 2021. During the year ended December 31, 2022, 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, 2022 or December 31, 2021.

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.

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,	
	2022	2021
Federal statutory income tax rate	(21.0)%	(21.0)%
State taxes, net of federal benefit	(5.4)	(6.4)
Research and development and orphan drug tax credits	(2.9)	(2.7)
Other permanent items	0.9	0.5
Change in deferred tax asset valuation allowance	28.4	29.6
Effective income tax rate	—%	—%

Net deferred tax assets as of December 31, 2022 and 2021 consisted of the following:

	December 31,	
	2022	2021
Deferred tax assets:		
Net operating loss carryforwards	$ 64,959	$ 61,934
Research and development and orphan drug tax credit carryforwards	6,606	5,725
Capitalized research and development expenses	4,380	52
Accrued expenses and reserves	61	290
Depreciation and amortization	—	445
Lease Liability	9	44
Stock compensation	1,442	1,231
Total deferred tax assets	77,457	69,721
Valuation allowance	(77,441)	(69,680)
Net deferred tax assets	$ 16	$ 41
Deferred Tax Liabilities:		
Depreciation and amortization	$ (5)	
Right of Use Asset	$ (11)	$ (41)
Total Deferred Tax Liabilities	$ (16)	$ (41)
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, 2022, the Company had net operating loss carryforwards for federal and state purposes of $239,638 and $231,570, respectively. $129,596 of the U.S. federal tax operating loss carryforwards will begin to expire in 2029. Approximately $110,042 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, 2022, the Company also had available research and development tax credit carryforwards for federal and state income tax purposes of $2,664 and $1,922, respectively, which begin to expire in 2025 and 2026, respectively. As of December 31, 2022, the Company also had available orphan drug credit carryforwards of $2,423 for federal income tax purposes, which begin to expire in 2039. On December 22, 2017, the Tax Cuts and Jobs Act (the "TCJA") was signed into law. Under the TCJA provisions, effective with tax years beginning on or after January 1, 2022, taxpayers can no longer immediately expense research and development expenditures. Taxpayers are now required to capitalize and amortize these costs over 5 years for research conducted within the United States or 15 years for research conducted abroad. As a result, the Company capitalized $17,705 of research and development expenses for the year ended December 31, 2022.

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 and similar state statutes 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 and similar state statutes, 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 and similar state statutes, 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, 2022 and 2021. 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, 2022 and 2021 related primarily to the increase in net operating loss carryforwards. Changes in the valuation allowance were as follows:

	Year Ended December 31,	
	2022	2021
Valuation allowance at beginning of year	$ (69,680)	$ (61,932)
Increases recorded to income tax provision	(7,761)	(7,748)
Valuation allowance at end of year	$ (77,441)	$ (69,680)

The Company has not recorded any amounts for unrecognized tax benefits as of December 31, 2022 or 2021.

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 2019 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, 2022 and 2021, 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. The Company provides a safe harbor match with a maximum amount of 4.0% of the participant's compensation, and vests 100% at time of match. The Company accrued approximately $105.0 for the estimated safe harbor matching contribution for the year ended December 31, 2022.

15. Subsequent Event

On February 16, 2023, the Board of Directors (the "Board") of the Company determined to reduce the Company's remaining workforce from nine to three employees. The determination to effect the workforce reduction was made in connection with the Company's decision, further described below, to terminate its Phase 1b breast cancer trial of ALRN-6924 and further development of ALRN-6924. The workforce reduction is designed to reduce the Company's operating expenses while the Company explores a range of strategic alternatives. The workforce reduction is expected to be completed in the second quarter of 2023.

Affected employees will be offered separation benefits, including severance payments along with temporary healthcare coverage assistance. The Company estimates that the severance and termination-related costs will be approximately $1.0 to $1.1 million and expects to record these costs in the first quarter of 2023. The Company expects that payment of these costs will be made through the second quarter of 2023. The Company's estimate of costs and the expected timing for recording and paying those costs are subject to a number of assumptions and actual results may differ. The Company may also incur other costs not currently contemplated due to events that may occur as a result of, or associated with, the workforce reduction.

The Company also announced that it is exploring a range of strategic alternatives to maximize stockholder value. The Company has engaged Ladenburg Thalmann & Co., Inc. to act as a strategic advisor for this process. Strategic alternatives that are being evaluated may include, but are not limited to, an acquisition, a merger, a business combination, a sale of assets or other transaction. There is no set timetable for this process and there can be

no assurance that this process will result in the Company pursuing a transaction or that any transaction, if pursued, will be completed on attractive terms.

Exhibit 10.12

AILERON THERAPEUTICS, INC.
STOCK OPTION AGREEMENT

Aileron Therapeutics, Inc. (the "Company") hereby grants the following stock option pursuant to its 2021 Stock Incentive Plan. The terms and conditions attached hereto are also a part hereof.

Notice of Grant

Name of optionee (the "Participant"):	
Grant Date:	
Incentive Stock Option or Nonstatutory Stock Option:	
Number of shares of the Company's Common Stock subject to this option ("Shares"):	
Option exercise price per Share:	
Number, if any, of Shares that vest immediately on the grant date:	
Shares that are subject to vesting schedule:	
Vesting Start Date:	
Final Exercise Date:	

Vesting Schedule:

Vesting Date:	Number of Options that Vest:
All vesting is dependent on the Participant remaining an Eligible Participant, as provided herein.	

This option satisfies in full all commitments that the Company has to the Participant with respect to the issuance of stock, stock options or other equity securities.

AILERON THERAPEUTICS, INC.

_____
Signature of Participant

_____
Street Address

_____
City/State/Zip Code

By:
Name of Officer
Title:

AILERON THERAPEUTICS, INC.

Stock Option Agreement
Incorporated Terms and Conditions

1. Grant of Option.

This agreement evidences the grant by the Company, on the grant date (the "Grant Date") set forth in the Notice of Grant that forms part of this agreement (the "Notice of Grant"), to the Participant of an option to purchase, in whole or in part, on the terms provided herein and in the Company's 2021 Stock Incentive Plan (the "Plan"), the number of Shares set forth in the Notice of Grant of common stock, $0.001 par value per share, of the Company ("Common Stock"), at the exercise price per Share set forth in the Notice of Grant. Unless earlier terminated, this option shall expire at 5:00 p.m., Eastern time, on the Final Exercise Date set forth in the Notice of Grant (the "Final Exercise Date").

The option evidenced by this agreement is intended to be an incentive stock option as defined in Section 422 of the Internal Revenue Code of 1986, as amended, and any regulations promulgated thereunder (the "Code") to the maximum extent permitted by law, solely to the extent designated as an incentive stock option in the Notice of Grant. Except as otherwise indicated by the context, the term "Participant", as used in this option, shall be deemed to include any person who acquires the right to exercise this option validly under its terms.

2. Vesting Schedule.

This option will become exercisable ("vest") in accordance with the vesting schedule set forth in the Notice of Grant.

The right of exercise shall be cumulative so that to the extent the option is not exercised in any period to the maximum extent permissible it shall continue to be exercisable, in whole or in part, with respect to all Shares for which it is vested until the earlier of the Final Exercise Date or the termination of this option under Section 3 hereof or the Plan.

3. Exercise of Option.

a. Form of Exercise. Each election to exercise this option shall be in writing, in the form of the Stock Option Exercise Notice attached as Annex A, signed by the Participant, and received by the Company at its principal office, accompanied by this agreement, or in such other form (which may be electronic) as is approved by the Company, together with payment in full in the manner provided in the Plan. The Participant may purchase less than the number of shares covered hereby, provided that no partial exercise of this option may be for any fractional share.

b. Continuous Relationship with the Company Required. Except as otherwise provided in this Section 3, this option may not be exercised unless the Participant, at the time he or she exercises this option, is, and has been at all times since the Grant Date, an employee, director or officer of, or consultant or advisor to, the Company or any other entity the employees, officers, directors, consultants, or advisors of which are eligible to receive option grants under the Plan (an "Eligible Participant").

c. Termination of Relationship with the Company. If the Participant ceases to be an Eligible Participant for any reason, then, except as provided in paragraphs (d) and (e) below, the right to exercise this option shall terminate three months after such cessation (but in no event after the Final Exercise Date), provided that this option shall be exercisable only to the extent that the Participant was entitled to exercise this option on the date of such cessation. Notwithstanding the foregoing, if the Participant, prior to the Final Exercise Date, violates the restrictive covenants (including, without limitation, the non-competition, non-solicitation, or confidentiality provisions) of any employment contract, any non-competition, non-solicitation, confidentiality or assignment agreement to which the Participant is a party, or any other agreement between the Participant and the Company, the right to exercise this option shall terminate immediately upon such violation.

d. Exercise Period Upon Death or Disability. If the Participant dies or becomes disabled (within the meaning of Section 22(e)(3) of the Code) prior to the Final Exercise Date while he or she is an Eligible Participant and the Company has not terminated such relationship for "cause" as specified in paragraph (e) below, this option shall be exercisable, within the period of one year following the date of death or disability of the Participant, by the Participant (or in the case of death by an authorized transferee), provided that this option shall be exercisable only to the extent that this option was exercisable by the Participant on the date of his or her death or disability, and further provided that this option shall not be exercisable after the Final Exercise Date.

e. Termination for Cause. If, prior to the Final Exercise Date, the Participant's employment is terminated by the Company for Cause (as defined in below), the right to exercise this option shall terminate immediately upon the effective date of such termination of employment. If, prior to the Final Exercise Date, the Participant is given notice by the Company of the termination of his or her employment by the Company for Cause, and the effective date of such employment termination is subsequent to the date of delivery of such notice, the right to exercise this option shall be suspended from the time of the delivery of such notice until the earlier of (i) such time as it is determined or otherwise agreed that the Participant's employment shall not be terminated for Cause as provided in such notice or (ii) the effective date of such termination of employment (in which case the right to exercise this option shall, pursuant to the preceding sentence, terminate upon the effective date of such termination of employment). If the Participant is subject to an individual employment agreement with the Company or eligible to participate in a Company severance plan or arrangement, in any case which agreement, plan or arrangement contains a definition of "cause" for termination of employment, "Cause" shall have the meaning ascribed to such term in such agreement, plan or arrangement. Otherwise, "Cause" shall mean willful misconduct by the Participant or willful failure by the Participant to perform his or her responsibilities to the Company (including, without limitation, breach by the Participant of any provision of any employment, consulting, advisory, nondisclosure, non-competition or other similar agreement between the Participant and the Company), as determined by the Company, which determination shall be conclusive. The Participant's employment shall be considered to have been terminated for Cause if the Company determines, within 30 days after the Participant's resignation, that termination for Cause was warranted.

4. Tax Matters.

a. Withholding. No Shares will be issued pursuant to the exercise of this option unless and until the Participant pays to the Company, or makes provision satisfactory to the Company for payment of, any federal, state or local withholding taxes required by law to be withheld in respect of this option.

b. Disqualifying Disposition. If this option is an incentive stock option and the Participant disposes of Shares acquired upon exercise of this option within two years from the Grant Date or one year after such Shares were acquired pursuant to exercise of this option, the Participant shall notify the Company in writing of such disposition.

5. Transfer Restrictions; Clawback.

(a) This option may not be sold, assigned, transferred, pledged, encumbered or otherwise disposed of by the Participant, either voluntarily or by operation of law, except by will or the laws of descent and distribution, and, during the lifetime of the Participant, this option shall be exercisable only by the Participant.

(b) In accepting this option, the Participant agrees to be bound by any clawback policy that the Company has in place or may adopt in the future.

6. Provisions of the Plan.

This option is subject to the provisions of the Plan (including the provisions relating to amendments to the Plan), a copy of which is furnished to the Participant with this option.

ANNEX A

AILERON THERAPEUTICS, INC.

Stock Option Exercise Notice

Aileron Therapeutics, Inc.
285 Summer Street, Unit 111
Boston, MA 02210

Dear Sir or Madam:

I, _____ (the "Participant"), hereby irrevocably exercise the right to purchase _____ shares of the Common Stock, $0.001 par value per share (the "Shares"), of Aileron Therapeutics, Inc. (the "Company") at $_____ per share pursuant to the Company's 2021 Stock Incentive Plan and a stock option agreement with the Company dated _____ (the "Option Agreement"). Enclosed herewith is a payment of $_____, the aggregate purchase price for the Shares. The certificate for the Shares should be registered in my name as it appears below or, if so indicated below, jointly in my name and the name of the person designated below, with right of survivorship.

Dated: _____

_____
Signature
Print Name:

Address:
_____
_____

Name and address of persons in whose name the Shares are to be jointly registered (if applicable):

_____

Exhibit 10.13

Aileron Therapeutics, Inc.
RESTRICTED STOCK UNIT AGREEMENT

Aileron Therapeutics, Inc. (the "Company") hereby grants the following restricted stock units pursuant to its 2021 Stock Incentive Plan. The terms and conditions attached hereto are also a part hereof.

Notice of Grant

Name of recipient (the "Participant"):	
Grant Date:	
Number of restricted stock units ("RSUs") granted:	
Vesting Start Date:	
Vesting Schedule:	
All vesting is dependent on the Participant remaining an Eligible Participant, as provided herein.	

This grant of RSUs satisfies in full all commitments that the Company has to the Participant with respect to the issuance of stock, stock options or other equity securities.

Aileron Therapeutics, Inc.

_____
Signature of Participant

By:
Name:
Title:

_____
Street Address

_____
City/State/Zip Code

IF " DOCVARIABLE "SWDocIDLocation" 1" = "1" " DOCPROPERTY "SWDocID" ActiveUS 186047966v.2" "" ActiveUS 186047966v.2

Aileron Therapeutics, Inc.

Restricted Stock Unit Agreement
Incorporated Terms and Conditions

For valuable consideration, receipt of which is acknowledged, the parties hereto agree as follows:

1. Award of Restricted Stock Units.

In consideration of services rendered and to be rendered to the Company, by the Participant, the Company has granted to the Participant, subject to the terms and conditions set forth in this Restricted Stock Unit Agreement (this "Agreement") and in the Company's 2021 Stock Incentive Plan (the "Plan"), an award with respect to the number of restricted stock units (the "RSUs") set forth in the Notice of Grant that forms part of this Agreement (the "Notice of Grant"). Each RSU represents the right to receive one share of common stock, $0.001 par value per share, of the Company (the "Common Stock") upon vesting of the RSU, subject to the terms and conditions set forth herein.

1. Vesting.

The RSUs shall vest in accordance with the Vesting Schedule set forth in the Notice of Grant (the "Vesting Schedule"). Any fractional shares resulting from the application of any percentages used in the Vesting Schedule shall be rounded down to the nearest whole number of RSUs. Upon the vesting of the RSU, the Company will deliver to the Participant, for each RSU that becomes vested, one share of Common Stock, subject to the payment of any taxes pursuant to Section 7. The Common Stock will be delivered to the Participant as soon as practicable following each vesting date, but in any event within 30 days of such date.

2. Forfeiture of Unvested RSUs Upon Cessation of Service.

In the event that the Participant ceases to be an employee, director or officer of, or consultant or advisor to, the Company or any other entity the employees, officers, directors, consultants, or advisors of which are eligible to receive awards under the Plan (an "Eligible Participant") for any reason or no reason, with or without cause, all of the RSUs that are unvested as of the time of such cessation shall be forfeited immediately and automatically to the Company, without the payment of any consideration to the Participant, effective as of such cessation. The Participant shall have no further rights with respect to the unvested RSUs or any Common Stock that may have been issuable with respect thereto. If the Participant provides services to a subsidiary of the Company, any references in this Agreement to provision of services to the Company shall instead be deemed to refer to service with such subsidiary.

3. Restrictions on Transfer.

The Participant shall not sell, assign, transfer, pledge, hypothecate, encumber or otherwise dispose of, by operation of law or otherwise (collectively "transfer") any RSUs, or any interest therein. The Company shall not be required to treat as the owner of any RSUs or issue

any Common Stock to any transferee to whom such RSUs have been transferred in violation of any of the provisions of this Agreement.

4. Rights as a Stockholder.

The Participant shall have no rights as a stockholder of the Company with respect to any shares of Common Stock that may be issuable with respect to the RSUs until the issuance of the shares of Common Stock to the Participant following the vesting of the RSUs.

5. Provisions of the Plan.

This Agreement is subject to the provisions of the Plan, a copy of which is furnished to the Participant with this Agreement.

6. Tax Matters.

a. Acknowledgments; No Section 83(b) Election. The Participant acknowledges that he or she is responsible for obtaining the advice of the Participant's own tax advisors with respect to the award of RSUs and the Participant is relying solely on such advisors and not on any statements or representations of the Company or any of its agents with respect to the tax consequences relating to the RSUs. The Participant understands that the Participant (and not the Company) shall be responsible for the Participant's tax liability that may arise in connection with the acquisition, vesting and/or disposition of the RSUs. The Participant acknowledges that no election under Section 83(b) of the Internal Revenue Code of 1986, as amended (the "Code"), is available with respect to RSUs.

b. Withholding. The Participant acknowledges and agrees that the Company has the right to deduct from payments of any kind otherwise due to the Participant any federal, state, local or other taxes of any kind required by law to be withheld with respect to the vesting of the RSUs. At such time as the Participant is not aware of any material nonpublic information about the Company or the Common Stock and is not prohibited from doing so by the Company's insider trading policy or otherwise, the Participant shall execute the instructions set forth in Schedule A attached hereto (the "Automatic Sale Instructions") as the means of satisfying such tax obligation. If the Participant does not execute the Automatic Sale Instructions prior to an applicable vesting date, then the Participant agrees that if under applicable law the Participant will owe taxes at such vesting date on the portion of the award then vested the Company shall be entitled to immediate payment from the Participant of the amount of any tax required to be withheld by the Company. The Company shall not deliver any shares of Common Stock to the Participant until it is satisfied that all required withholdings have been made.

7. Miscellaneous.

a. No Right to Continued Service. The Participant acknowledges and agrees that, notwithstanding the fact that the vesting of the RSUs is contingent upon his or her continued service to the Company, this Agreement does not constitute an express or implied promise of continued service relationship with the Participant or confer upon the Participant any rights with respect to a continued service relationship with the Company or any affiliate of the Company.

b. Section 409A. The RSUs awarded pursuant to this Agreement are intended to be exempt from or comply with the requirements of Section 409A of the Code and the Treasury Regulations issued thereunder ("Section 409A"). The delivery of shares of Common Stock on the vesting of the RSUs may not be accelerated or deferred unless permitted or required by Section 409A.

c. Participant's Acknowledgments. The Participant acknowledges that he or she: (i) has read this Agreement; (ii) has been represented in the preparation, negotiation and execution of this Agreement by legal counsel of the Participant's own choice or has voluntarily declined to seek such counsel; (iii) understands the terms and consequences of this Agreement; (iv) is agreeing, in accepting this award, to be bound by any clawback policy that the Company has in place or may adopt in the future; and (iv) is fully aware of the legal and binding effect of this Agreement.

d. Governing Law. This Agreement shall be construed, interpreted and enforced in accordance with the internal laws of the State of Delaware without regard to any applicable conflicts of laws provisions.

Schedule A

Automatic Sale Instructions

The undersigned hereby consents and agrees that any taxes due on a vesting date as a result of the vesting of RSUs on such date shall be paid through an automatic sale of shares as follows:

(a) Upon any vesting of RSUs pursuant to Section 2 hereof, the Company shall arrange for the sale of such number of shares of Common Stock issuable with respect to the RSUs that vest pursuant to Section 2 as is sufficient to generate net proceeds sufficient to satisfy the Company's minimum statutory withholding obligations with respect to the income recognized by the Participant upon the vesting of the RSUs (based on minimum statutory withholding rates for all tax purposes, including payroll and social security taxes, that are applicable to such income), and the net proceeds of such sale shall be delivered to the Company in satisfaction of such tax withholding obligations.

(b) The Participant hereby appoints the Company's Chief Executive Officer and principal financial officer, and any of them acting alone and with full power of substitution, to serve as his or her attorneys in fact to arrange for the sale of the Participant's Common Stock in accordance with this Schedule A. The Participant agrees to execute and deliver such documents, instruments and certificates as may reasonably be required in connection with the sale of the shares pursuant to this Schedule A.

(c) The Participant represents to the Company that, as of the date hereof, he or she is not aware of any material nonpublic information about the Company or the Common Stock and is not prohibited from entering into these Automatic Sale Instructions by the Company's insider trading policy or otherwise. The Participant and the Company have structured this Agreement, including this Schedule A, to constitute a "binding contract" relating to the sale of Common Stock, consistent with the affirmative defense to liability under Section 10(b) of the Securities Exchange Act of 1934 under Rule 10b5-1(c) promulgated under such Act.

The Company shall not deliver any shares of Common Stock to the Participant until it is satisfied that all required withholdings have been made.

_____

Participant Name: _____

Date: _____

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-1 (Nos. 333-231143 and 333-249319), Form S-3 (Nos. 333-244367, 333-252587 and 333-265470) and Form S-8 (Nos. 333-219158, 333-224785, 333-230592, 333-237480, 333-254659, and 333-258717) of Aileron Therapeutics, Inc. of our report dated March 20, 2023 relating to the financial statements, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts
March 20, 2023

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, 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 20, 2023

/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, Susan L. Drexler, 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 20, 2023

/s/ Susan L. Drexler

Susan L. Drexler

Principal Financial Officer and Interim 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, 2022 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 20, 2023

/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, 2022 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 20, 2023

/s/ Susan L. Drexler

Susan L. Drexler

Principal Financial Officer and Interim Chief Financial Officer

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K/A
(Amendment No. 1)

(Mark One)

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

For the fiscal year ended December 31, 2022

OR

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

Commission File Number 001-38130

Aileron Therapeutics, Inc.
(Exact name of Registrant as specified in its Charter)

Delaware	**13-4196017**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
738 Main Street, Unit #398 Waltham, MA	**02451**
(Address of principal executive offices)	**(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 ☒

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

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

As of June 30, 2022, 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 Capital Market was $19,137,097.

Auditor Name:	**Auditor Location:**	**Auditor Firm ID:**
PricewaterhouseCoopers LLP	Boston, MA	238

As of March 16, 2023, the Registrant has 4,541,167 shares of Common Stock, $0.001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

None.

EXPLANATORY NOTE

This Amendment No. 1 on Form 10-K/A (this "Amendment") is filed with respect to our Annual Report on Form 10-K for the year ended December 31, 2022 (the "Original Filing"), filed with the Securities and Exchange Commission(the "SEC") on March 20, 2023. We are filing this Amendment solely for the purpose of including the information required by Part III of Form 10-K, which information was omitted from the Original Filing in reliance on General Instruction G(3) to Form 10-K, which permits the information required by Part III of Form 10-K to be incorporated by reference from a registrant's definitive proxy statement if it is filed with the SEC no later than 120 days after the fiscal year end. However, we do not intend to file a definitive proxy statement for our 2023 annual meeting of stockholders within 120 days of the end of our fiscal year ended December 31, 2022.

Accordingly, this Amendment is being filed solely to (i) provide the information required by Items 10 through 14 of Part III of the Original Filing, and (ii) delete the reference on the cover page of the Original Filing to the incorporation by reference of portions of our definitive proxy statement into Part III of the Original Filing. In addition, as required by Rule 12b-15 under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), new certifications by our principal executive officer and principal financial officer are filed herewith as exhibits to this Amendment pursuant to Rule 13a-14(a) or 15d-14(a) of the Exchange Act.

This Amendment speaks as of the date of the Original Filing and, except as described above, this Amendment makes no changes to the Original Filing. This Amendment does not amend, update or change the financial statements or any other information presented in the Original Filing and does not otherwise reflect events occurring after the date of the Original Filing. Accordingly, this Amendment should be read in conjunction with our filings with the SEC subsequent to the filing of the Original Filing.

On November 11, 2022, we effected a 1-for-20 reverse stock split of our issued and outstanding common stock. As a result of the reverse stock split, every 20 shares of our common stock issued and outstanding were converted into one share of common stock, without any change in the par value per share. No fractional shares were issued in connection with the reverse stock split. Stockholders who would otherwise have been entitled to a fractional share of our common stock were instead entitled to receive a proportional cash payment. Unless otherwise indicated, all historical share and per share amounts in this Amendment have been adjusted to reflect the reverse stock split. Proportionate adjustments were made to the per share exercise price and the number of shares of common stock that may be purchased upon exercise of outstanding stock options, and the number of shares of common stock reserved for future issuance under our 2006 Equity Incentive Plan, as amended, our 2016 Stock Incentive Plan, our 2017 Stock Incentive Plan, our 2021 Stock Incentive Plan, and our 2017 Employee Stock Purchase Plan.

Unless indicated otherwise, throughout this Amendment, references to "Aileron," "the Company," "we," "us" and "our" refer Aileron Therapeutics, Inc. and its subsidiaries, except where the context otherwise requires or indicates.

Aileron and the other trademarks or service marks of Aileron appearing in this Amendment are the property of Aileron. All other trademarks, service marks or other trade names appearing in this Amendment are the property of their respective owners.

Table of Contents

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Executive Officers

The following table sets forth the name, age as of April 25, 2023, and position of each of our executive officers.

Name	Age	Position(s)
Manuel C. Alves Aivado, M.D., Ph.D.*	53	President and Chief Executive Officer, Director
Susan L. Drexler**	53	Interim Chief Financial Officer

* *Dr. Aivado is a member of our board of directors. See "– Board of Directors" below for more information about Dr. Aivado.*

** *Ms. Drexler is not directly compensated by Aileron for her services to us as our interim chief financial officer.*

Susan L. Drexler has served as our interim chief financial officer since June 2022. Since January 2022, Ms. Drexler has served as a chief financial officer consultant at Danforth Advisors, a firm that specializes in outsourced corporate functions for life sciences companies. From October 2019 to March 2021, Ms. Drexler served as chief financial officer at Harmony Biosciences, a life sciences company. From April 2018 to June 2019, Ms. Drexler served in various roles as interim chief financial officer and vice president of business development at Ocugen, Inc., a biotechnology company. From August 2015 to November 2017, Ms. Drexler served in senior roles in business development and market intelligence at AmerisourceBergen Corporation, a company that provides distribution, logistics and technology solutions to life sciences companies. From July 2007 to June 2015, Ms. Drexler held a senior business development finance role at Shire Pharmaceuticals, a biopharmaceutical company. Earlier in her career, Ms. Drexler held roles of increasing responsibility in finance consulting at Duff & Phelps, LLC, a financial consultancy firm, and senior audit roles at PricewaterhouseCoopers LLP. Ms. Drexler earned a B.S. in Accounting from Albright College and an M.B.A. from the Joseph M. Katz Graduate School of Business at the University of Pittsburgh. Ms. Drexler is a Certified Public Accountant in the State of Pennsylvania.

Board of Directors

Our restated certificate of incorporation, as amended, provides for a classified board of directors. This means that our board of directors is divided into three classes, with each having as nearly as possible an equal number of directors, with terms of service of each class of directors staggered for three-year terms, so that the term of one class expires at each annual meeting of stockholders.

Our board of directors currently consists of seven members. There are currently two Class I directors (Jeffrey A. Bailey and Jodie P. Morrison), whose terms expire at the 2024 annual meeting of stockholders; two Class II directors (William T. McKee and Nolan Sigal, M.D., Ph.D.), whose terms expire at the 2025 annual meeting of stockholders; and three Class III directors (Manuel C. Alves Aivado, M.D., Ph.D., Reinhard J. Ambros, Ph.D. and Josef H. von Rickenbach), whose terms expire at the 2023 annual meeting of stockholders (in all cases until his or her successor has been duly elected and qualified).

Name	Age	Position(s)
Class I Directors		
Jeffrey A. Bailey (1)	61	Chair of the Board of Directors
Jodie P. Morrison (2) (3)	47	Director
Class II Directors		
William T. McKee (2)	61	Director
Nolan Sigal, M.D., Ph.D. (1)(3)	73	Director

Name	Age	Position(s)
Class III Directors		
Manuel C. Alves Aivado, M.D., Ph.D.	53	President and Chief Executive Officer, Director
Reinhard J. Ambros, Ph.D. (3)	67	Director
Josef H. von Rickenbach (1)(2)	68	Director

(1) Member of compensation committee.
(2) Member of audit committee.
(3) Member of nominating and corporate governance committee.

Set forth below are the names of and certain information for each member of our board of directors as of April 25, 2023. The information presented includes each director's principal occupation and business experience for the past five years, and the names of other public companies of which he or she has served as a director during the past five years. The information presented below regarding the specific experience, qualifications, attributes and skills of each director led our nominating and corporate governance committee and our board of directors to conclude that he or she should serve as a director. In addition, we believe that all of our directors possess the attributes or characteristics described below in "–Corporate Governance Matters" that the nominating and corporate governance committee expects of each director. There are no family relationships among any of our directors or executive officers.

Class I Directors (Term Expires at 2024 Annual Meeting)

Jeffrey A. Bailey has served as chair of our board of directors and as a member of our board of directors since March 2018. Since March 2022, Mr. Bailey has served as an advisor to various life sciences companies. From November 2020 to March 2022, Mr. Bailey served as chief executive officer and director of BioDelivery Sciences, Inc., a publicly-traded commercial-stage specialty pharmaceutical company that Collegium Pharmaceutical, Inc. acquired in March 2022. From December 2015 until March 2017, Mr. Bailey served as chair and chief executive officer of Neurovance, Inc., a biotechnology firm acquired by Otsuka Pharmaceutical in 2017. Previously, from January 2013 through June 2015, Mr. Bailey served as president and chief executive officer and as a director of Lantheus Medical Imaging, Inc., a public medical diagnostic company. Prior to 2013, Mr. Bailey held various leadership positions with several public and private pharmaceutical and medical device companies, including operating unit president at Novartis Pharmaceuticals, a multinational pharmaceutical company, and a 22-year career with Johnson & Johnson, a multinational medical devices, pharmaceutical and consumer packaged goods manufacturing company (including Janssen Pharmaceutica NV). Mr. Bailey has served as a trustee of Tekla Capital since September 2020 and as an advisor to Venture Investors / Madison Vaccines since October 2017. Mr. Bailey received a B.S. from Rutgers University. We believe Mr. Bailey is qualified to serve on our board of directors due to his extensive management experience in the life sciences industry and his experience on corporate boards of companies in the life sciences industry.

Jodie P. Morrison has served as a member of our board of directors since June 2017. Since September 2022, Ms. Morrison has served as acting chief executive officer at Q32 Bio, a life sciences company, and, since July 2021, has served as a venture advisor at Atlas Ventures, a leading early-stage venture capital firm. From February 2019 to March 2021, Ms. Morrison served as chief executive officer of Cadent Therapeutics, Inc., a privately-held biotechnology company, that was acquired by Novartis in 2021. From April 2018 to December 2018, Ms. Morrison served as interim chief executive officer of Keryx Biopharmaceuticals, Inc., a biopharmaceutical company. Since May 2017, Ms. Morrison has provided services to venture capital, biotechnology, and pharmaceutical companies, including serving as acting chief operating officer of Syntimmune, Inc., a clinical stage biotechnology company, from January 2018 to July 2018 and as president and chief executive officer of eGenesis, Inc., a private life sciences company, from September 2017 to November 2017. Prior to founding Morrison Advisory, Ms. Morrison served as the president and chief executive officer of Tokai Pharmaceuticals, Inc, now Novus Therapeutics, Inc., or Novus, a biopharmaceutical company, from March 2013 until May 2017. From December 2006 until March 2013, Ms. Morrison held other senior positions with

Tokai, including chief operating officer, head of clinical affairs and program operations, and vice president of clinical affairs and program operations. Prior to joining Novus, Ms. Morrison served as director of clinical operations and medical affairs at Dyax Corporation, or Dyax. Prior to joining Dyax, Ms. Morrison held clinical management positions at both Curis, Inc. and Diacrin, Inc. Ms. Morrison serves as a chair of the board of directors of Ribon Therapeutics, Inc., and as a member of the board of directors at Rectify Pharmaceuticals, Inc. Ms. Morrison previously served on the board of directors of Cadent Therapeutics, Inc., prior to its acquisition by Novartis; on the board of directors of Keryx Biopharmaceuticals, Inc., prior to its merger with Akebia Therapeutics, Inc.; on the board of directors of Akebia and on the board of directors of Novus Therapeutics. Ms. Morrison received a B.A. in neuroscience from Mount Holyoke College, a clinical research certification from the Boston University School of Medicine, and business training through the Greater Boston Executive Program at the MIT Sloan School of Management. We believe Ms. Morrison is qualified to serve on our board of directors due to her extensive management experience in the life sciences industry and her experience on corporate boards of public companies.

Class II Directors (Term Expires at 2025 Annual Meeting)

William T. McKee has served as a member of our board of directors since June 2019. Mr. McKee is NACD Directorship Certified®. Mr. McKee has served as the chief executive officer of MBJC Associates, LLC, a business consulting firm serving the pharmaceutical and biotechnology industry, since June 2010. From April 2020 to June 2021, Mr. McKee served as interim chief financial officer of C4 Therapeutics, Inc., a clinical-stage biopharmaceutical company. Mr. McKee served as chief operating officer and chief financial officer for EKR Therapeutics, Inc., or EKR, a specialty pharmaceutical company, from July 2010 until June 2012, when EKR was sold to Cornerstone Therapeutics Inc. From December 2008 until March 2010, Mr. McKee served as the executive vice president, chief financial officer, and treasurer of Barr Pharmaceuticals, LLC, a subsidiary of Teva Pharmaceutical Industries Limited, or Teva, and the successor entity to Barr Pharmaceuticals, Inc., or Barr, which was acquired by Teva in December 2008. Mr. McKee was also executive vice president and chief financial officer of Barr prior to its acquisition by Teva, after having served in positions of increasing responsibility at Barr from 1995 until its acquisition. Prior to joining Barr, Mr. McKee served as director of international operations and vice president-finance at Absolute Entertainment, Inc. from June 1993 until December 1994. From 1990 until June 1993, Mr. McKee worked at Gramkow & Carnevale, CPA's, and from 1983 until 1990, he worked at Deloitte & Touche LLP. Mr. McKee serves as a member of the board of directors and chairman of the audit committee of Assertio Therapeutics, Inc., a specialty pharmaceutical company. Mr. McKee received a B.B.A. from the University of Notre Dame. We believe Mr. McKee is qualified to serve on our board of directors due to his extensive management and financial experience in the life sciences industry and his experience on corporate boards of public companies.

Nolan Sigal, M.D., Ph.D. has served as a member of our board of directors since April 2019. Dr. Sigal has served as a partner at Alerce Management Co., L.P., a private investment firm, since January 2018. From March 2008 to December 2017, Dr. Sigal was founder and chief executive officer of Tunitas Therapeutics, Inc., a biopharmaceutical company. Prior to Tunitas, Dr. Sigal's biotechnology experience included president of Trellis Bioscience, Inc., a biotechnology company, EVP of research and development, and chief scientific officer at Cytokinetics, Inc., a biopharmaceutical company, and SVP, research at Pharmacopeia, Inc., a biotechnology company, where he was one of Pharmacopeia's founders. He served at Merck & Company Inc. as executive director of the Department of Immunology Research. Prior to Merck, he was an assistant professor at the University of Toronto. Dr. Sigal graduated from Princeton University with an A.B. in chemistry, and he completed an M.D./Ph.D. program at the University of Pennsylvania. We believe Dr. Sigal is qualified to serve on our board of directors due to his significant experience as an executive of a biopharmaceutical company and his background in life sciences investing.

Class III Directors (Term Expires at 2023 Annual Meeting)

Manuel C. Alves Aivado, M.D., Ph.D. has served as our president and chief executive officer and as a member of our board of directors since September 2018. Previously, Dr. Aivado served as our senior vice president, chief

medical officer from September 2014 to September 2018. From March 2012 to September 2014, Dr. Aivado served as vice president of clinical development and pharmacovigilance at Taiho Oncology, Inc., a pharmaceutical company. From October 2006 to March 2012, Dr. Aivado served as senior medical director in the clinical development group at GlaxoSmithKline, Inc., a global pharmaceutical company. Dr. Aivado has also served as an instructor in medicine at Beth Israel Deaconess Medical Center/Harvard Medical School. Prior to his industry experience, Dr. Aivado practiced clinical medicine in Germany for nearly ten years. During that time, he was awarded the Dr. Mildred Scheel cancer research scholarship award in 2002. Dr. Aivado is a German board-certified physician for internal medicine, hematology, and medical oncology. He received an M.D. and Ph.D. from the Medical School of the University of Dusseldorf in Germany. We believe that Dr. Aivado is qualified to serve on our board of directors due to his service as our president and chief executive officer, previous role as our chief medical officer, extensive knowledge of our company, and significant background in pharmaceutical research and development.

Reinhard J. Ambros, Ph.D. has served as a member of our board of directors since June 2013. From 2005 until 2017, Dr. Ambros served as global head of Novartis Venture Funds, a globally acting corporate biotechnology venture fund. Prior to that, from 1999 until 2005, he served as head of group strategic planning and as global head of business development and licensing for cardiovascular and metabolic diseases at Novartis AG, a multinational pharmaceutical company. He currently serves on the boards of several biotechnology companies in Europe and the United States. He also served as advisor to German and Swiss Government Biotechnology Funds. Dr. Ambros received an M.S. from the University of Regensburg, Germany, and a Ph.D. in medicinal chemistry and pharmacology from the University of Regensburg, Germany. We believe Dr. Ambros is qualified to serve on our board of directors due to his management experience in the biotechnology sector and his service on other boards of directors.

Josef H. von Rickenbach has served as a member of our board of directors since June 2019. Mr. von Rickenbach has served as managing director of Stet Vision LLC, a life sciences business advisory firm, since December 2018. He co-founded and served as president and chief executive officer of HelioVision, Inc., a biotechnology company, from April 2017 until its acquisition by Aldeyra Therapeutics, Inc. in February 2019. Previously, Mr. von Rickenbach was a founder of Parexel International Corporation, a global clinical research organization and biopharmaceutical services company, in 1982 and served as a director, chairman of the board, and chief executive officer of Parexel from 1983 until the company's acquisition by Pamplona Capital Management, LLP in September 2017. Mr. von Rickenbach received an M.B.A. from Harvard Business School and a B.A. in business economics from the University of Lucerne in Switzerland. We believe Mr. von Rickenbach is qualified to serve on our board of directors due to his management experience in the biotechnology sector, his decades of experience in drug development, and his service on other boards of directors.

Corporate Governance Matters

Our board of directors believes that good corporate governance is important to ensure that our company is managed for the long-term benefit of stockholders. This section describes key corporate governance guidelines and practices that our board of directors has adopted. Complete copies of our corporate governance guidelines, committee charters and code of conduct are available on the "Investors & Media—Corporate Governance" section of our website, which is located at *www.aileronrx.com*. Alternatively, you can request a copy of any of these documents by writing us at Aileron Therapeutics, Inc., 738 Main Street, Unit #398, Waltham, MA 02451, Attention: Interim Chief Financial Officer.

Corporate Governance Guidelines

Our board of directors has adopted corporate governance guidelines to assist in the exercise of its duties and responsibilities and to serve the best interests of our company and our stockholders. These guidelines, which provide a framework for the conduct of our board of directors' business, provide that:

- the principal responsibility of our board of directors is to oversee our management;

- a majority of the members of the board of directors must be independent directors, unless otherwise permitted by the Nasdaq Stock Market, or Nasdaq, rules;
- the independent directors meet at least twice a year in executive session;
- directors have full and free access to management and, as necessary and appropriate, independent advisors;
- our nominating and corporate governance committee will oversee an annual self-evaluation of the board to determine whether it and its committees are functioning effectively; and
- new directors participate in an orientation program and all directors are expected to participate in continuing director education on an ongoing basis.

Board Leadership Structure

Our corporate governance guidelines provide that the nominating and corporate governance committee shall periodically assess the board of directors' leadership structure, including whether the offices of chief executive officer and chair of the board of directors should be separate. Our guidelines provide the board of directors with flexibility to determine whether the two roles should be combined or separated based upon our needs and the board of directors' assessment of its leadership from time to time. We currently separate the roles of chief executive officer and chair of the board of directors. Separating the duties of the chair of the board from the duties of the chief executive officer allows our chief executive officer to focus on our day-to-day business, while allowing the chair of the board to lead the board of directors in its fundamental role of providing advice to and independent oversight of management. Specifically, the chair of our board of directors presides over meetings of the board of directors, facilitates communications between management and the board of directors and assists with other corporate governance matters.

Our board of directors has three standing committees that currently consist of, and are chaired by, independent directors. Our board of directors delegates substantial responsibilities to the committees, which then report their activities and actions back to the full board of directors. We believe that the independent committees of our board of directors and their chairpersons promote effective independent governance. We believe this structure represents an appropriate allocation of roles and responsibilities for our company at this time because it strikes an effective balance between management and independent leadership participation in our board of director proceedings.

Our board of directors oversees our risk management processes directly and through its committees. Our management is responsible for risk management on a day-to-day basis. The role of our board of directors and its committees is to oversee the risk management activities of management. Our board of directors fulfills this duty by discussing with management the policies and practices utilized by management in assessing and managing risks and providing input on those policies and practices. In general, our board of directors oversees risk management activities relating to business strategy, acquisitions, capital allocation, organizational structure and certain operational risks; our audit committee oversees risk management activities related to financial controls and legal and compliance risks; our compensation committee oversees risk management activities relating to our compensation policies and practices; and our nominating and corporate governance committee oversees risk management activities relating to the composition of our board of directors and management succession planning. Each committee reports to the full board of directors on a regular basis, including reports with respect to the committee's risk oversight activities as appropriate. In addition, since risk issues often overlap, committees from time to time request that the full board of directors discuss particular risks.

Board Determination of Independence

Applicable Nasdaq rules require a majority of a listed company's board of directors to be comprised of independent directors within one year of listing. In addition, the Nasdaq rules require that, subject to specified

exceptions, each member of a listed company's audit, compensation and nominating and corporate governance committees be independent. Audit committee members must also satisfy the independence criteria set forth in Rule 10A-3 under the Securities Exchange Act of 1934, as amended, or the Exchange Act, and compensation committee members must also satisfy the independence criteria set forth in Rule 10C-1 under the Exchange Act. Under applicable Nasdaq rules, a director will only qualify as an "independent director" if, in the opinion of the listed company's board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In order to be considered independent for purposes of Rule 10A-3, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee, accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries or otherwise be an affiliated person of the listed company or any of its subsidiaries. In order to be considered independent for purposes of Rule 10C-1, the board must consider, for each member of a compensation committee of a listed company, all factors specifically relevant to determining whether a director has a relationship to such company which is material to that director's ability to be independent from management in connection with the duties of a compensation committee member, including, but not limited to: the source of compensation of the director, including any consulting, advisory or other compensatory fee paid by such company to the director; and whether the director is affiliated with the company or any of its subsidiaries or affiliates.

In March 2022, our board of directors undertook a review of the composition of our board of directors and its committees and the independence of each director. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board of directors has determined that each of our directors, with the exception of Manuel C. Alves Aivado, M.D., Ph.D., is an "independent director" as defined under applicable Nasdaq rules, including, in the case of all the members of our audit committee, the independence criteria set forth in Rule 10A-3 under the Exchange Act, and in the case of all the members of our compensation committee, the independence criteria set forth in Rule 10C-1 under the Exchange Act. In making such determination, our board of directors considered the relationships that each such non-employee director has with our company and all other facts and circumstances that our board of directors deemed relevant in determining his or her independence, including the beneficial ownership of our capital stock by each non-employee director. Dr. Aivado is not an independent director under these rules because he is our president and chief executive officer.

Board of Director Meetings and Attendance

Our board of directors held nine meetings during the year ended December 31, 2022, or fiscal 2022. During fiscal 2022, each of the directors then in office attended at least 75% of the aggregate of the number of board of director meetings held during the period which the person has been a director and the number of meetings held by all committees of the board of directors on which such director then served (during the periods that such person served). Our corporate governance guidelines provide that directors are expected to attend the annual meeting of stockholders. All directors then serving on our board of directors attended the 2022 annual meeting of stockholders.

Communicating with our Directors

Our board of directors provides a process for stockholders to send communications to the board. Any interested party with concerns about our company may report such concerns to the board of directors, or the chair of our board of directors, or otherwise the chair of the nominating and corporate governance committee, by submitting a written communication to the attention of such director at the following address:

c/o Aileron Therapeutics, Inc.
738 Main Street, Unit #398
Waltham, MA 02451

You may submit your concern anonymously or confidentially by postal mail. You may also indicate whether you are a stockholder, customer, supplier, or other interested party.

A copy of any such written communication may also be forwarded to our legal counsel, and a copy of such communication may be retained for a reasonable period of time. The director may discuss the matter with our legal counsel, with independent advisors, with non-management directors, or with our management, or may take other action or no action as the director determines in good faith, using reasonable judgment and discretion.

Communications may be forwarded to all directors if they relate to important substantive matters and include suggestions or comments that may be important for the directors to know. In general, communications relating to corporate governance and long-term corporate strategy are more likely to be forwarded than communications relating to ordinary business affairs, personal grievances, and matters as to which we tend to receive repetitive or duplicative communications.

The audit committee oversees the procedures for the receipt, retention, and treatment of complaints received by us regarding accounting, internal accounting controls, or audit matters, and the confidential, anonymous submission by employees of concerns regarding questionable accounting, internal accounting controls, or auditing matters. We have also established a toll-free telephone number for the reporting of such activity, which is 866-869-5217.

Committees of the Board of Directors

We have established an audit committee in accordance with Section 3(a)(58)(A) of the Exchange Act, a compensation committee, and a nominating and corporate governance committee. Each of these committees operates under a charter that has been approved by our board of directors. A copy of each committee's charter can be found under the "Investors & Media—Corporate Governance" section of our website, located at *www.aileronrx.com*.

Audit Committee

The current members of our audit committee are William T. McKee, Jodie P. Morrison, and Josef H. von Rickenbach. Mr. McKee serves as chair of our audit committee. In fiscal 2022, our audit committee met seven times. Our audit committee's responsibilities include:

- appointing, approving the compensation of, and assessing the independence of our independent registered public accounting firm;
- overseeing the work of our independent registered public accounting firm, including through the receipt and consideration of reports from that firm;
- reviewing and discussing with management and our independent registered public accounting firm our annual and quarterly financial statements and related disclosures;
- monitoring our internal control over financial reporting, disclosure controls, and procedures, and code of business conduct and ethics;
- overseeing our internal audit function, if any;
- discussing our risk assessment and risk management policies;
- establishing policies regarding hiring employees from our independent registered public accounting firm and procedures for the receipt and retention of accounting-related complaints and concerns;
- meeting independently with our internal auditing staff, if any, our independent registered public accounting firm and management;

- reviewing and approving or ratifying any related person transactions; and
- preparing the audit committee report required by the SEC rules.

All audit and non-audit services, other than *de minimis* non-audit services, to be provided to us by our independent registered public accounting firm must be approved in advance by our audit committee.

Our board of directors has determined that Mr. McKee is an "audit committee financial expert" as defined in applicable SEC rules and that each of the members of our audit committee possesses the financial sophistication required for audit committee members under Nasdaq rules. We believe that the composition of our audit committee meets the requirements for independence under current Nasdaq and SEC rules and regulations.

Compensation Committee

The current members of our compensation committee are Jeffrey A. Bailey, Nolan Sigal, M.D., Ph.D., and Josef H. von Rickenbach. Mr. Bailey has served as the chair of the compensation committee since June 15, 2022. Mr. von Rickenbach was appointed as a member of the compensation committee on June 15, 2022. Reinhard J. Ambros, Ph.D. served as a member and chair of the compensation committee, and Jodie P. Morrison served as a member of the compensation committee until June 15, 2022. In fiscal 2022, our compensation committee met five times. Our compensation committee's responsibilities include:

- reviewing and approving or making recommendations to our board of directors concerning the compensation of our chief executive officer and our other executive officers;
- overseeing an evaluation of our senior executives;
- reviewing and making recommendations to our board of directors concerning our incentive-compensation and equity-based compensation plans;
- overseeing and administering our equity-based plans;
- reviewing and making recommendations to our board of directors concerning director compensation;
- reviewing and discussing annually with management our "Compensation Discussion and Analysis" disclosure if and to the extent then required by SEC rules; and
- preparing the compensation committee report if and to the extent required by SEC rules.

Our compensation committee may delegate to one or more executive officers the power to grant options or other stock awards pursuant to our incentive plans to employees of the company who are not executive officers or senior vice presidents.

We believe that the composition of our compensation committee meets the requirements for independence under current Nasdaq and SEC rules and regulations.

Nominating and Corporate Governance Committee

The current members of our nominating and corporate governance committee are Reinhard J. Ambros, Ph.D., Jodie Morrison and Nolan Sigal, M.D., Ph.D. Dr. Sigal has served as the chair of the nominating and corporate governance committee since June 15, 2022. Ms. Morrison was appointed as a member of the nominating and corporate governance committee on June 15, 2022. Josef H. von Rickenbach served as a member and chair of the nominating and corporate governance committee until June 15, 2022. In fiscal 2022, our nominating and corporate governance committee met one time. Our nominating and corporate governance committee's responsibilities include:

- identifying individuals qualified to become members of our board of directors;

- recommending to our board of directors the persons to be nominated for election as directors and to each of our board's committees;
- developing and recommending to our board of directors corporate governance principles; and
- overseeing an annual evaluation of our board of directors.

We believe that the composition of our nominating and corporate governance committee meets the requirements for independence under current Nasdaq and SEC rules and regulations.

Director Nomination Process

The process followed by our nominating and corporate governance committee to identify and evaluate director candidates includes requests to board members and others for recommendations, meetings from time to time to evaluate biographical information and background material relating to potential candidates and interviews of selected candidates by members of the nominating and corporate governance committee and our board of directors.

Criteria and Diversity

In considering whether to recommend to our board of directors any particular candidate for inclusion in our board of directors' slate of recommended director nominees, including candidates recommended by stockholders, the nominating and corporate governance committee of our board of directors applies the criteria set forth in our corporate governance guidelines. These criteria include the candidate's integrity, business acumen, knowledge of our business and industry, the ability to act in the interests of all stockholders and lack of conflicts of interest.
Our nominating and corporate governance committee does not have a policy (formal or informal) with respect to diversity, but believes that our board, taken as a whole, should embody a diverse set of skills, experiences and backgrounds. In this regard, the nominating and corporate governance committee also takes into consideration the diversity (for example, with respect to gender, race and national origin) of our board members. The nominating and corporate governance committee does not make any particular weighting of diversity or any other characteristic in evaluating nominees and directors.

Stockholder Nominations

Stockholders may recommend individuals to our nominating and corporate governance committee for consideration as potential director candidates by submitting their names, together with appropriate biographical information and background materials and a statement as to whether the stockholder or group of stockholders making the recommendation has beneficially owned more than 5% of our common stock for at least a year as of the date such recommendation is made, to Aileron Therapeutics, Inc., Attention: Nominating and Corporate Governance Committee, 738 Main Street #398, Waltham, MA 02451. Assuming that appropriate biographical and background material has been provided on or before the dates set forth in our definitive proxy statement for our 2022 annual meeting of stockholders filed with the SEC on April 29, 2022 (the "2022 Proxy Statement") under the heading "Other Matters – Stockholder Proposals for our 2023 annual meeting", the committee will evaluate stockholder-recommended candidates by following substantially the same process, and applying substantially the same criteria, as it follows for candidates submitted by others. If the board of directors determines to nominate a stockholder-recommended candidate and recommends his or her election, then his or her name will be included in our proxy card for the next annual meeting.

Stockholders also have the right under our by-laws to directly nominate director candidates, without any action or recommendation on the part of the nominating and corporate governance committee or our board of directors, by following the procedures set forth in our 2022 Proxy Statement under "Other Matters – Stockholder Proposals for our 2023 annual meeting."

There were no material changes to the procedures described in our 2022 Proxy Statement by which stockholders may recommend nominees to our board of directors.

Board Diversity Matrix

In accordance with Nasdaq's recently adopted board diversity listing standards, we are also disclosing aggregated statistical information about the members of our board directors as voluntarily identified to us by each of our directors.

Board Diversity Matrix (As of April 28, 2023)

Total Number of Directors	**7**			
	Female	**Male**	**Non-Binary**	**Did not Disclose Gender**
Part I: Gender Identity				
Directors	1	6	—	—
Part II: Demographic Background				
African American or Black	—	—	—	—
Alaskan Native or Native American	—	—	—	—
Asian	—	—	—	—
Hispanic or Latinx	—	1	—	—
Native Hawaiian or Pacific Islander			—	—
White	1	5	—	—
Two or More Races or Ethnicities	—	—	—	—
LGBTQ+			—	
Did Not Disclose Demographic Background			—	

Anti-Hedging Policy

Our insider trading policy expressly prohibits all of our employees, including our named executive officers, as well as our directors, from engaging in speculative transactions in our stock, including short sales, puts/calls, hedging transactions and margin accounts or pledges.

Compensation Committee Interlocks and Insider Participation

None of our executive officers serve, or in the past has served, as a member of the board of directors or compensation committee, or other committee serving an equivalent function, of any entity that has one or more executive officers who serve as members of our board of directors or our compensation committee. None of the members of our compensation committee is, or ever has been, an officer or employee of our company.

Code of Business Conduct and Ethics

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer and principal financial officer. A copy of the code is available on the "Investors & Media—Corporate Governance" section of our website, which is located at *www.aileronrx.com*. Our board of directors is responsible for overseeing the code of business conduct and ethics and must approve any waivers of the code for directors, officers and employees. If we make any substantive amendments to, or grant any waivers from, the code of business conduct and ethics for any officer or director, we will disclose the nature of such amendment or waiver on our website or in a current report on Form 8-K.

Item 11. Executive Compensation.

This section discusses the material elements of our executive compensation policies for our "named executive officers" and the most important factors relevant to an analysis of these policies. For 2022, our "named executive

officers" are Manuel C. Alves Aivado, M.D., Ph.D., our current president and chief executive officer; our other most highly compensated executive officer serving at year end (other than our chief executive officer), D. Allen Annis, our former senior vice president, research; and one additional individual no longer serving as an executive officer at year end, Vojislav Vukovic, M.D., Ph.D., our former senior vice president, chief medical officer. In addition, this section provides qualitative information regarding the manner and context in which compensation is awarded to and earned by our named executive officers and is intended to place in perspective the data presented in the following tables and the corresponding narrative.

Summary Compensation Table

The following table sets forth information regarding compensation awarded to, earned by or paid to our named executive officers during the years indicated.

Name and Principal Position	Year	Salary ($)	Bonus ($) (1)	Option Awards ($) (2)	All Other Compensation ($) (3)	Total ($)
Manuel C. Alves Aivado, M.D., Ph.D.	2022	587,336	—	543,850	113,234(4)	1,244,420
President and Chief Executive Officer	2021	564,736	254,131	2,368,000	93,512(4)	3,280,379
D. Allen Annis, Ph.D. (5)	2022	404,100	—	150,250	17,914	572,264
Former Senior Vice President, Research						
Vojislav Vukovic, M.D., Ph.D. (6)	2022	248,566	—	72,010	225,127(7)	545,703
Former Senior Vice President, Chief Medical Officer	2021	423,225	133,316	388,197	17,648	962,386

(1) Unless otherwise noted, the amounts reported in the "Bonus" column represent discretionary annual cash bonuses awarded to our named executive officers for service during the year referenced, although paid in the following year.

(2) The amounts reported in the "Options Awards" column reflect the aggregate grant date fair value of share-based compensation awarded during the year computed in accordance with the provisions of Financial Accounting Standards Board Accounting Standards Codification, or ASC, Topic 718. See Note 10 to our financial statements included in our Annual Report on Form 10-K regarding assumptions underlying the valuation of equity awards.

(3) Unless otherwise noted, the amounts represent Health Savings Account, or HSA, contributions and the dollar value of group life insurance paid with respect to life insurance, and, beginning in fiscal 2021, company contributions under the 401(k) match program described below under "401(k) Retirement Plan" for the named executive officer consistent with those provided to all of our employees.

(4) In addition to the HSA contribution, 401k contribution, and the dollar value of group life insurance paid, the amounts for Dr. Aivado consist of $49,816 and $50,070 in commuting reimbursements in fiscal 2022 and 2021, respectively, and $45,504 and $25,794 in tax gross-ups in fiscal 2022 and 2021, respectively, for the payment of taxes associated with the reimbursement of commuting expenses

(5) Dr. Annis ceased to serve as our senior vice president, research, effective as of April 15, 2023. Because Dr. Annis was not an NEO prior to 2022, compensation information is not provided for 2021.

(6) Dr. Vukovic ceased to serve as our senior vice president, chief medical officer, effective as of July 8, 2022.

(7) In addition to the HSA contribution and the dollar value of group life insurance paid, this amount for Dr. Vukovic also includes $209,732 in severance paid to Dr. Vukovic in 2022 in connection with his separation from his position as our senior vice president, chief medical officer in July 2022.

Narrative Disclosure to Summary Compensation Table

We review compensation for our executive officers annually. The material terms of the elements of our executive compensation program for 2022 are described below.

Our compensation committee sets base salaries and bonus targets, and grants bonuses and equity incentive awards to our executive officers. In setting base salaries and bonus targets and granting equity incentive awards,

our compensation committee considers compensation for comparable positions in the market, the historical compensation levels of our executives, individual and corporate performance as compared to our expectations and objectives, our desire to motivate our employees to achieve short- and long-term results that are in the best interests of our stockholders, and a long-term commitment to our company. In granting bonuses, our compensation committee considers corporate and individual performance.

As part of our annual compensation process, our president and chief executive officer prepares performance evaluations for the other executive officers and recommends annual salary increases, annual stock option awards and cash bonuses to the compensation committee. The compensation committee conducts a performance evaluation of our president and chief executive officer. The compensation committee consults with the board of directors as to the achievement of corporate objectives that drive compensation awards.

In March 2021, February 2022 and December 2022, the compensation committee engaged Radford as its independent compensation consultant to provide comparative data on executive and director compensation practices in our industry and assess our executives' and directors' compensation relative to comparable companies for 2021, 2022, and 2023 respectively.

Base Salary

We use base salaries to recognize the experience, skills, knowledge and responsibilities required of all our employees, including our named executive officers. None of our named executive officers is currently party to an employment agreement or other agreement or arrangement that provides for automatic or scheduled increases in base salary.

In March 2021, based upon comparative data on executive compensation provided by Radford and annual performance reviews of our named executive officers, our compensation committee increased (i) Dr. Aivado's annual base salary to $564,736 and (ii) Dr. Annis' annual base salary to $354,900, in each case retroactively effective to January 1, 2021.

In March 2022, based upon comparative data on executive compensation provided by Radford and annual performance reviews conducted by our compensation committee of our named executive officers, our compensation committee increased (i) Dr. Aivado's annual base salary to $587,336, (ii) Dr. Annis' annual base salary to $404,100, and (iii) Dr. Vukovic's annual base salary to $435,925, in each case retroactively effective to January 1, 2022.

Our compensation committee determined not to make any adjustments to our named executive officers' base salaries in 2023.

Cash Incentives

The compensation committee awards annual performance-based cash bonuses to our executive officers for up to a specific percentage of his salary as a vehicle to reward achievement of value-driving milestones and recognize individual performance.

Pursuant to the terms of Dr. Aivado's September 2018 employment agreement, Dr. Aivado is eligible to receive, commencing in 2019 and for each calendar year thereafter that Dr. Aivado is employed by us, a discretionary performance target bonus of up to 50% of his annual base salary based on the achievement of performance milestones set by either our board of directors or the compensation committee of the board.

Pursuant to the terms of Dr. Annis' November 2007 employment offer letter, Dr. Annis is eligible to receive a performance-based cash bonus of up to 20% of his annual base salary, subject to the achievement of performance

milestones as determined by our board of directors in its sole discretion. Between November 2007 and November 2018, Dr. Annis' target performance-based cash bonus was subsequently increased from 20% to 30% of his annual base salary as Dr. Annis assumed additional responsibilities. In connection with Dr. Annis' promotion to senior vice president, research in November 2018, Dr. Annis' target performance-based cash bonus was increased from 30% to 35% of his annual base salary, effective for 2019 and each calendar year thereafter.

Pursuant to the terms of Dr. Vukovic's November 2018 employment offer letter, Dr. Vukovic is eligible to receive a performance-based cash bonus of up to 35% of his annual base salary, subject to the achievement of performance milestones as determined by our board of directors in its sole discretion.

In January 2022, we paid cash bonus awards of $254,131 to Dr. Aivado, $111,794 to Dr. Annis and $133,316 to Dr. Vukovic based on the compensation committee's assessment of achievement of corporate and individual goals in calendar year 2021.

The compensation committee determined not to award cash bonuses to our executive officers for their performance in 2022. In addition, the compensation committee determined not to change the target performance-based cash bonuses for our executive officers for 2023, which will remain at 50% for Dr. Aivado.

Equity Incentives

Although we do not have a formal policy with respect to the grant of equity incentive awards to our executive officers, or any formal equity ownership guidelines applicable to them, we believe that equity grants provide our executives with a strong link to our long-term performance, create an ownership culture and help to align the interests of our executives and our stockholders. In addition, we believe that equity grants with a time-based vesting feature promote executive retention because this feature incents our executive officers to remain in our employment during the vesting period, and equity grants with a performance-based feature incents our executive officers to focus on what we see as key business goals. Accordingly, the compensation committee periodically reviews the equity incentive compensation of our named executive officers and from time to time may grant equity incentive awards to them in the form of stock options.

In June 2021, our board of directors granted options to purchase 120,000, 23,700 and 20,000 shares of our common stock to Dr. Aivado, Dr. Annis and Dr. Vukovic, respectively. 25% of the shares underlying each option vest on June 15, 2022 and the remaining shares underlying each option vest and become exercisable thereafter in 36 monthly installments through June 15, 2025.

In March 2022, our board of directors granted options to purchase 56,650, 15,650 and 7,500 shares of our common stock to Dr. Aivado, Dr. Annis and Dr. Vukovic, respectively. Each of the options vest in equal monthly installments over four years from March 30, 2022.

The compensation committee determined not to grant equity awards to our executive officers in 2023.

Outstanding Equity Awards at Fiscal Year End 2022

The following table sets forth information regarding outstanding equity awards held by our named executive officers as of December 31, 2022:

Name	Number of Securities Underlying Unexercised Options Exercisable (#)		Number of Securities Underlying Unexercised Options Unexercisable (#)		Option Exercise Price ($/ share)	Option Expiration Date
Manuel C. Alves Aivado, M.D., Ph.D.	6,290		—		101.40	3/9/2025
	7,196		—		115.40	3/1/2027
	2,870		—		260.00	7/24/2027
	11,646		—		67.80	9/5/2028
	22,917	(1)	2,084	(1)	35.00	4/14/2029
	14,589	(2)	5,412	(2)	13.60	1/30/2030
	45,752	(3)	76,249	(3)	25.80	6/14/2031
	10,629	(4)	46,022	(4)	9.60	3/29/2032
D. Allen Annis, Ph.D.	2,789		—		101.40	3/12/2024
	403		—		101.40	3/9/2025
	1,208		—		115.40	3/1/2027
	1,251		—		260.00	7/24/2027
	7,085	(1)	416	(1)	35.00	4/14/2029
	4,561	(2)	1,690	(2)	13.60	1/30/2030
	8,890	(3)	14,811	(3)	25.80	6/14/2031
	2,941	(4)	12,710	(4)	9.60	3/29/2032
Vojislav Vukovic, M.D., Ph.D.	7,500		—		43.20	11/4/2028
	5,001	(1)	416	(1)	35.00	4/14/2029
	5,026		—		35.00	4/14/2029
	8,204	(2)	3,047	(2)	13.60	1/30/2030
	7,502	(3)	12,499	(3)	25.80	6/14/2031
	1,413	(4)	12,499	(4)	9.60	3/29/2032

(1) These options were granted on April 15, 2019 and vest as to 2.0833% of the shares in equal monthly installments through April 15, 2023.
(2) These options were granted on January 31, 2020 and vest as to 2.0833% of the shares in equal monthly installments through January 31, 2024.
(3) These options were granted on June 15, 2021 and vest as to 25% of the shares on June 15, 2022 with the remaining shares vesting in equal monthly installments of 2.0833% of the shares through June 15, 2025.
(4) These options were granted on March 30, 2022 and vest as to 2.0833% of the shares in equal monthly installments through March 30, 2026.

Director Compensation

Our non-employee directors receive compensation under our director compensation program.

Cash Retainer

Under this program, we pay our non-employee directors a cash retainer for service on the board of directors and for service on each committee on which the director is a member. The chair of each committee and the chair of the board of directors receive higher retainers for such service. These fees are payable in arrears in four equal quarterly installments on the last day of each quarter, subject to proration for any portion of such quarter that the

director is not serving on our board of directors, on such committee or in such position. The fees paid to non-employee directors for service on the board of directors and for service on each committee of the board of directors on which the director is a member are as follows:

	Base	Incremental — Chair	Incremental — Non-Chair
Board of Directors	$35,000	$ 50,000	—
Audit Committee	—	$ 22,500	$ 15,000
Compensation Committee	—	$ 15,000	$ 10,000
Nominating and Corporate Governance Committee	—	$ 11,250	$ 7,500

Equity Grants

In June 2021, based upon comparative data on board compensation provided by Radford and following the recommendation of our compensation committee, our board granted each current non-employee director an option award in the amount of 4,800 shares of our common stock, contingent upon the approval of our 2021 Stock Incentive Plan, or the 2021 Plan, by our stockholders at the 2021 annual meeting of our stockholders. The June 2021 options vested in full on the earlier of the 1-year anniversary of the date of grant or the date of the 2022 annual meeting of stockholders, subject to continued service, with full acceleration upon a change in control of our company. In June 2021, our board also revised our director compensation program to provide that, commencing with the 2022 annual meeting of stockholders, each non-employee director who has served on our board of directors for at least six months will receive an option to purchase 2,400 shares of our common stock immediately following each annual meeting of our stockholders. Such annual option grants vest in full on the earlier of the first anniversary of the date of grant and the date of the next annual meeting of stockholders, subject to continued service, with full acceleration upon a change in control of our company. The board also revised the director compensation program to provide that each new member of the board will receive an initial grant of 4,800 shares of our common stock, which shall vest over 48 equal monthly installments, subject to continued service, with full acceleration upon a change in control of our company. In all cases, options granted pursuant to our director compensation program have an exercise price equivalent to fair market value of a share of common stock at the time of grant and have a term of 10 years.

In March 2022, based upon comparative data on board compensation provided by Radford, the board of directors further revised the director compensation program to increase the annual stock option grants, such that each non-employee director who has served on our board of directors for at least six months will receive an option to purchase will receive an option to purchase 2,725 shares of our common stock immediately following each annual meeting of our stockholders. In addition, the compensation committee revised the director compensation program to increase the initial grant, such that each new member of the board will receive an option to purchase 5,450 shares of our common stock upon election to the board. All other provisions of the director compensation program, including the vesting terms for such grants, remain unchanged.

We also reimburse our non-employee directors for reasonable travel and out-of-pocket expenses incurred in connection with attending our board of directors and committee meetings.

We do not pay any compensation to our president and chief executive officer in connection with his service on our board of directors. The compensation that we pay to our president and chief executive officer is discussed earlier in this “Executive Compensation” section.

The following table sets forth information regarding compensation earned by our non-employee directors for service during fiscal 2022.

Name	Fees Earned or Paid in Cash ($)	Option Awards ($) [1]	Total ($)
Jeffrey A. Bailey	97,500	21,637	119,137
Reinhard J. Ambros, Ph.D.	50,000	21,637	71,637
William T. McKee	57,500	21,637	79,137
Jodie P. Morrison	58,750	21,637	80,387
Nolan Sigal, M.D., Ph.D.	54,375	21,637	76,012
Josef H. von Rickenbach	60,625	21,637	82,262

(1) The amounts reported in the "Option Awards" column reflect the aggregate grant date fair value of stock-based compensation awarded during the year computed in accordance with the provisions of ASC Topic 718. See Note 10 to our financial statements included in our Annual Report on Form 10-K regarding assumptions underlying the valuation of equity awards.

As of December 31, 2022, our non-employee directors that served in such capacity during fiscal 2022 held the following stock options, all of which were granted under (a) our 2017 Stock Incentive Plan, or 2017 Plan, and (b) our 2021 Plan:

Name	Option Awards
Jeffrey A. Bailey	12,150
Reinhard J. Ambros, Ph.D.	12,150
William T. McKee	9,400
Jodie P. Morrison	10,900
Nolan Sigal, M.D., Ph.D.	9,400
Josef H. von Rickenbach	9,400

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

Unless otherwise provided below, the following table sets forth information regarding beneficial ownership of our common stock as of April 25, 2023, by:

- each person, or group of affiliated persons, known to us to be the beneficial owner of 5% or more of the outstanding shares of our common stock;
- each of our current directors;
- our named executive officers; and
- all of our current executive officers and directors as a group.

Beneficial ownership is determined in accordance with the rules and regulations of the SEC and includes voting or investment power with respect to our common stock. Percentage of beneficial ownership is based on 4,541,167 shares of our common stock outstanding as of April 25, 2023. In addition, shares of common stock subject to options, warrants, or other rights currently exercisable or exercisable within 60 days of April 25, 2023, are deemed outstanding and beneficially owned for the purpose of computing the percentage beneficially owned by (i) the person or entity holding such options, warrants or other rights (but not any other person or entity) and (ii) the directors and executive officers as a group. Except as otherwise noted, the persons and entities in this table have sole voting and investing power with respect to all of the shares of our common stock beneficially

owned by them, subject to community property laws, where applicable. Except as otherwise set forth below, the address of the beneficial owner is c/o Aileron Therapeutics, Inc., 738 Main Street, Unit #398, Waltham, Massachusetts 02451.

Name of Beneficial Owner	Total Beneficial Ownership	
	Shares Beneficially Owned	Percentage of Shares Beneficially Owned
5% Stockholders		
Muneer A. Satter (1)	907,779	19.9%
Scott B. Kapnick (2)	379,608	8.4%
BVF Inc. (3)	236,835	5.2%
Named Executive Officers and Directors		
Manuel C. Aivado, M.D., Ph.D. (4)	147,260	3.2%
D. Allen Annis, Ph.D. (5)	35,165	*
Vojislav Vukovic, M.D., Ph.D. (6)	42,854	*
Jeffrey A. Bailey (7)	15,895	*
Reinhard J. Ambros, Ph.D. (8)	12,440	*
William T. McKee (9)	9,400	*
Jodie P. Morrison (10)	10,900	*
Josef H. von Rickenbach (11)	34,160	*
Nolan Sigal, M.D., Ph.D. (12)	9,400	*
All Executive Officers and Directors as a Group (7 persons)	239,455	5.0%

* Represents beneficial ownership of less than 1% of our outstanding stock.

(1) Based on information provided in a Schedule 13D/A filed on January 8, 2021, Muneer A. Satter's beneficial ownership consists of (i) 51,254 shares of common stock that are held by Muneer A. Satter Revocable Trust for which Mr. Satter serves as trustee and, in such capacity, has sole voting and dispositive power over all such shares; (ii) 61,552 shares of common stock that are held by various other trusts and other entities for which Mr. Satter serves as trustee, investment advisor or manager and, in such capacity, has sole voting and dispositive power over all such shares; (iii) 717,666 shares of common stock that are held by Satter Medical Technology Partners, L.P., or SMTP, for which Mr. Satter has sole voting and dispositive power over all such shares and (iv) 77,307 shares of common stock which may be acquired upon the exercise of warrants held by SMTP for which Mr. Satter has sole voting and dispositive power. As a result of the application of a beneficial ownership cap in the warrants, the table above does not include 109,260 shares of common stock issuable upon exercise of warrants to purchase common stock held by SMTP. Under the terms of the warrants issued to SMTP, SMTP is not permitted to exercise such warrants to purchase common stock to the extent that such exercise would result in SMTP and its affiliates beneficially owning more than 19.99% of the number of shares of our common stock outstanding immediately after giving effect to the issuance of shares of common stock issuable upon exercise of such warrants to purchase common stock. The address for Mr. Satter is c/o Alerce Management Co., L.P., 676 N. Michigan Avenue, Suite 4000, Chicago, IL 60611.

(2) Based on information provided in a Schedule 13G/A filed on February 14, 2023. Mr. Kapnick has sole voting and dispositive power over all of his shares of common stock. As a result of the application of a beneficial ownership cap in the warrants issued to Mr. Kapnick, the table above does not include 74,626 shares of common stock issuable upon exercise of warrants to purchase common stock held by Mr. Kapnick. Under the terms of the warrants, Mr. Kapnick is not permitted to exercise such warrants to purchase common stock to the extent that such exercise would result in Mr. Kapnick and his affiliates beneficially owning more than 4.999% of the number of shares of our common stock outstanding immediately after giving effect to the issuance of shares of common stock issuable upon exercise of such warrants to purchase common stock. Mr. Kapnick has the right to increase this beneficial ownership limitation at his discretion on

61 days' prior written notice to us. Mr. Kapnick is a former member of our board of directors. The address for Mr. Kapnick is 20 East 73rd St, New York, New York 10021.

(3) Based on information provided in a Schedule 13G/A filed on February 14, 2023, BVF, Inc. ("BVF") has shared voting and dispositive power over all of its shares of common stock. BVF's beneficial ownership is comprised of 236,835 shares of common stock owned by certain private investment vehicles managed by BVF. The principal business address of BVF is 44 Montgomery St., 40th Floor San Francisco, California 94104.

(4) Consists of (i) 50 shares of common stock held directly and (ii) 147,210 shares of common stock issuable upon the exercise of options exercisable within 60 days after April 25, 2023.

(5) Consists of (i) 377 shares of common stock held directly and (ii) 34,788 shares of common stock issuable upon the exercise of options exercisable within 60 days after April 25, 2023.

(6) Consists of (i) 3,750 shares of common stock held directly and (ii) 39,104 shares of common stock issuable upon the exercise of options exercisable within 60 days after April 25, 2023.

(7) Consists of (i) 3,745 shares of common stock held directly and (ii) 12,150 shares of common stock issuable upon the exercise of options exercisable within 60 days after April 25, 2023.

(8) Consists of (i) 290 shares of common stock held directly and (ii) 12,150 shares of common stock issuable upon the exercise of options exercisable within 60 days after April 25, 2023.

(9) Consists of 9,400 shares of common stock issuable upon the exercise of options exercisable within 60 days after April 25, 2023.

(10) Consists of 10,900 shares of common stock issuable upon the exercise of options exercisable within 60 days after April 25, 2023.

(11) Consists of (i) 22,273 shares of common stock held directly, (ii) 2,487 shares of common stock issuable upon the exercise of warrants to purchase common stock exercisable within 60 days after April 25, 2023, and (iii) 9,400 shares of common stock issuable upon the exercise of options exercisable within 60 days after April 25, 2023.

(12) Consists of 9,400 shares of common stock issuable upon the exercise of options exercisable within 60 days after April 25, 2023.

Securities Authorized for Issuance Under Equity Compensation Plans

The following table contains information about our equity compensation plans as of December 31, 2022. As of December 31, 2022, we had five equity compensation plans, each of which was approved by our stockholders: our 2006 Equity Incentive Plan, as amended, or the 2006 Plan, our 2016 Stock Incentive Plan, or the 2016 Plan, our 2017 Plan, our 2021 Plan, and our 2017 Employee Stock Purchase Plan, or 2017 ESPP.

Equity Compensation Plan Information

Plan Category	Number of securities to be issued upon exercise of outstanding options, warrants and rights (a)	Weighted average exercise price of outstanding options, warrants and rights ($/share) [1] (b)	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a)) (c)
Equity compensation plans approved by security holders	537,112[2]	29.77	323,448[3][4]
Equity compensation plans not approved by security holders	—	—	—
Total	537,112	29.77	323,448

Equity Compensation Plan Information

(1) Represents the weighted average exercise price of the 537,112 stock options that were outstanding as of December 31, 2022.

(2) Consists of (i) 9,784 shares to be issued upon exercise of outstanding options under our 2006 Plan as of December 31, 2022, (ii) 8,807 shares to be issued upon exercise of outstanding options under our 2016 Plan as of December 31, 2022, (iii) 183,057 shares to be issued upon exercise of outstanding options under our 2017 Plan as of December 31, 2022, and (iv) 335,464 shares to be issued upon exercise of outstanding options under our 2021 Plan as of December 31, 2022.

(3) Consists of (i) 315,948 shares that remained available for future issuance under our 2021 Plan as of December 31, 2022, and (ii) 7,500 shares that remained available for future issuance under our 2017 ESPP as of December 31, 2022. No shares remained available for future issuance under the 2006 Plan, the 2016 Plan, or the 2017 Plan as of December 31, 2022.

(4) Our 2017 ESPP has an evergreen provision that allows for an annual increase in the number of shares available for issuance under the 2017 ESPP to be added on the first day of each fiscal year through the fiscal year ending December 31, 2027, in an amount equal to the least of 31,120 shares of our common stock, 1% of the total number of shares of our common stock outstanding on the first day of the applicable fiscal year and an amount determined by our board of directors. On January 1, 2023, no additional shares were reserved for issuance under the 2017 ESPP pursuant to this provision.

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

Transactions with Related Persons

Since January 1, 2021, we have engaged in the following transactions in which the amount involved exceeded the lesser of $120,000 or one percent of our total assets at year end for fiscal years 2022 and 2021, and any of our executive officers, directors, or beneficial holders of more than 5% of any class of voting securities, or any of their affiliates, had a direct or indirect material interest. We believe that all of these transactions were on terms comparable to terms that could have been obtained from unrelated third parties.

January 2021 Registered Direct Offering

In January 2021, we issued and sold an aggregate of 1,631,549 shares of common stock in a registered direct offering at a purchase price per share of $22.00 for gross proceeds of approximately $35.9 million before deducting the placement agent's fees and other offering expenses payable by us. Entities affiliated with Satter Medical Technology Partners, L.P. purchased 450,000 shares in the registered direct offering for a purchase price of $9.9 million. Dr. Nolan Sigal, a partner at Satter Management Co., L.P., an affiliate of Satter Medical Technology Partners, L.P., is a member of our board of directors. Scott Kapnick purchased 210,750 shares in the registered direct offering for a purchase price of $4.6 million.

Indemnification Agreements

Our restated certificate of incorporation, as amended, provides that we will indemnify our directors and officers to the fullest extent permitted by Delaware law. In addition, we have entered into indemnification agreements with each of our officers and directors that may be broader in scope than the specific indemnification provisions contained in the Delaware General Corporation Law. See "Executive Compensation—Limitations on Liability and Indemnification" for additional information regarding these agreements.

Policies and Procedures for Related Person Transactions

Our board of directors has adopted a written related person transaction policy to set forth policies and procedures for the review of any transaction, arrangement, or relationship in which we are a participant, the amount involved

exceeds $120,000, and one of our executive officers, directors, or 5% stockholders, or their immediate family members, each of whom we refer to as a "related person," has a direct or indirect material interest.

If a related person proposes to enter into such a transaction, arrangement, or relationship, which we refer to as a "related person transaction," the related person must report the proposed related person transaction to our chief executive officer or our chief financial officer. The policy calls for the proposed related person transaction to be reviewed and approved by our audit committee. Whenever practicable, the reporting, review, and approval will occur prior to entry into the transaction. If advance review and approval is not practicable, the committee will review and, in its discretion, may ratify the related person transaction. The policy also permits the chair of the audit committee to review and, if deemed appropriate, approve proposed related person transactions that arise between committee meetings, subject to ratification by the committee at its next meeting. Any related person transactions that are ongoing in nature will be reviewed annually.

A related person transaction reviewed under the policy will be considered approved or ratified if it is authorized by the audit committee after full disclosure of the related person's interest in the transaction. As appropriate for the circumstances, the committee will review and consider:

- the related person's interest in the related person transaction;
- the approximate dollar value of the amount involved in the related person transaction;
- the approximate dollar value of the amount of the related person's interest in the transaction without regard to the amount of any profit or loss;
- whether the transaction was undertaken in the ordinary course of our business;
- whether the terms of the transaction are no less favorable to us than terms that could have been reached with an unrelated third party;
- the purpose of, and the potential benefits to us of, the transaction; and
- any other information regarding the related person transaction or the related person in the context of the proposed transaction that would be material to investors in light of the circumstances of the particular transaction.

The audit committee may approve or ratify the transaction only if the committee determines that, under all of the circumstances, the transaction is in our best interests. The committee may impose any conditions on the related person transaction that it deems appropriate.

In addition to the transactions that are excluded by the instructions to the SEC's related-person transaction disclosure rule, our board of directors has determined that the following transactions do not create a material direct or indirect interest on behalf of related persons and, therefore, are not related-person transactions for purposes of this policy:

- interests arising solely from the related person's position as an executive officer of another entity, whether or not the person is also a director of such entity, that is a participant in the transaction, where (a) the related person and all other related persons own in the aggregate less than a 10% equity interest in such entity; (b) the related person and his or her immediate family members are not involved in the negotiation of the terms of the transaction and do not receive any special benefits as a result of the transaction; (c) the amount involved in the transaction equals less than the greater of $1 million or 2% of the annual gross revenues of the other entity that is a party to the transaction; and (d) the amount involved in the transaction equals less than 2% of our annual gross revenues; and
- a transaction that is specifically contemplated by provisions of our charter or bylaws.

The policy provides that transactions involving compensation of executive officers shall be reviewed and approved by the compensation committee in the manner specified in its charter.

Employment Agreements

Manuel C. Alves Aivado, M.D., Ph.D.

In September 2018, in connection with our appointment of Dr. Aivado as our president and chief executive officer, we entered into a new employment agreement with Dr. Aivado, which superseded his July 2014 employment agreement with us. Pursuant to the terms of Dr. Aivado's September 2018 employment agreement, we agreed to pay Dr. Aivado a base salary at a rate of $41,666.67 per month, which was based on an annualized base salary of $500,000. Beginning in 2019, following the end of each calendar year that Dr. Aivado is employed by us, Dr. Aivado will be eligible to receive a discretionary performance target bonus of up to 50% of his then annual base salary based on the achievement of performance milestones set by either our board of directors or the compensation committee of the board. The employment agreement also provided that following the end of the 2018 calendar year, Dr. Aivado was eligible to receive a discretionary performance target bonus calculated on the basis of 35% of his base salary as of August 31, 2018 pro-rated for the first eight months of the fiscal year, and 50% of his current base salary under the employment agreement pro-rated for the remaining four months of the fiscal year. The amount of such bonus and the achievement of such milestones were determined by our board in its sole discretion. Dr. Aivado is also entitled to receive reimbursement of up to $4,400 per month for travel and living accommodations pursuant to the employment agreement.

Pursuant to the employment agreement, in September 2018 we granted Dr. Aivado options to purchase 11,646 shares of our common stock under our 2017 Stock Incentive Plan. The options have an exercise price of $67.80, which was the closing price of our common stock on September 6, 2018. The options vest in equal monthly installments over four years from September 6, 2018.

D. Allen Annis, Ph.D.

In November 2007, we entered into an employment offer letter with D. Allen Annis, Ph.D. The offer letter established Dr. Annis' title, his base salary, his eligibility for an annual bonus, and his eligibility for benefits made available to employees generally. The offer letter established that Dr. Annis' employment was at will. Pursuant to the offer letter, we granted Dr. Annis options to purchase 3,750 shares of our common stock under our 2006 Plan, at a price per share equal to the fair market value of one share of our common stock on the date of the option grant as determined by our board.

On April 24, 2023, we entered into a separation and release of claims agreement with Dr. Annis, which provided for Dr. Annis' separation of employment as our senior vice president, research, effective as of April 15, 2023. In accordance with the terms of the separation agreement, we agreed to provide Dr. Annis with (i) a lump sum payment representing an aggregate amount equal to nine months of Dr. Annis' salary as of April 15, 2023, subject to applicable taxes and withholdings, and (ii) payment on Dr. Annis' behalf of the monthly premiums for group medical insurance coverage under COBRA until the earlier of the date that is nine months after April 15, 2023 and the date on which Dr. Annis becomes eligible to receive the same or substantially similar group health insurance coverage through another employer. The separation agreement also contains a release of claims by Dr. Annis, subject to customary exceptions, and covenants not to solicit or disparage and to cooperate with us.

In April 2023, we also entered into a consulting agreement with Dr. Annis for an initial term of six months. We will pay Dr. Annis an hourly consulting fee equal to $500 per hour for his services under the consulting agreement, which may not exceed 10 hours per month without our prior written consent. The consulting agreement also provides that Dr. Annis may be eligible to receive a cash bonus award in recognition of his services under the consulting agreement, in an amount not to exceed $50,000, as determined in the sole discretion of our compensation committee. Pursuant to the terms of the consulting agreement, Dr. Annis' options to purchase shares of our common stock continue to vest and be exercisable during the term of the consulting agreement. The consulting agreement may be terminated by Dr. Annis or us for any reason upon fifteen days' advance written notice to the other party.

Vojislav Vukovic, M.D., Ph.D.

In November 2018, we entered into an employment offer letter with Vojislav Vukovic, M.D., Ph.D. pursuant to which Dr. Vukovic agreed to serve as our senior vice president, chief medical officer. The offer letter established Dr. Vukovic's title, his base salary, his eligibility for an annual bonus, and his eligibility for benefits made available to employees generally. Dr. Vukovic's employment was at will. Pursuant to his offer letter, we granted Dr. Vukovic options to purchase 150,000 shares of our common stock under our 2017 Plan, which options were subject to service-based vesting, at an exercise price equal to $2.16, which was the fair market value of one share of our common stock on the date of grant.

On July 8, 2022, we entered into a separation and release of claims agreement with Dr. Vukovic, which provided for Dr. Vukovic's separation of employment as our senior vice president, chief medical officer. In accordance with the terms of the separation agreement, we agreed to provide Dr. Vukovic with (i) nine months of semi-monthly salary continuation payments, payable in equal installments in accordance with our regular payroll practices, in an aggregate amount equal to nine (9) months of Dr. Vukovic's base salary as of July 8, 2022, subject to applicable taxes and withholdings, and (ii) payment on Dr. Vukovic's behalf of the monthly premiums for group medical insurance coverage under COBRA until the earlier of the date that is nine months after July 8, 2022 and the date on which Dr. Vukovic becomes eligible to receive the same or substantially similar group health insurance coverage through another employer. The separation agreement also contains a release of claims by Dr. Vukovic, subject to customary exceptions, and covenants not to solicit or disparage and to cooperate with us.

In July 2022, we also entered into a consulting agreement with Dr. Vukovic for an initial term of twelve months. Pursuant to the terms of the consulting agreement, Dr. Vukovic's options to purchase shares of our common stock continue to vest and be exercisable during the term of the consulting agreement. Dr. Vukovic does not receive any cash compensation from us under the consulting agreement. The consulting agreement may be terminated by Dr. Vukovic or us for any reason upon thirty days' advance written notice to the other party.

Severance and Change in Control Agreements

We have entered into a severance agreement with Dr. Aivado. Under the terms of the severance agreement, if we terminate Dr. Aivado's employment other than for cause or by reason of death or disability, or if Dr. Aivado terminates his employment for good reason and, in each case, not upon or within twelve months following a change in control event, as such terms are defined in the severance agreement, Dr. Aivado will be entitled to receive his then current base salary for twelve months following the date of Dr. Aivado's termination and (B) payments on Dr. Aivado's behalf of the monthly premiums for medical insurance coverage under COBRA until the earlier of the date that is 12 months following the date of Dr. Aivado's termination or the date on which Dr. Aivado becomes eligible to receive group health insurance coverage through another employer, which we refer to as the standard severance benefits. If we terminate Dr. Aivado's employment other than for cause or by reason of death or disability, or if Dr. Aivado terminates his employment for good reason, in each case upon or within 12 months following a change in control event, Dr. Aivado will be entitled to receive the standard severance benefits for a period of 18 months following the date of Dr. Aivado's termination and a lump sum payment equal to one and one-half times Dr. Aivado's target bonus for the year in which he is terminated, and the vesting of any unvested equity awards will accelerate in full on the date of Dr. Aivado's termination. Dr. Aivado's receipt of any post-separation benefits under the severance agreement is conditioned upon his execution of a severance and release of claims agreement in a form satisfactory to us. Upon the execution of his severance agreement, Dr. Aivado ceased to be entitled to the severance and post-employment payments and benefits provided under any preexisting agreements between us and Dr. Aivado.

Other Agreements

We have also entered into employee confidentiality, inventions, non-solicitation and non-competition agreements with each of our named executive officers. Under the employee confidentiality, inventions, non-solicitation and

non-competition agreements, each named executive officer has agreed (1) not to compete with us during his employment and for a period of one year after the termination of his employment, (2) not to solicit our employees during his employment and for a period of two years after the termination of his employment, (3) to protect our confidential and proprietary information and (4) to assign to us related intellectual property developed during the course of his employment.

401(k) Retirement Plan

We maintain a 401(k) retirement plan that is intended to be a tax-qualified defined contribution plan under Section 401(k) of the Internal Revenue Code. In general, all of our employees are eligible to participate, beginning on the first day of the month following commencement of their employment. The 401(k) plan includes a salary deferral arrangement pursuant to which participants may elect to reduce their current compensation by up to the statutorily prescribed limit, equal to $19,500 in 2021 and $20,500 in 2022 and have the amount of the reduction contributed to the 401(k) plan. Participants over the age of 50 are entitled to an additional catch-up contribution up to the statutorily prescribed limit, equal to $6,500 in 2021 and 2022.

Prior to the 2021 calendar year, we did not match employee contributions.

In March 2021, our compensation committee adopted a 100% match on the first 4% of eligible compensation, retroactively effective to January 1, 2021, which remained applicable in 2022. This was a non-voluntary contribution by the Company for 2021 and 2022 and will be a non-voluntary contribution by the Company for 2023.

Limitations on Liability and Indemnification

As permitted by Delaware law, we adopted provisions in our restated certificate of incorporation, as amended, that limit or eliminate the personal liability of our directors. Our restated certificate of incorporation, as amended, limits the personal liability of directors for breach of fiduciary duty to the maximum extent permitted by the General Corporation Law of the State of Delaware and provides that no director will have personal liability to us or to our stockholders for monetary damages for breach of fiduciary duty. However, these provisions do not eliminate or limit the liability of any of our directors:

- for any breach of the director’s duty of loyalty to us or our stockholders;
- for acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
- for voting for or assenting to unlawful payments of dividends, stock repurchases or other distributions; or
- for any transaction from which the director derived an improper personal benefit.

Any amendment to or repeal of these provisions will not eliminate or reduce the effect of these provisions in respect of any act, omission or claim that occurred or arose prior to such amendment or repeal. If the General Corporation Law of the State of Delaware is amended to provide for further limitations on the personal liability of directors of corporations, then the personal liability of our directors will be further limited to the greatest extent permitted by the General Corporation Law of the State of Delaware.

In addition, our restated certificate of incorporation, as amended, provides that we must indemnify our directors and officers and we must advance expenses, including attorneys’ fees, to our directors and officers in connection with legal proceedings, subject to very limited exceptions.

We maintain a general liability insurance policy that covers specified liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers. In addition, we entered

into indemnification agreements with each of our officers and directors. These indemnification agreements require us, among other things, to indemnify each such director or officer for some expenses, including attorneys' fees, judgments, fines and settlement amounts, incurred by him or her in any action or proceeding arising out of his or her service as one of our directors or officers.

Some of our non-employee directors may, through their relationships with their employers, be insured or indemnified against specified liabilities incurred in their capacities as members of our board of directors.
Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, executive officers or persons controlling us, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

Item 14. Principal Accounting Fees and Services.

Audit Fees and Services

Audit Fees and Services

PricewaterhouseCoopers was our independent registered public accounting firm for the years ended December 31, 2022 and December 31, 2021. The following table summarizes the fees of PricewaterhouseCoopers billed to us for each of the last two fiscal years. All such services and fees were pre-approved by our audit committee in accordance with the "Pre-Approval Policies and Procedures" described below.

Fee Category	2022	2021
Audit Fees (1)	$546,200	$477,600
All Other Fees (2)	3,081	3,000
Total Fees	$549,281	$480,600

(1) "Audit Fees" consist of fees for the audit of our annual financial statements, the review of the interim financial statements included in our quarterly reports on Form 10-Q and other professional services provided in connection with regulatory filings or engagements.
(2) "All Other Fees" consist of database subscription fees paid to PricewaterhouseCoopers.

Pre-Approval Policies and Procedures

Our audit committee has adopted procedures requiring the pre-approval of all non-audit services performed by our independent registered public accounting firm in order to assure that these services do not impair the auditor's independence. These procedures generally approve the performance of specific services subject to a cost limit for all such services. This general approval is to be reviewed, and if necessary modified, at least annually. Management must obtain the specific prior approval of the audit committee for each engagement of the independent registered public accounting firm to perform other audit-related or other non-audit services. The audit committee does not delegate its responsibility to approve services performed by the independent registered public accounting firm to any member of management. Our audit committee has delegated authority to the committee chair to pre-approve any audit or non-audit service to be provided to us by our independent registered public accounting firm provided that the fees for such services do not exceed $100,000. Any approval of services by the committee chair pursuant to this delegated authority must be reported to the audit committee at the next meeting of the committee.

The standard applied by the audit committee, or the chair of the audit committee, in determining whether to grant approval of any type of non-audit service, or of any specific engagement to perform a non-audit service, is whether the services to be performed, the compensation to be paid therefore and other related factors are consistent with the independent registered public accounting firm's independence under guidelines of the SEC and applicable professional standards. Relevant considerations include whether the work product is likely to be

subject to, or implicated in, audit procedures during the audit of our financial statements, whether the independent registered public accounting firm would be functioning in the role of management or in an advocacy role, whether the independent registered public accounting firm's performance of the service would enhance our ability to manage or control risk or improve audit quality, whether such performance would increase efficiency because of the independent registered public accounting firm's familiarity with our business, personnel, culture, systems, risk profile and other factors, and whether the amount of fees involved, or the non-audit services portion of the total fees payable to the independent registered public accounting firm in the period would tend to reduce the independent registered public accounting firm's ability to exercise independent judgment in performing the audit.

PART IV

Item 15. Exhibits and Financial Statement Schedules.

(a) Financial Statements

The response to this portion of Item 15 is incorporated by reference from the Original Filing into this Amendment.

(b) Exhibits.

Exhibit Number	Description	Incorporation by Reference			Filed Herewith
		Form	Date of Filing	Exhibit Number	
3.1	Restated Certificate of Incorporation of the Registrant, as amended	10-Q	8/11/2021	3.1	
3.2	Certificate of Amendment of Restated Certificate of Incorporation of the Registrant	8-K	11/10/2022	3.2	
3.3	Amended and Restated By-laws of the Registrant	8-K	7/5/2017	3.3	
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*	2021 Stock Incentive Plan	8-K	6/17/2021	99.1	
10.12*	Form of Stock Option Agreement under 2021 Stock Incentive Plan	10-K	3/20/2023	10.12	
10.13*	Form of Restricted Stock Unit Agreement under 2021 Stock Incentive Plan	10-K	3/20/2023	10.13	
10.14	Form of Director and Officer Indemnification Agreement	S-1^	6/19/2017	10.12	

Exhibit Number	Description	Incorporation by Reference			Filed Herewith
		Form	Date of Filing	Exhibit Number	
10.15	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	
10.16+	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	
10.17*	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	
10.18*	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	
10.19*	Offer Letter, dated as of November 15, 2007, between the Registrant and D. Allen Annis, Ph.D.	10-K	3/29/2019	10.21	
10.20*	Severance Agreement, dated as of November 5, 2018, between the Registrant and D. Allen Annis, Ph.D.	10-K	3/29/2019	10.22	
10.21	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	
10.27	Sublease Agreement, dated March 26, 2021, by and among the Company, Vittoria Industries North America, Inc. and Waterfront Equity Partners, LLC	10-Q	5/11/2021	10.1	
10.28*	Separation and Release of Claims Agreement, dated July 8, 2022, by and between the Company and Vojislav Vukovic, M.D., Ph.D.	10-Q	8/15/2022	10.1	
23.1	Consent of PricewaterhouseCoopers LLP, independent registered public accounting firm.	10-K	3/20/2023	23.1	

Exhibit Number	Description	Incorporation by Reference			Filed Herewith
		Form	Date of Filing	Exhibit Number	
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.	10-K	3/20/2023	31.1	
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.	10-K	3/20/2023	31.2	
31.3	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
31.4	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.	10-K	3/20/2023	32.1	
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.	10-K	3/20/2023	32.2	
101.INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.				
101.SCH	Inline XBRL Taxonomy Extension Schema Document				
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document				
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document				
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document				
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document				
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)				

* 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: April 28, 2023

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)

Exhibit 31.3

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 Amendment No. 1 to the Annual Report on Form 10-K of Aileron Therapeutics, Inc.; and

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.

Date: April 28, 2023

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

Manuel C. Alves Aivado, M.D., Ph.D.
President and Chief Executive Officer

Exhibit 31.4

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, Susan L. Drexler, certify that:

1. I have reviewed this Amendment No. 1 to the Annual Report on Form 10-K of Aileron Therapeutics, Inc.; and

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.

Date: April 28, 2023

/s/ Susan L. Drexler

Susan L. Drexler
Principal Financial Officer and Interim Chief Financial Officer