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, 2018

OR

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

Commission File Number 001-38130

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

Delaware **(State or other jurisdiction of incorporation or organization)**	**13-4196017** **(I.R.S. Employer Identification No.)**
490 Arsenal Way, Suite 210 **Watertown, MA** **(Address of principal executive offices)**	**02472** **(Zip Code)**

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

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

Title of each class	**Name of each exchange on which registered**
Common Stock, $0.001 par value	**The Nasdaq Global Market**

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

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

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 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 if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405) is not contained herein, and will not be contained, to the best of Registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☒

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 is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES ☐ NO ☒

As of June 29, 2018, the last 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 $40,753,229.

As of March 26, 2019, the Registrant has 14,875,035 shares of Common Stock, $0.001 par value per share, outstanding.

Portions of the Registrant's definitive proxy statement for its 2019 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, 2018, are incorporated by reference into Part III of this Annual Report on Form 10-K.

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

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

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

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

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

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.

PART I

Item 1. Business.

Overview

We are a clinical-stage biopharmaceutical company that is focused on developing and commercializing a novel class of stabilized cell-permeating alpha-helical peptides to address intracellular targets in oncology and other therapeutic areas. Our lead product candidate, ALRN-6924, is a cell-permeating peptide that disrupts the interaction of p53 suppressors MDM2 and MDMX with tumor suppressor p53 to reactivate tumor suppression in non-mutant, or wild-type, p53 cancers. Based on preclinical data and preliminary evidence of safety and anti-tumor activity in our ongoing clinical trials, we believe that there may be a significant opportunity to develop ALRN-6924 in combination with other drugs for a wide variety of cancers. Our clinical development program for ALRN-6924 is currently focused on our ongoing Phase 2a clinical trial of the combination of ALRN-6924 and palbociclib (Ibrance), marketed by Pfizer, Inc., for the treatment of MDM2-amplified advanced solid tumors and our planned Phase 1b/2 clinical trial to evaluate ALRN-6924 as a myelopreservative agent, to protect against chemotherapy-induced bone marrow toxicity. Our first planned clinical trial to assess the myelopreservation opportunity will be in small cell lung cancer patients who will be treated with the chemotherapy topotecan.

We have conducted other clinical trials of ALRN-6924 as a single agent and in combination with other therapies. For instance, we have conducted a single-agent Phase 2a trial for the treatment of peripheral T-cell lymphoma, or PTCL, a single-agent Phase 1 trial for the treatment of acute myeloid leukemia, or AML, and advanced high-risk myelodysplastic syndrome, or MDS, and a Phase 1b trial testing the combination of ALRN-6924 and cytarabine, or Ara-C, in patients with MDS. We have observed anticancer activity with ALRN-6924 in each of these trials. However, despite that activity, in light of our resources, and our assessment of the commercial opportunities in these indications, as well as the changed competitive landscape in myeloid cancers where seven drugs were approved for AML in the United States in the last two years, we have determined to cease enrollment in these trials and further clinical development for these indications at this time. We plan to present data from our AML/MDS trials in the fourth quarter of 2019.

We believe that by using our proprietary stabilized cell-permeating peptide platform, we can develop first-in-class molecules, like ALRN-6924, that contain a novel set of properties. As such, our stabilized cell-permeating peptide drugs may be able to address historically undruggable targets, such as intracellular protein-protein interactions like p53 and MDM2/MDMX, that underlie many diseases with high unmet medical need. We believe that stabilized cell-permeating peptide therapeutics have the potential to become a major class of drugs, like small molecules and monoclonal antibodies, for oncology and other therapeutic areas, and may significantly improve treatment paradigms and clinical outcomes for patients. We believe that the ability of our stabilized cell-permeating peptides to target and activate or inhibit key intrinsic cellular functions, such as the p53 signaling pathway and affect key cellular functions such as cell cycle control and apoptosis, along with our scientific expertise in the design, application and development of these stabilized cell-permeating alpha-helical peptides, has the potential to positively impact patients' lives and treatment strategies for a wide variety of cancers. Our belief is based on the scientific evidence that these cellular functions play a key role in cancer formation, maintenance and treatment resistance. As such, we believe the ability to directly affect these key intrinsic cellular functions, which we are seeking to do with ALRN-6924 and p53 reactivation, may have potential advantages over approved drugs and drug candidates that are directed against other targets or systemically by stimulating immune responses. By targeting a key signaling pathway like p53 that is critical and preserved across a multitude of different cancers, we believe our approach may allow for utility in a broader set of cancer patients.

P53 has been a focus of researchers and the pharmaceutical industry due to its central role in preventing the initiation and progression of most cancers, and has long been referred to as "the guardian of the genome" because of its central role in cellular defense mechanisms against cancers. P53 is activated when DNA damage is detected and, among other functions, is capable of regulating a variety of tumor suppression responses, including cell cycle arrest, DNA repair, apoptosis, or senescence. The effect of p53 activation is to facilitate the repair of the cell, or trigger killing of the damaged cell, a process known as apoptosis, before it can become cancerous. P53 function is believed to be primarily regulated by the suppressor proteins MDM2 and MDMX, which bind to p53 to either reduce its levels through degradation or control its activity, including the suppression of effect on cell repair and apoptotic activities, so that normal cells are able to function as expected. Approximately half of all cancer patients at initial diagnosis have cancers that prevent this tumor suppression response by mutation of the p53 gene. The remaining cancer patients have a p53 gene that is not mutated and is otherwise known as wild type, or WT, but that is functionally suppressed through the activation or overexpression of regulatory proteins, including, MDM2 and MDMX. ALRN-6924 reactivates non-mutant or WT p53 by disrupting the interactions between p53 and these two suppressor proteins, thereby freeing p53 to proceed to its DNA targets in the nucleus and initiate cell cycle arrest, DNA repair, apoptosis, or senescence in damaged cells. Although p53 and its tumor suppression responses have been well characterized in the scientific literature, no product that directly engages p53 and its function has been approved. Moreover, we believe that the only product candidates in clinical development targeted at p53 activation, including one product candidate that is in Phase 3 testing, are small molecule inhibitors that are designed to engage only the p53-MDM2 interaction and not the p53-MDMX interaction, which we believe, based on published data and our clinical results, is also important in determining clinical outcomes. We believe that ALRN-6924 is the first and only product candidate in clinical development that can bind to and disrupt the interaction of MDM2 and MDMX with p53 with equivalent effectiveness, or equipotently. As such, we believe that ALRN-6924's ability to bind to both MDM2 and MDMX may enable it to have an effect in a broader range of tumors and to have a favorable safety profile.

Our integrated understanding of peptide chemistry and molecular biology as it relates to the physiological functions of stabilized and cell-permeating peptides forms the basis of our ability to generate novel product candidates. We seek to rationally design sequences of amino acids and "staple" or stabilize them with hydrocarbon bonds that maintain their natural alpha-helical shape. The broad potential of maintaining the alpha helix is derived from the fact that it is the most common protein structure at the interface of protein-protein interactions and, as exploited by our stabilized cell-permeating alpha-helical peptides, is a necessary shape to retain the intended biological activity of the therapeutic molecule. Our approach is to target high value and historically undruggable intracellular and extracellular targets with this novel class of molecules. In the case of cancer, pathways that incorporate protein-protein interactions with an alpha helix, and that, therefore, may be amenable to our approach and the focus of our future research, include p53 and may include other transcription factors and signaling proteins such as Ras, Myc, ß-Catenin, the Bcl family of proteins and HIF-1a. Importantly, while the critical role of these targets in biological processes has been known for decades, there are no approved therapeutics that directly engage these targets other than one therapeutic that inhibits Bcl-2. In addition to oncology, we are currently exploring research and business development strategies to develop certain non-cancer applications.

Since our inception, we have created and evaluated over 10,000 cell-permeating peptides against multiple targets in a variety of therapeutic areas. We believe that a number of these molecules and targets warrant further study and development and could, in the future, contribute to a pipeline of novel therapeutics. Subject to our resources, we intend to continue to make selective investments into early research programs as part of our ongoing research. Where we believe it will be beneficial to the success of the program, we will also seek academic and industry collaborations to advance this work.

We strive to protect the proprietary product candidates and technologies that we believe are important to our business, including seeking and maintaining patent protection intended to cover the composition of matter of our product candidates, including ALRN-6924, their methods of use, related platform technology and other inventions. As of January 31, 2019, we owned or had an exclusive license to over 240 patents and over 190 provisional or non-provisional patent applications throughout the world directed toward various aspects of our product candidates and research programs. We own worldwide rights to ALRN-6924.

Our Strategy

Our goal is to be a leader in the discovery, development and commercialization of novel therapeutics for the treatment of cancer by targeting high-value and historically undruggable targets through our proprietary stabilized cell-permeating peptide technology. Key elements of our strategy to achieve this goal include the following:

Pursue a targeted development strategy for our lead product candidate, ALRN-6924, across multiple oncology indications. We are advancing our lead product candidate, ALRN-6924, into several clinical trials, focusing on areas in which we believe ALRN-6924 may have anti-tumor activity or myelopreservative effects and in which there are significant unmet medical needs. We are initially focusing our development efforts on cancers that commonly present with WT p53. One of the key benefits of targeting p53 is that the MDMX/MDM2-dependent mechanism by which cancers overcome p53 control is found in a broad range of cancers. We have demonstrated evidence of anti-tumor activity of ALRN-6924 as a single agent in our Phase 1 All-comers trial in which we have treated patients with 24 different tumor types as well as in our Phase 2a PTCL trial and our Phase 1/1b AML/MDS trials.

We plan to conduct, alone and in collaboration with third parties, additional clinical trials of ALRN-6924, as warranted by the clinical data. The goal of these clinical trials will be to broaden the application of ALRN-6924 by studying safety and potential anti-tumor activity in additional distinct subgroups of patients with specific cancers that commonly present with WT p53. Because many approved drugs and drug candidates for cancer require a functioning p53 pathway to exert their anti-cancer effect, we have expanded and advanced our non-clinical and clinical research to test a variety of approved drugs in combination with ALRN-6924, including cyclin-dependent kinase inhibitors, traditional chemotherapeutic agents, and immuno-oncology agents. We believe the mechanism of action and safety profile of ALRN-6924 may provide the potential for its combination with a wide variety of conventional and novel therapies.

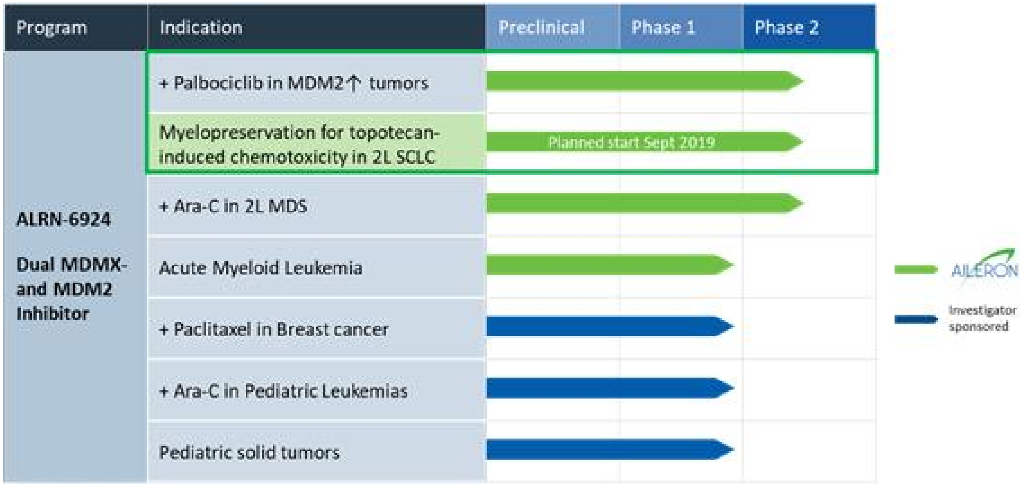
Design and execute on clinical trial programs with the expectation of presenting data within the next twelve months. We plan to disclose interim data from our Phase 2a trial of the combination of ALRN-6924 and palbociclib in patients with MDM2-amplified solid tumors at a medical conference in the second half of 2019. Additionally, we intend to initiate our planned Phase 1b/2 clinical trial to evaluate ALRN-6924 as a myelopreservative agent which protects against chemotherapy-induced bone marrow toxicity. We anticipate initiating this trial in September of 2019 and presenting interim data from the trial in the first half of 2020. Additionally, we plan to disclose data from our Phase 1b trial of the combination of ALRN-6924 and Ara-C in patients with advanced MDS in the fourth quarter of 2019.

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

Leverage our proprietary stabilized cell-permeating peptide technology to develop additional product candidates across oncology and other diseases with unmet medical need. Over 3,000 known protein-protein interactions are mediated by a helical peptide interface. Based on our data related to stabilized cell-permeating peptides, as well as the growing body of third-party publications that support the utility of these peptides against a wide variety of targets, we believe that our stabilized peptides have the potential for therapeutic benefits across a broad range of oncology indications and other diseases with unmet medical need. Subject to available resources, we plan to invest in and conduct research on those product candidates for which our prior work or published literature suggests a stabilized cell-permeating peptide may confer advantages over small molecule or biologic therapeutics in delivering therapeutic benefits. We may also seek to develop additional stabilized cell-permeating peptides to target p53 as changes in the chemical structures of our stabilized peptides may engender peptides with varying affinities to MDM2 and MDMX. Additionally, we may seek to selectively form collaborations to expand our capabilities and potentially accelerate research and development activities for certain of these oncology indications and other diseases.

Our Development Pipeline

The following table summarizes key information about our ongoing and planned ALRN-6924 clinical trials.



Cancer and the Need for Novel and Improved Treatment Options

Cancer is a major public health problem in the United States and worldwide. The U.S. National Cancer Institute estimated that approximately 40% of all men and women in the United States will be diagnosed with cancer during their lifetime. According to the U.S. Centers for Disease Control, cancer is currently the second leading cause of death in the United States and is expected to surpass heart disease as the leading cause of death in the next several years. Although progress has been made in the diagnosis and treatment of cancer, the American Cancer Society estimates that over 1.75 million new cancer cases will be diagnosed in the United States and more than 600,000 people will die from cancer in 2019. Thus, there remains a significant need for novel and improved treatment options for cancer patients.

Most cancers begin as a result of DNA damage or the mutation of certain important genes that alters or inhibits the cell's mechanism for making the proteins it needs to function, survive and grow. When DNA becomes damaged or mutated, either as a result of natural processes, inherited traits or other exogenous factors such as radiation or exposure to chemicals in the environment, abnormal cells begin to replicate and spread into surrounding tissue, interfere with the body's normal function and eventually invade and destroy the body's healthy tissue.

Surgery, radiation and drug therapy, either individually or in combination, are currently the most common methods used in treating patients with cancer and can be effective in specific situations. Surgery and radiation are particularly effective for patients in whom the disease is localized, but cannot fully address the needs of a patient with metastasized tumors. For these patients, or for patients where surgery or radiation is ineffective, physicians typically prescribe a treatment program using systemic drug therapies. The goal of drug therapy is to directly or indirectly kill cancer cells or to damage cellular components required for the proliferation of cancer cells. Drug therapy often is administered as a combination of several different drugs. Drug therapy has been evolving from non-specific drugs that kill both healthy and cancer cells, to drugs that target specific molecular pathways to preferentially or selectively kill cancer cells. While heightened vigilance, new diagnostic tests, combination regimens and targeted therapies have resulted in improvements in overall survival for some cancer patients, continued innovation in the treatment of cancer is necessary.

The conventional approaches to oncology drug development, which are based primarily on small molecules and antibodies, have limitations that restrict their ability to fully treat cancer. Small molecule drugs can target proteins inside the cell, but are often limited to a subset of proteins with accessible functional domains or, in most cases, a single intended target protein, while antibodies are unable to directly bind to intracellular targets and are thereby limited to targeting circulating proteins or those expressed on the cell surface. We believe that the ability to target and activate or inhibit key intrinsic cellular proteins and their functions, such as p53 and apoptosis, using our proprietary stabilized cell-permeating peptide platform, has the potential to significantly impact patients' lives and treatment strategies for a wide variety of cancers. Our belief is based on the mounting scientific evidence that these cellular functions play a key role in cancer formation, maintenance and treatment resistance. As such, the ability to directly impact these key intrinsic cellular functions, which we are seeking to do with ALRN-6924, may have potential advantages over approved drugs and drug candidates that work upstream at the cell surface or systemically by stimulating immune responses. By targeting a downstream pathway like p53 that is critical and preserved across a multitude of different cancers, our approach may allow for utility in a broader set of cancer patients. In addition, we believe that our approach may circumvent resistance mechanisms that characterize many of the most aggressive cancers.

P53 and its Interaction with MDM2 and MDMX

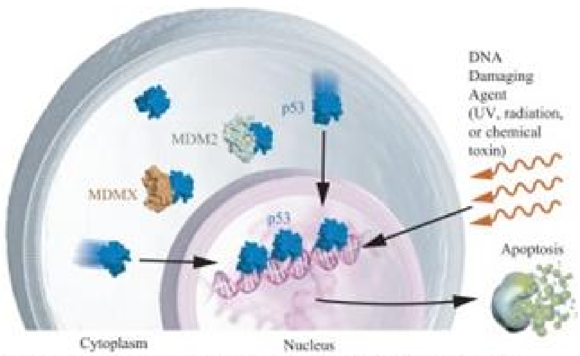
P53 is considered to be one of the most important tumor suppressor proteins due to its central role in preventing the initiation and progression of most cancers. The role of p53 in cancer was first described in 1979. Since then, it has become clear that inactivation of p53's tumor suppression activity is an almost universal step in the development and progression of virtually all human cancers. Research on the function and role of the p53 mechanism has been the subject of over 75,000 scientific publications. Targeting p53 has been tested clinically in at least 18 prior and ongoing clinical trials that were sponsored by six of the world's largest pharmaceutical companies. The magnitude and persistence of this effort demonstrates the importance of the mechanism and the enormous challenge that drugging this mechanism presents. Recent clinical data from certain of these p53 development efforts has shown encouraging progress, possibly an indication that the field is maturing to a point where these efforts may start to yield valuable cancer treatments.

The main function of p53 is to activate genes that will interrupt the cell cycle when DNA damage is first detected. The effect of this process is to ensure that damaged, or cancerous, cells do not continue to grow and propagate. This is why functional p53 is critical to human health and the main reason it has been called the "guardian of the genome." P53 normally protects cells by monitoring and controlling how quickly cells divide into new cells, repairing DNA mutations and controlling when a cell dies. When p53 itself is mutated or pathologically inhibited by its natural regulators, cells grow uncontrollably and may eventually form a cancerous tumor. Approximately half of all cancer patients at initial diagnosis have cancers that circumvent the p53 mechanism by activating or overexpressing the natural suppressor proteins of p53, including, MDM2 and MDMX, making them an ideal target for novel cancer therapies. In the remaining cancer patients, the p53 mechanism is circumvented by deactivating mutations in p53 itself, commonly referred to as mutant p53.

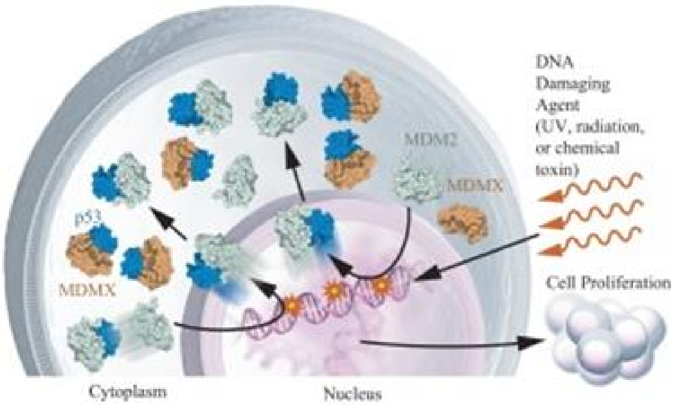
In recent years there have been numerous publications that describe the relationship between p53-activation and the immune response to cancer, in addition to its effects on cell cycle, DNA repair and cell death. P53 regulates the expression of various chemokines, interferons and related receptors, as well as other elements of the adaptive and innate immune response.

As depicted in the figures below, p53 is regulated by MDM2 and MDMX, which are two proteins known to bind to p53 and play non-redundant roles in modulating p53 protein activity. In normal 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 act to suppress p53's apoptotic activity so that cells can function as expected. In the event of DNA damage, these two suppressor proteins detach from p53 so that it is activated to respond to DNA damage. Once activated, p53 either enables the repair of the DNA damage or triggers apoptosis. This is the body's natural response against cancer and a defense mechanism for dealing with DNA damage and maintaining normal cellular function. However, activation and overexpression of MDM2 and MDMX are found in a significant number of cancers that commonly present with WT p53. In these cancers, cancer cells co-opt and over-activate some of the mechanisms used by normal cells to restrain p53 function, thereby nullifying the tumor suppression capabilities of WT p53. In this environment, the cancer cell growth is left unchecked.

p53 ACTIVATION IN NORMAL CELLS



p53 SUPPRESSION IN CANCER CELLS



Despite the structural similarity between MDM2 and MDMX, there is important diversity in the p53 binding sites of these proteins that make the development of therapeutic antagonists that can bind to both MDM2 and MDMX challenging. MDM2 has a deep binding pocket that offers potential for small molecule selectivity. MDMX, in comparison, has a structural difference in its p53 binding cleft, making it larger and shallower and less accessible to small molecules. We are not aware of any small molecules in clinical development that are capable of binding to MDMX in a therapeutically meaningful way. We are aware of selective small molecule inhibitors that are designed to target only the p53-MDM2 interaction. Certain of these small molecule inhibitors have been publicly reported to shrink tumors in certain cancers and have thereby provided clinical proof of concept that restoration of p53 activity can lead to the killing of cancer cells and tumor shrinkage in select cancers. However, these MDM2-only small molecule inhibitors have also been publicly reported to have caused meaningful levels of neutropenia of grade 3 or worse and thrombocytopenia of grade 3 or worse in patients. For instance, in Phase 1 dose escalation trials of these small molecule inhibitors that are currently in active development, approximately 20% to 26% of patients in the trials experienced neutropenia of grade 3 or grade 4 and 15% to 44% of patients experienced thrombocytopenia of grade 3 or grade 4.

As tumor cells can have different levels of, and differential reliance on, MDM2 and MDMX, the current data suggests that there is a limited set of tumors that are highly sensitive to MDM2 inhibition, while a broader set of tumors may be sensitive to both MDM2 and MDMX inhibition. We believe that ALRN-6924 is the first and only product candidate in clinical development that can equipotently bind to and disrupt the interaction of MDM2 and MDMX with p53. As such, we believe that ALRN-6924 may have an effect in a broad range of tumors and may be less prone to resistance as a result of different levels of MDM2 and MDMX in tumor cells. We believe ALRN-6924 should also be less prone to resistance from the likely compensatory mechanisms, such as activation or overexpression of MDMX, that may result from selective pressure on MDM2 alone.

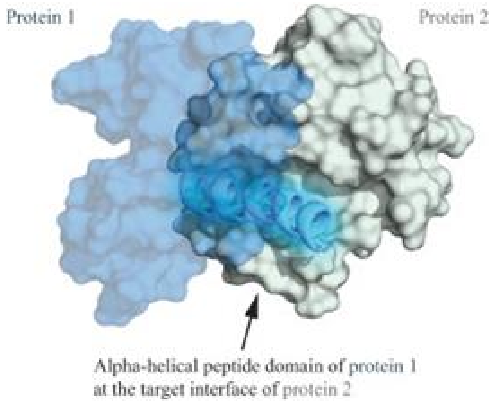
Our Platform – Stabilized Cell-Permeating Peptides

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

Our goal is to create a broad range of first-in-class therapeutics through our proprietary stabilized peptide technology. Our platform enables us to chemically stabilize and improve the performance and activity of a broad range of alpha-helical peptides that we believe may have benefit in oncology and other diseases. We believe that our stabilized peptides can potentially activate and inhibit key cellular functions that underlie disease and that are otherwise difficult to target with existing drug technologies, including small molecules and monoclonal antibodies. Our strategy is to target high value and historically undruggable targets with stabilized peptides.

The Value and Intrinsic Limitations of Peptide Drugs

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

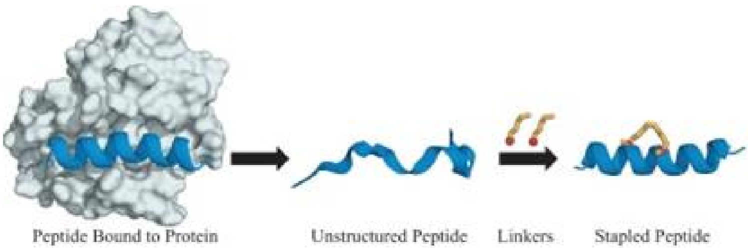


There are presently more than 60 approved peptide drugs, including insulin, liraglutide (Victoza), exenatide (Byetta), teriparatide (Forteo) and Linaclotide (Linzess), that have benefitted patients and improved their quality of life. Attractive attributes of peptide drugs include high specificity and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

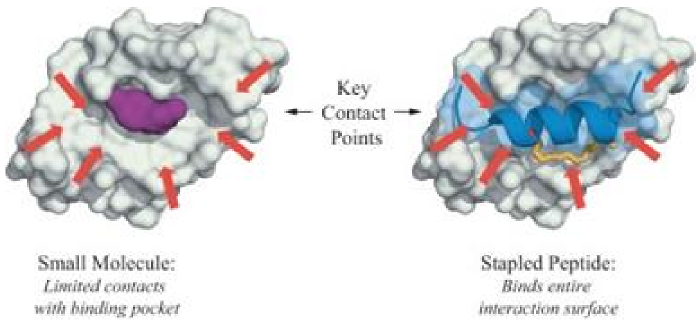
Small molecules currently represent the dominant therapeutic modality underlying the majority of approved drugs and are the only modality that can directly engage protein targets and protein-protein interactions that are contained inside our cells. However, protein-protein interactions are still viewed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

Our Solution

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

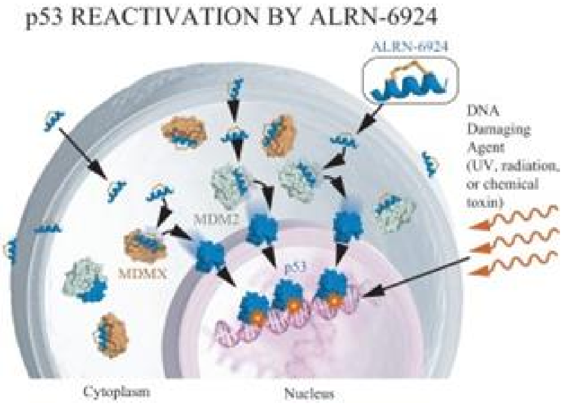


Unlike large proteins, such as monoclonal antibodies or other naturally occurring proteins, that do not penetrate cell membranes due to their size and biophysical properties, stabilized alpha-helical peptides can in many circumstances penetrate cells and still maintain high affinity to their large protein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



Our Lead Product Candidate – ALRN-6924

ALRN-6924, a stabilized cell-permeating peptide, is designed to reactivate WT p53 by inhibiting both MDM2 and MDMX. We believe that ALRN-6924, by inhibiting both MDM2 and MDMX, may enable p53 to perform its natural function of responding to DNA damage and repairing the DNA damage or triggering apoptosis. In so doing, ALRN-6924 may help to restore the body's natural defense against its existing cancer. The figure below shows ALRN-6924 inhibiting both MDM2 and MDMX and reactivating WT p53. ALRN-6924 enters the cell and mimics p53 and in so doing acts as a higher-affinity decoy that attracts and binds to MDM2 and MDMX, thereby causing the release of the bound p53.

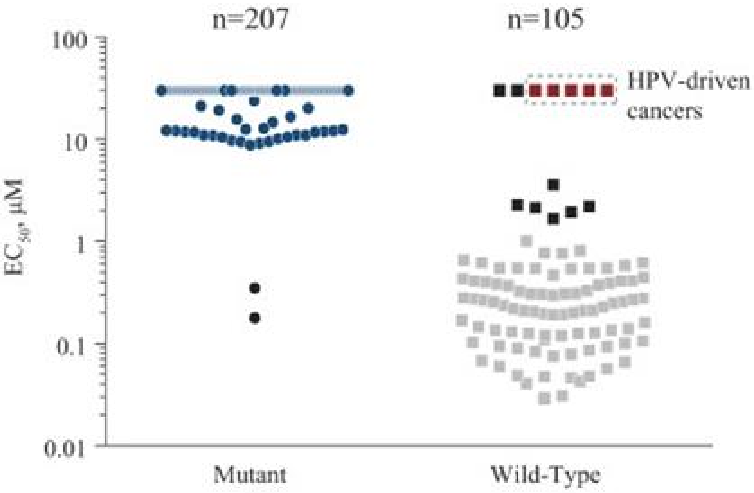


Preclinical Studies

We conducted several *in vivo* and *in vitro* studies of ALRN-6924 that informed our approach to the design of our clinical trials and provided safety information needed to initiate patient selection and dosing in our trials. In these preclinical studies, ALRN-6924 bound to both MDM2 and MDMX with nanomolar affinities, indicating a high level of binding between ALRN-6924 and these proteins, and demonstrated evidence of specific on-target engagement *in vitro* by gene expression profiling. In addition, in preclinical studies ALRN-6924 as a single agent and in combination with other anticancer drugs has demonstrated tumor growth suppression, p53-dependent cell cycle arrest, apoptosis and anti-tumor activity in an MDM2/MDMX-overexpressing xenograft cancer model with clear correlation to on-target pharmacokinetics, or PK, and pharmacodynamic activity.

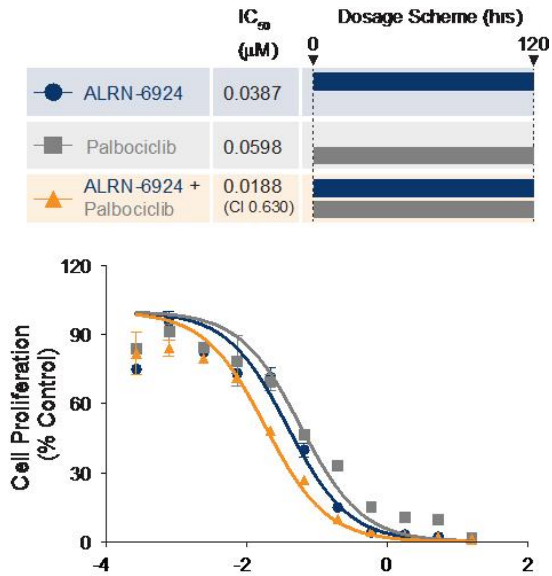
In Vitro

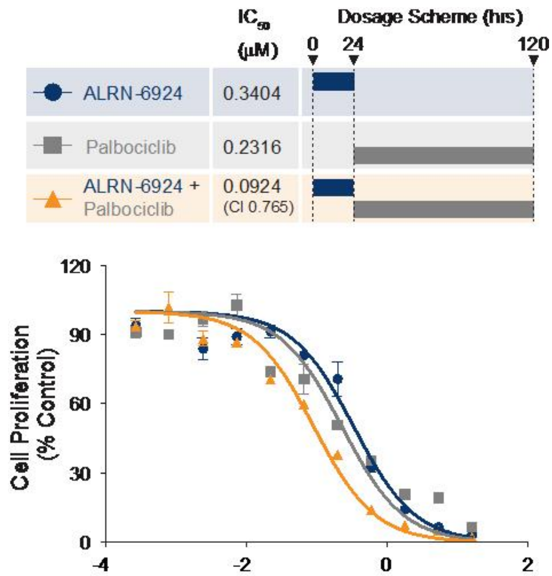
We conducted a p53 signal activation preclinical study to determine if ALRN-6924 has a differential effect on cancer cell lines with mutant p53 compared to WT p53. In the study, we measured the effect of ALRN-6924 in 312 cell lines across a variety of different cancers to compare the effect of ALRN-6924 in cell lines with mutant p53 and cell lines with WT p53. In all but two of the 207 mutant p53 cell lines, ALRN-6924 had no discernable effect, but 98 of the 105 WT p53 cell lines showed tumor cell death and seven of the 105 WT p53 cell lines did not show tumor cell death. Five of the seven WT p53 cell lines that did not show tumor cell death were derived from human papilloma virus-, or HPV, related cancers. We believe these HPV-derived cell lines were not responsive due to the presence of HPV-generated protein that destroys p53. By concentrating on WT p53 and responsive tumors, we believe we are better able to enrich for patient populations that may have a better chance of response to ALRN-6924. We used the results from this preclinical study to inform entry criteria in our ongoing Phase 1 All-comers trial. The figure below shows the results from this study.



EC_{50} = Drug conc. at which 50% of tumor cells are killed
EC_{50} values ≥ 30 μM are shown as 30 μM

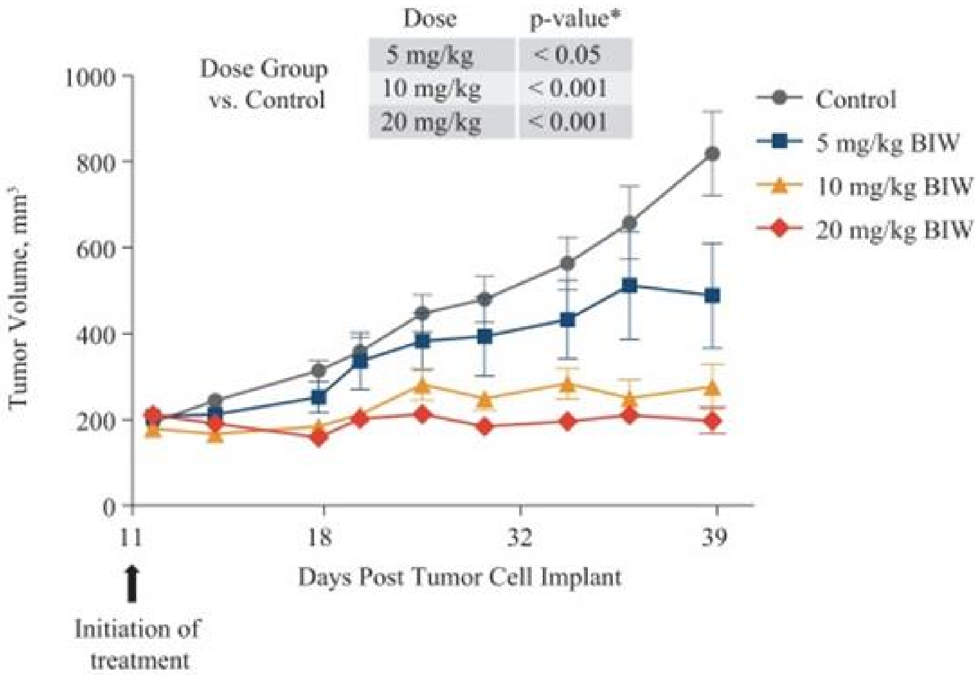
Due to the fact that p53 plays a central role in a variety of signal transduction pathways, including cell cycle and apoptosis, which are critical to the treatment of cancer, we believe reactivation of p53 by ALRN-6924 can play an important role in combination therapy. We believe such combinations therapy could provide a greater anti-tumor response than single-agent treatment, and may minimize resistance to individual drugs. CDK4/6 inhibitors can induce apoptosis, senescence, and cell growth arrest via the retinoblastoma protein (Rb) pathway, which converges on the p53 pathway through interrelated mechanisms. Co-amplification of MDM2 and cyclin-dependent kinase 4, or CDK4, which are both located on chromosome 12, are oncogenic events. This suggests that combinations of MDM2-inhibitors such as ALRN-6924 and CDK4/6 inhibitors, including palbociclib, may be synergistic. In a preclinical *in vitro* study, we observed that the anticancer activity of palbociclib was enhanced when combined with ALRN- 6924 in SJSA1 osteosarcoma cancer cells. SJSA1 cancer cells harbor DNA amplification of both MDM2 and CDK4 genes. Treatment for 120 hours with ALRN-6924 alone inhibited cellular proliferation with an IC50 value of 0.04 µM, and treatment with palbociclib alone yielded an IC50 of 0.06 µM. IC50 refers to the concentration of an inhibitor required to inhibit a specific target by half. However, treatment with increasing concentrations of ALRN-6924 combined with palbociclib in a 1:1 ratio resulted in an improved IC50 of 0.02 µM, suggesting that there may be a synergistic complementarity of the two agents when dosed together. We observed that the combination treatment was also effective against SJSA1 cancer cells when ALRN-6924 was administered first and then washed out, in order to mimic its six-hour pharmacokinetic half-life in patients, prior to treatment with palbociclib. We believe that the sustained anti-proliferative effects of ALRN-6924 may be enhanced by palbociclib.





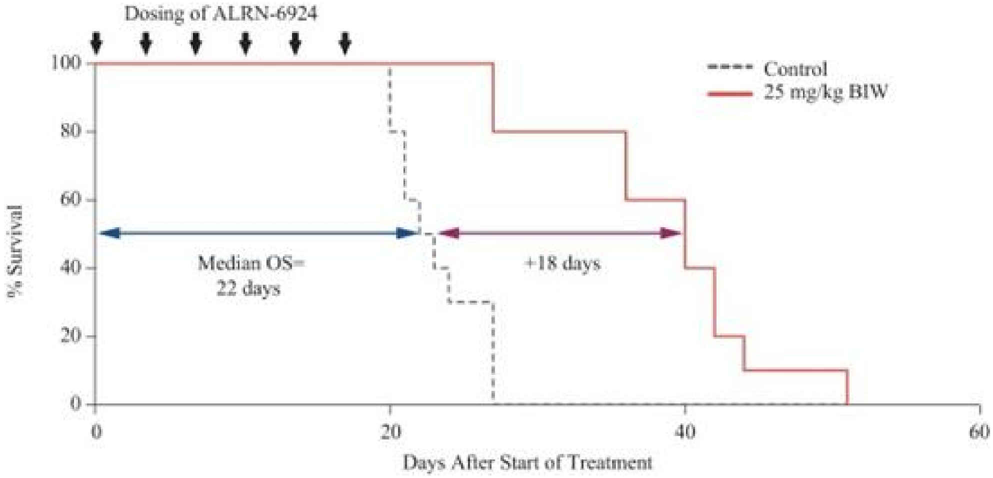
In Vivo

In our *in vivo* preclinical studies of ALRN-6924, we have studied the effects of ALRN-6924 in both solid tumors and hematological malignancies. In this study graphically depicted below, we evaluated the effect of ALRN-6924 administered by an intravenous injection in an MDMX-driven MCF-7 breast cancer xenograft model in mice. We further evaluated doses ranging from 1.25 mg/kg to 20 mg/kg, dosed twice weekly (BIW) over four weeks, to determine effect on tumor volume growth as measured by physical examination. ALRN-6924 showed statistically significant tumor growth inhibition at doses ranging from 5 mg/kg to 20 mg/kg 28 days after initiation of treatment. At 5, 10 and 20 mg/kg in this model, when measured against the control, we observed 55%, 84% and 102% tumor growth inhibition in each dose group, with 10%, 20% and 60% of individual mice demonstrating tumor shrinkage, respectively.

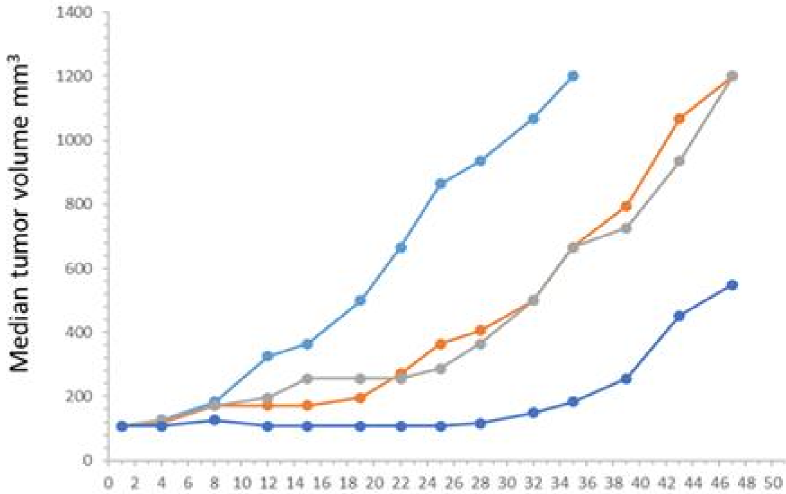


* P-value is a conventional statistical method for measuring the statistical significance of scientific results. A p-value of 0.05 or less represents statistical significance, meaning that there is a 1-in-20 or less statistical probability that the observed results occurred by chance.

In a preclinical study, we used an MV(4;11) human leukemia xenograft model in mice to assess the ability of ALRN-6924 to inhibit tumor growth and improve overall survival in AML. In this study, we administered a 25 mg/kg dose of ALRN-6924 in six twice weekly doses and compared the results to mice treated with only cyclophosphamide, the control group. Mice were monitored individually for an endpoint of survival due to progression of leukemia. Because all ten mice that received the control exited the study between days 21 and 28, we believe that this study offered a sensitive assay for drug activity. Treatment with ALRN-6924 resulted in median overall survival of 40 days as compared to 22 days for untreated mice, an 82% increase for those receiving ALRN-6924. In our view, these results, among others, support our belief that ALRN-6924 may potentially have an effect in cancers with WT p53. The figure below shows the results of the preclinical study.



In another preclinical study, we tested the combination of ALRN-6924 and palbociclib in the MCF-7 mouse xenograft breast cancer model. In this study, MCF-7 cells were transplanted in mice which were then treated with ALRN-6924 alone once-weekly for 21 days, palbociclib alone once daily for 21 days, or a combination of the two agents. At the doses administered in this study, we observed that the combination of ALRN-6924 and palbociclib yielded 14% greater tumor growth inhibition and 31% longer time-to-progression than either single-agent alone.



	%TGI (±SEM) on d22	Median days to >500 mm³	Median days to >1000 mm³
Vehicle	---	20	29
ALRN-6924 20 mg/kg BIW	65 (5)	31	44
Palbociclib 75 mg/kg qdx22	80 (3)	32	45
ALRN-6924 + palbociclib	94 (2)	42	*Not reached*

Clinical Development of ALRN-6924

Our clinical development program for ALRN-6924 is currently focused on our ongoing Phase 2a clinical trial of the combination of ALRN-6924 and palbociclib (Ibrance), marketed by Pfizer, Inc., for the treatment of MDM2-amplified advanced solid tumors and our planned Phase 1b/2 clinical trial to evaluate ALRN-6924 as a myelopreservative agent, to protect against chemotherapy-induced bone marrow toxicity. Our first planned clinical trial to assess the myelopreservation opportunity will be in small cell lung cancer patients who will be treated with the chemotherapy topotecan.

We have conducted other clinical trials of ALRN-6924 as a single agent and in combination with other therapies. For instance, we have conducted a single-agent Phase 2a trial for the treatment of peripheral T-cell lymphoma, or PTCL, a single-agent Phase 1 trial for the treatment of acute myeloid leukemia, or AML, and advanced high-risk myelodysplastic syndrome, or MDS, and a Phase 1b trial testing the combination of ALRN-6924 and cytarabine, or Ara-C, in patients with MDS. We have observed anticancer activity with ALRN-6924 in each of these trials. However, despite that activity, in light of our resources, and our assessment of the commercial opportunities in these indications, as well as the changed competitive landscape in myeloid cancers where seven drugs were approved for AML in the United States in the last two years, we have determined to cease enrollment in these trials and further clinical development for these indications at this time. We plan to present data from our AML/MDS trials in the fourth quarter of 2019.

Combination Trials:

A standard treatment practice in oncology is the use of multiple agents in combination regimens to improve patient outcomes. Since many approved drugs and drug candidates for cancer require a functioning p53 pathway, we have expanded and advanced our non-clinical research to test a variety of approved drugs in combination with ALRN-6924 including cyclin-dependent kinase inhibitors, traditional chemotherapeutic agents and immuno-oncology agents for solid tumors and hematologic malignancies. We believe the mechanism of action and the safety profile of ALRN-6924 may provide potential benefits to cancer patients in combination with a wide variety of conventional and novel therapies.

We have observed the potential benefits of combining ALRN-6924 with other anti-cancer agents in combination therapy in preclinical studies. We have investigated the combination of more than 20 drugs with ALRN-6924 in *in vitro* studies, including drugs that target a variety of pathways mediated by p53, including mitogen-activated protein kinase, or MAPK, molecular target of rapamycin, or mTOR, and CDK4/6 inhibitors, and traditional chemotherapeutic agents, including demethylating agents, such as rituximab (Rituxan), obinutuzumab (Gazyva), palbociclib (Ibrance), everolimus (Afinitor), dabrafenib (Tafinlar), vemurafenib (Zelboraf), capecitabine (Xeloda) and triflurdine/tipiracil (Lonsurf). In each combination, with the exception of dexamethasone, which was expected to have no effect on ALRN-6924 activity, the selected drugs were additive or synergistic with ALRN-6924. To date, ALRN-6924 has not been found to diminish, or antagonize, the activity of any drug tested in combination.

Combination with Palbociclib (Ibrance) in MDM2-Amplified Tumors

In November 2018, we announced a collaboration with Pfizer to evaluate the combination of ALRN-6924 and palbociclib in patients with MDM2-amplified solid tumors. We determined to evaluate this combination based on the frequent co-existence of genetic aberrations, or gene copy amplifications for the MDM2 and CDK4 genes. Their corresponding proteins, MDM2 and CDK4, are believed to have a role in promoting tumor growth and are targeted and inhibited by ALRN-6924 and palbociclib, respectively. We believe that MDM2 amplification or MDM2/CDK4 co-amplification is present in approximately 2.5-3.5% of all human cancers. Tumors with the highest frequency of these genetic abnormalities include liposarcomas, sarcomas, urothelial cancers, lung cancers, gliomas and a number of other tumor types. In most MDM2-amplified or MDM2/CDK4 co-amplified tumors the p53 protein is not mutated. In January 2019, we commenced a Phase 2a trial of ALRN-6924 in combination with palbociclib in patients with MDM2-amplified tumors. We currently expect to report interim results from this trial in the second half of 2019. At this time, there are no approved therapies that specifically target MDM2 amplification or MDM2/CDK4 co-amplification, thus representing an opportunity to develop ALRN-6924 in this area of unmet medical need.

We believe our Phase 1 All-comers trial of ALRN-6924 in patients with solid tumors provided an initial indication of potential anti-tumor activity of ALRN-6924 in MDM2-amplified tumors. In this trial, we evaluated ALRN-6924 as a single-agent, and the patient population included ten patients with tumors harboring MDM2 amplifications. In those patients, we observed a preliminary dose-effect relationship for ALRN-6924. Patients receiving subtherapeutic doses (2-10 times lower than the recommended Phase 2 dose of ALRN-6924) did not appear to benefit from treatment. However, three patients with three different tumor types (liposarcoma, breast cancer and urothelial cancer) with MDM2-amplification were treated with ALRN-6924 doses that have resulted in pharmacodynamic effects of engaging the intracellular targets and reactivating p53 in patients. Two of these three patients treated with pharmacologically relevant ALRN-6924 doses had tumor shrinkage, including one durable confirmed partial response lasting more than two years, and one patient had progressive disease.

Our Phase 2a combination trial of ALRN-6924 and palbociclib in patients with tumors harboring MDM2 amplifications or MDM2/CDK4 co-amplifications is a multicenter, non-randomized trial which is designed to enroll up to 25 patients in the United States. The objectives of this trial include evaluation of safety, tolerability, and activity of the combination, including determination of the overall response rate, or ORR and other measures of activity. Most of the patients in this trial are expected to have liposarcomas, other sarcomas, glioblastomas, lung cancer, breast cancer and other cancers, according to the frequency of this genetic profile in the respective tumor types. Eligible patients must meet standard inclusion and exclusion criteria, must have exhausted reasonable standard treatments for their cancer and must have tumors harboring WT p53 as well as MDM2 amplification or MDM2/CDK4 co-amplification, diagnosed with a validated or approved assay. The combination treatment regimen includes administration of ALRN-6924 at 3.1 mg/kg on days 1, 8 and 15 of every 28-day treatment cycle. Palbociclib is administered at a dose of 100 mg daily on days 1-21 of every 28-day treatment cycle. A safety evaluation will be conducted after the first six to eight patients have been enrolled and treated for a minimum of one treatment cycle.

Myelopreservation with ALRN-6924 to protect against chemotherapy-induced bone marrow damage in patients with small cell lung cancer

Many cancer patients experience clinically significant decreases in white and red blood cells, as well as platelets, or cytopenias, caused by the malignant disease and/or the treatment of the malignant disease. Cytopenias are managed with transfusions or with stimulating factors that induce increased production of white and red blood cells, as well as platelets and therefore allow the bone marrow function to improve or recover following treatment with anti-cancer drugs, which we refer to as "myelopreservation."

Recent data from G1 Therapeutics Inc. that was presented at the 2018 annual conference of the European Society for Medical Oncology (ESMO) demonstrated that pharmacologically induced cell-cycle arrest in normal bone marrow cells could significantly reduce the frequency, intensity and duration of hematological side effects such as anemia or neutropenia in patients receiving chemotherapy for treatment of small cell lung cancer.

We believe there is a significant opportunity for the use of ALRN-6924 as a myelopreservative agent. In preclinical research studies ALRN-6924 successfully activated WT p53 and induced cell-cycle arrest in normal tissues, including bone marrow cells, and tumors in a dose and schedule dependent manner but ALRN-6924 did not induce apoptosis or cell-cycle arrest in mutant p53 cancers. Bone marrow toxicity is the dose limiting toxicity of many chemotherapeutics, and cell-cycle arrest has been shown to reduce bone marrow toxicity. ALRN-6924 also induced cell-cycle arrest in normal tissues in these preclinical studies, including the WT p53 harboring bone marrow, when administered at the appropriate dose and schedule. As such, we believe ALRN-6924 may serve as a myelopreservative agent in bone marrow cells, while having no effect on the cell cycle of mutant p53 cancers. Therefore, rapidly-dividing cancer cells will remain fully susceptible to bone marrow-toxic chemotherapy. We plan to start enrolling patients in a Phase 1b/2 trial ofALRN-6924 in September of 2019 in patients with small cell lung cancer who are treated with topotecan to assess ALRN-6924 as a myelopeservative agent protecting against chemotherapy-induced bone marrow toxicity.

Phase 1 All-comers Clinical Trial in Advanced Solid Tumors or Lymphomas

We have completed enrollment in our single-agent ALRN-6924 Phase 1 All-comers trial for patients with advanced solid tumors or lymphomas. Several patients in this trial have achieved durable tumor responses, and as of March 1, 2019, two patients remained on therapy with ALRN-6924.

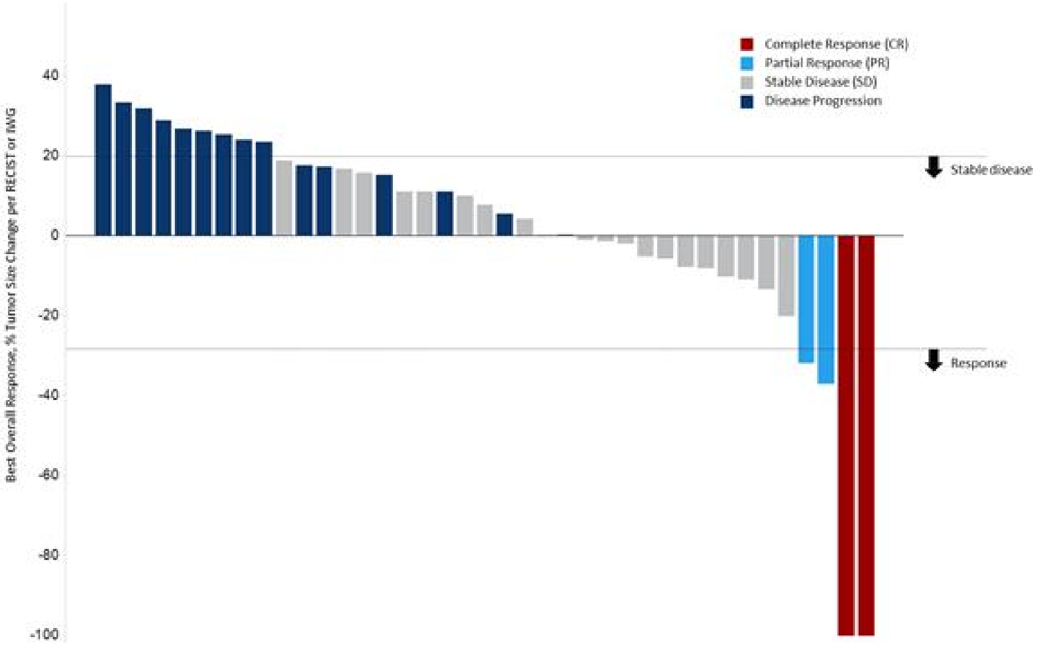
In the trial, ALRN-6924 is administered by intravenous infusion in patients with advanced solid tumors or lymphomas that are refractory to or intolerant of standard therapy or for which no standard therapy exists. We initiated the trial in October 2014 and completed enrollment in January 2017 with a total of 71 patients enrolled. Of the 71 enrolled, 67 patients had solid tumors and four patients had lymphomas, with a total of 24 different tumor types. The trial was designed to determine the recommended Phase 2 dose, to evaluate the safety, tolerability and PK of ALRN-6924 and to provide a preliminary assessment of anti-tumor activity. Treatment of patients in the trial continues until documentation of progressive disease, unacceptable toxicity or patient or physician decision to discontinue study medication. Four patients in this trial achieved a durable tumor response and were on treatment for more than two years each, and two remain on study.

The trial used a "3+3" dose escalation design. For the first two dose levels, patients received ALRN-6924 once a week for three consecutive weeks over a 28-day cycle. After the first two dose levels, patients were included in one of two arms. In Arm A, patients receive ALRN-6924 once a week for three consecutive weeks over a 28-day cycle (days 1, 8 and 15), with doses ranging from 0.64 mg/kg to 4.4 mg/kg. Patients in Arm B receive a lower dose level twice a week for two consecutive weeks over a 21-day cycle (days 1, 4, 8 and 11), with doses ranging from 0.32 mg/kg to 2.7 mg/kg. Arm A, with its less frequent dosing and higher peak levels of ALRN-6924, and Arm B, with its more frequent dosing and more continuous exposure to ALRN-6924, provided us with PK information, safety profiles and preliminary clinical activity data that informed the dose selection for our Phase 2a PTCL trial. Starting with the fourth dose level (1.25 mg/kg in Arm A and 0.53 mg/kg in Arm B), patients were required to test positive for WT p53 through next-generation sequencing in order to participate in the trial and patients who had cancers with known HPV, association were excluded from enrollment because HPV is known to destroy WT p53. Because we started dosing at relatively low dose levels, the protocol did not require patients in the first three dose levels to have WT p53 or have cancers that are not associated with HPV.

To determine tumor p53 mutation status, we relied upon commercially available third-party assays and a central laboratory to conduct next generation sequencing on archived tumor tissue samples or fresh biopsy samples from patients taken prior to enrollment. Based on the results of the trial, we concluded that the recommended Phase 2 dose and dosing schedule for ALRN-6924 was administration of a 3.1 mg/kg infusion once per week on days 1, 8 and 15 of a 28-day treatment cycle.

Of the 71 patients enrolled in the trial, 63 were evaluable. Of these 63 evaluable patients, 30 patients (or 48%) demonstrated disease control, including two patients who achieved complete responses, two patients who achieved partial responses and 26 patients who achieved stable disease, with 46% of the stable disease patients experiencing shrinkage of their tumors. For the patients to be evaluable, they had to have received at least one dose of ALRN-6924 and have undergone at least one tumor imaging with computed tomography per protocol post-baseline or have experienced clinical progression as determined by the investigator without formal imaging. Of the 71 enrolled patients, eight patients were not evaluable because they had discontinued treatment without an efficacy assessment, including two patients who discontinued treatment due to adverse events, three patients who discontinued treatment due to noncompliance, and three patients who withdrew their informed consent.

We also evaluated the anti-tumor activity in our Phase 1 All-comers trial in a subset of WT p53 patients who were treated at doses of at least 0.8 mg/kg, which, based on pharmacodynamic evaluations, we believe to be the minimal clinically relevant dose in this trial. Consequently, we excluded patients who were mutant p53 patients and patients who received doses at one of the three lowest dose levels in the trial of ALRN-6924 from the efficacy analysis. In this figure, the percent change in tumor volume for each evaluable patient is plotted from highest to lowest value, or worst to best response, and each bar of the histogram colored by the best overall response measure for that patient per RECIST 1.1 or International Working Group (Cheson 2014), or IWG 2014 criteria. In this subset of 41 evaluable patients, 39 are represented in the “waterfall” plot below as two patients with clinical or objective evidence of disease progression did not receive a scan. Further, 24 of these 41 evaluable patients (or 59%) demonstrated disease control in at least one scan following the start of ALRN-6924 treatment, including two patients who achieved complete responses, two patients who achieved partial responses, and 20 patients who achieved stable disease, with 55% of the patients with stable disease experiencing shrinkage of their tumors.



ALRN-6924 was well tolerated by patients in our ongoing Phase 1 All-comers trial. Adverse events were reported in all 71 patients (100%), and 29 (41%) had adverse events of grade 3 or 4. The most common adverse events were nausea, vomiting and fatigue. Seven patients reported a total of nine serious adverse events which were deemed possibly, probably or definitely related to ALRN-6924 by the investigators. Notably, hematologic toxicity was mild. Fewer than 10% of patients with solid tumors had any National Cancer Institute's Common Toxicity Criteria, or NCI CTC, Grade thrombocytopenia or neutropenia; no patients had thrombocytopenia of NCI CTC Grade 3 or higher, and two patients had neutropenia Grade 3 or 4 (one each).

Peripheral T-Cell Lymphoma

We conducted a Phase 2a open label, multi-center clinical trial of ALRN-6924 in WT p53 patients who have relapsed/refractory PTCL after at least one prior systemic chemotherapy. In determining to evaluate ALRN-6924 in PTCL, we considered our preclinical results, data from our Phase 1 All-comers trial, and published literature regarding the role of p53 in T-cell related malignancies.

We initiated the trial in August 2016 and completed enrollment in December 2018 with a total of 35 patients enrolled. As of March 25, 2019, three patients remain on study. We conducted the Phase 2a PTCL trial to provide preliminary insight into the responsiveness of this patient population to ALRN-6924, to evaluate its safety and confirm the optimal dosing regimen. The primary endpoint of this trial was overall response rate as well as the safety and tolerability of ALRN-6924 in relapsed/refractory PTCL patients. Important secondary endpoints were the duration of response, progression-free and overall survival as well as time-to-response. Treatment of patients continued until documentation of unacceptable toxicity or patient or physician decision to discontinue therapy, or disease progression that is either symptomatic, rapidly progressive, required urgent intervention, or associated with a decline in performance status.

In this trial, ALRN-6924 was administered by intravenous infusion in patients with refractory or relapsed peripheral T-cell lymphoma who failed previous treatments for that disease. Tumor response by positron emission tomography/computed tomography scans were evaluated by investigators and by an independent radiologist, using IWG 2014 and International Working Group (Cheson 2007), or Modified Cheson 2007 criteria, respectively.

We presented preliminary/interim data at the 60^{th} Annual Meeting of the American Society of Hematology in December 2018. ALRN-6924 was well-tolerated by patients in this Phase 2a trial and its safety profile was consistent with the profile observed in our Phase 1 All-comers trial.

As of October 8, 2018, the data cutoff date for the presentation, the tumor response rates in evaluable patients treated on the weekly dosing schedule (N=14 IWG 2014 criteria; N=15 Modified Cheson 2007 criteria; defined as patients with WT p53, at least one dose of ALRN-6924, and at least one post-baseline scan or non-radiographic disease progression) were 21% and 27%, for IWG 2014 and Modified Cheson 2007 criteria, respectively. The PTCL patients in the trial had a median of four prior therapies. Nevertheless, we achieved a response rate that we believe is generally in line with the overall response rates reported for other agents approved for second line treatment in this patient population.

Based on these results, we believe ALRN-6924 has established single-agent proof-of-concept in PTCL, showing complete and partial remissions for single-agent therapy along with a favorable safety profile. Given the competitive landscape in this very rare disease with three drugs already approved and three more drugs in Phase 3 clinical trials or entering Phase 3 clinical trials, we made the strategic decision to not further develop ALRN-6924 for the treatment of PTCL.

AML/MDS single-agent ALRN-6924

AML is a cancer of the myeloid line of blood cells, characterized primarily by the rapid growth of abnormal white blood cells that build up in the bone marrow and interfere with the production of normal blood cells. The American Cancer Society, or ACS, estimates for 2019 that there will be 21,450 new cases of AML and 10,920 deaths from AML in the United States. MDS is a group of diverse bone marrow disorders in which the bone marrow does not produce enough healthy blood cells. MDS is often referred to as a “bone marrow failure disorder”. The Leukemia and Lymphoma Society estimated that there are 14,275 new MDS cases each year in the United States. AML and MDS are often treated similarly in clinical practice because both disorders can originate from the same cell type and have numerous other features in common. As a result, it is difficult to distinguish between AML and MDS. Irrespective of diagnostic challenges, about one-third of MDS patients progress to AML.

We conducted a Phase 1 open label, multi-center clinical trial of ALRN-6924 as a single agent for the treatment of AML or MDS patients whose cells contain WT p53.

The trial intended to establish the recommended Phase 2 dose of ALRN-6924 as a single agent in patients with AML or MDS, to evaluate the safety, tolerability and PK of ALRN-6924 in patients with AML or MDS and to provide a preliminary assessment of anti-leukemic activity. The trial used a 3+3 dose escalation design.

We initiated this Phase 1 trial in August 2016 and ceased enrollment in December 2018 with a total of 27 patients enrolled. ALRN-6924 was administered as a single agent by intravenous infusion in patients with relapsed or refractory AML or MDS according to WHO criteria, who were not responsive to, were intolerant of, or had shown progression after hypomethylating agents. Two ALRN-6924 dosing regimens were evaluated: once-weekly dosing on days 1, 8 and 15 of a 28-day treatment cycle, and three-times-per week dosing on days 1, 3, 5, 8, 10 and 12 of a 21-day treatment cycle. The doses of ALRN-6924 ranged from 3.1 to 5.8 mg/kg for the once-weekly dosing regimen, and 2.7 to 3.8 for the three-time-per week dosing regimen. After the first cohort of three patients cleared safety review committee oversight at the 2.7 mg/kg dose, three new patients were enrolled at 3.8 mg/kg, the next dose level per protocol. One of those three patients died of tumor lysis syndrome related to treatment with ALRN-6924. We reported the death to the FDA and after the death, we dosed three additional patients at the 2.7 mg/kg dose level as per trial protocol.

While none of the AML or MDS patients treated with ALRN-6924 as a single agent achieved a hematologic response or improvement based on IWG criteria for MDS (Cheson 2006) or AML Response Criteria for AML (Dohner 2010, Appendix F), several of the AML patients had disease stabilization and remained on treatment for up to seven cycles.

Combination with Cytarabine (Ara-C) in AML/MDS

We are evaluating ALRN-6924 in high-risk MDS patients in combination with Ara-C in a Phase 1/1b trial. These MDS patients are diagnosed according to the World Health Organization classification, or WHO criteria, and have either progressed after treatment with hypomethylating agents or are intolerant or unresponsive to them. We initiated this trial in August 2016 and, ceased enrollment in the trial in February 2019 with 28 patients in this trial consisting of 22 patients in the dose escalation and six patients in the dose expansion portions of the study. Patients are being treated with ALRN-6924 dosed on a weekly regimen on days 1, 8 and 15 of a 28-day treatment cycle. Cytarabine is administered on a weekly regimen on days 1, 8 and 15 of a 28-day treatment cycle. The doses of ALRN-6924 ranged from 3.1 to 4.4 mg/kg, and the doses of cytarabine ranged from 100 to 200 mg/m^2.

The trial is intended to establish the recommended Phase 2 dose of ALRN-6924 in combination with cytarabine in patients with AML or MDS, to evaluate the safety, tolerability and PK of ALRN-6924 in patients with AML or MDS, and to provide a preliminary assessment of anti-leukemic activity. The trial uses a 3+3 dose escalation design.

We presented preliminary data from this trial at the 60th Annual Meeting of the American Society of Hematology in December 2018. In these data, as of October 8, 2018, the data cutoff date for the presentation, a preliminary signal of clinical activity was observed in five of six evaluable MDS patients treated at the highest ALRN-6924 and cytarabine dose levels (4.4 mg/kg and 200 mg/m^2, for ALRN-6924 and cytarabine, respectively). Three patients achieved a bone marrow complete response, two patients experienced hematologic improvements in platelets and/or neutrophils, and one patient responded sufficiently to proceed to stem-cell transplant after treatment in the trial. In addition, one patient had disease stabilization.

On the basis of this data, we determined to enroll additional high-risk MDS patients into an expansion cohort of this trial at the highest dose levels (4.4 mg/kg of ALRN-6924 and 200 mg/m^2 of cytarabine). However, in light of our resources, and our assessment of the commercial opportunities in these indications, as well as the changed competitive landscape in myeloid cancers, we have determined to cease enrollment in this trial and further clinical development for these indications at this time. We plan to continue to conduct preclinical research to explore whether alternative dose and schedule strategies for ALRN-6924 in AML and MDS can improve the activity of ALRN-6924 and warrant resumption of clinical development for these indications. We plan to present data from this trial in the fourth quarter of 2019.

Investigator-Sponsored Trials

Principal investigators at two world-class cancer centers have initiated three investigator sponsored trials of ALRN-6924. In November 2018, we provided support to the Dana-Farber/Boston Children's and Blood Disorder Center to initiate an investigator sponsored trial for pediatric patients with solid tumors to receive ALRN-6924 as a single agent and an investigator sponsored trial for pediatric patients with acute leukemia to be treated with a combination of ALRN 6924 and cytarabine. We also provided support to The University of Texas MD Anderson Cancer Center to conduct an investigator sponsored Phase 1b study of ALRN-6924 in combination with paclitaxel in WT TP53 advanced or metastatic solid tumors including estrogen-receptor positive breast cancer. We do not have control or influence on the conduct, timelines or readouts from investigator sponsored trials. We expect the results to be presented at scientific conferences and published in scientific journals in the future.

Next Generation WT p53 Reactivators

We intend to leverage the knowledge we have obtained from our ALRN-6924 development program to develop next-generation p53-reactivating stabilized peptides. We believe that specific changes in the chemical structures of our stabilized peptides may create peptides with varying affinities to MDM2 and MDMX, enabling better targeting of cancers that are more dependent on one or the other p53 suppressor protein. In addition to novel chemical and anti-tumor properties, our next-generation p53 program may also yield new chemical entities, or NCEs, with differential PK and safety profiles relative to ALRN-6924.

Other Targets

Based on our preclinical research, along with third-party scientific publications, we believe that stabilized cell-permeating peptides may be effective against a variety of cancer targets, as well as targets in other therapeutic areas, such as infectious, metabolic and autoimmune diseases. Pathways that incorporate protein-protein interactions with an alpha helix, and that, therefore, may be amenable to our approach and the focus of our future research may include transcriptional factors and signaling proteins, such as Ras, which is implicated in colorectal cancer, lung cancer and pancreatic cancer, Myc, which is implicated in breast cancer and colorectal cancer, ß-Catenin, which is implicated in colorectal cancer, gastric cancer, hepatocellular carcinoma, cholangiocarcinoma, melanoma and breast cancer, among others, the Bcl family of proteins, which are implicated in hematologic cancers such as AML, MDS, NHL as well as melanoma, lung cancer and breast cancer, among others and HIF-α, which is implicated in renal cancer.

Since our inception, we have created and evaluated over 10,000 cell-permeating peptides against multiple targets in a variety of therapeutic areas. We believe that a number of these molecules and targets warrant further study and development and could, in the future, contribute to a pipeline of novel therapeutics. Subject to our resources, we intend to continue to make selective investments into early research programs as part of our ongoing research. Where we believe it will be beneficial to the success of the program, we also expect to seek academic and industry collaborations to advance this work.

Manufacturing

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

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

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

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

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

Companion Diagnostic

If we decide to seek marketing approval of ALRN-6924 with a label limited to WT p53 and/or MDM2-amplified cancer patients, we may be required to have a companion *in vitro* diagnostic approved for use with ALRN-6924. We may also be required to obtain similar approvals from comparable foreign regulatory authorities. In such cases, we will need to contract with a third party for the supply of a commercially available diagnostic to identify patients with WT p53 and/or MDM2-amplified status, or develop such a diagnostic ourselves or in collaboration with a third party, in each case requiring approval of the diagnostic by regulatory authorities. We are currently evaluating the risks and benefits of each approach. We currently rely upon commercially available third-party assays and employ a central laboratory to test both archived tumor tissue samples and fresh biopsy samples from patients taken prior to enrollment in our clinical trials to identify WT p53 and/or MDM2-amplified status.

Competition

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

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

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

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

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

MDM2-amplified tumors

Amplification of the MDM2 gene is a genetic aberration present in approximately 2.5 – 3.5% of all cancers. Cancers that most frequently harbor this genetic aberration include sarcomas, glioblastomas, urothelial, stomach, lung, and breast cancers and melanoma. Cancers that harbor MDM2 amplification rarely have co-existent mutations in p53.

MDM2 amplification is diagnosed with commercially available genetic assay, such as FoundationOne CDx. We are not aware of any approved cancer therapy directed specifically against this genetic aberration. However, there are drugs approved to treat these tumors, as well as drugs in clinical development for the treatment of these tumors.

Myelopreservation

G-CSF or Granulocyte-colony-stimulating-factor, also known as colony-stimulating-factor 3 (CSF 3), 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. Erythropoietin, also known as hematopoietin or hemopoietin, 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 these supportive care measures are widely used in the medical management of cancer patients who experience cytopenias, numerous scientific publications suggest the possibility that those drugs may stimulate cancer cells and contribute to cancer therapy resistance and aggressiveness. In addition, these growth factors are often used once cytopenias are diagnosed and patients are at risk of infection and bleeding.

Novel and optimized supportive care drugs should ideally address both considerations by having mechanisms of action that are specific for normal cells (thus rendering cancer cells insensitive to their action) and ideally should prevent the onset of cytopenia rather than improving the recovery of the bone marrow.

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

Intellectual Property

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

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

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

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

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

Because patent applications in the United States and certain other jurisdictions are maintained in secrecy for 18 months, and since publication of discoveries in the scientific or patent literature often lags actual discoveries, we cannot be certain of the priority of inventions covered by pending patent applications. Moreover, we may have to participate in interference proceedings declared by the United States Patent and Trademark Office, or USPTO, to determine priority of invention or in post-grant challenge proceedings at the USPTO or at a foreign patent office, such as inter partes review and post grant review proceedings at the USPTO and opposition proceedings at the European Patent Office, that challenge priority of invention or other features of patentability. Such proceedings could result in substantial cost, even if the eventual outcome is favorable to us.

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

Patent Portfolio

As of January 31, 2019, we owned or had an exclusive license to at least 47 U.S. patents, at least 44 pending U.S. provisional or non-provisional patent applications, at least 198 foreign patents and at least 147 pending foreign applications. The claims of these owned or in-licensed patents and patent applications are directed toward various aspects of our product candidates and research programs. Specifically, the claims of these patents and patent applications include compositions of matter, methods of use, drug product formulations, diagnostics, methods of manufacture and methods of identifying active compounds. Such owned and in-licensed patents and patent applications, if issued, are expected to expire on various dates from 2020 through 2037, without taking into account any possible patent term adjustments or extensions. In addition, within our patent portfolio, as of January 31, 2019, we owned or had an exclusive license to at least 21 U.S. patents, at least 14 pending U.S. provisional or non-provisional patent applications, at least 95 foreign patents and at least 90 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 2020 through 2037, with the owned patents and patent applications, if issued, expiring on various dates from 2029 to 2037, in each case without taking into account any possible patent term adjustment or extensions. More specifically, such owned and in-licensed patents claiming compositions of matter covering ALRN-6924 are expected to expire on various dates from 2020 through 2033, with the owned patents and patent applications, if issued, expiring on various dates from 2029 to 2033, in each case without taking into account any possible patent term adjustments or extensions. Lastly, within our patent portfolio, as of January 31, 2018, at least 14 U.S. patents, at least 4 pending U.S. non-provisional patent applications, at least 110 foreign patents and at least 15 foreign patent applications are licensed to us by President and Fellows of Harvard College, or Harvard, and Dana-Farber Cancer Institute, or DFCI, pursuant to our license agreement with such parties, which patents and patent applications, if issued, are expected to expire on various dates from 2020 through 2028, without taking into account any possible patent term adjustments or extensions. We also have rights to certain patents and pending patent applications throughout the world licensed on a non-exclusive basis to us by Materia and other third parties pursuant to our license agreements with such parties.

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

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

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

License Agreements

Harvard and Dana-Farber License Agreement

In August 2006, we entered into a license agreement with Harvard and DFCI. This agreement was amended and restated in February 2010. Pursuant to the amended and restated agreement, Harvard and DFCI granted us an exclusive worldwide license, with the right to sublicense, under certain patents and patent applications to develop, make, have made, market, use, sell, offer for sale, and import products covered by the patents and patent rights. The licensed patents cover ALRN-6924. 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, 2018, we have paid non-refundable fees, consisting of license and maintenance fees, milestone payments and sublicense fees, of $4.6 million. We are obligated to pay annual maintenance fees totaling $145,000, which on an annual basis are creditable against royalties due for commercial sales of licensed products. We are obligated to make additional milestone payments of up to a maximum of $7.5 million upon our achievement of certain specified clinical, regulatory and sales milestones with respect to ALRN-6924. In the future, we may be obligated to pay up to a maximum of $7.7 million per additional licensed therapeutic product upon our achievement of certain specified clinical, regulatory and sales milestones with respect to such product with the first milestone being payable upon initiation of clinical development of the product. We may also be obligated to pay up to a maximum of $700,000 per licensed diagnostic product upon our achievement of certain specified regulatory and sales milestones with respect to such product. We also have agreed to pay low single-digit percentage royalties on aggregate worldwide net sales of licensed products, including sales by our sublicensees, on a licensed product-by-licensed product and country-by-country basis until the expiration of the last-to-expire applicable licensed patent. Our royalty obligations are subject to specified reductions in the event that we are required to obtain additional licenses from third parties and to make payments to such third parties under such licenses. We must also pay a percentage, up to the mid-twenties, of all sublicense income received from sublicensees, less certain costs, such as research and development costs and, in the event our patent rights are licensed to the sublicensee as part of the same transaction, less the portion of sublicense income allocated to our licensed patent rights. Under specified circumstances, portions of our sublicense payments may be creditable against royalty payments payable for sales of a licensed product. Finally, we must also reimburse all future patent expenses related to the prosecution and maintenance of the licensed patents and applications in-licensed.

Materia 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 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, 2018, we paid non-refundable fees, consisting of an up-front technology access fee and annual maintenance payments and milestone payments, of $850,000. We are obligated to pay Umicore an annual maintenance fee of $50,000. We are obligated to make additional milestone payments up to a maximum of $6.25 million upon our achievement of certain specified clinical, regulatory and sales milestones with respect to ALRN-6924. In the future, we may be obligated to pay to Umicore up to a maximum of $6.25 million per additional licensed product upon our achievement of certain specified clinical, regulatory and sales milestones with respect to such licensed product. We must also pay Umicore tiered royalties ranging in the low single-digit percentages on aggregate worldwide net sales of licensed products, including sales by our sublicensees, on a licensed product-by-licensed product and country-by-country basis until the expiration of the last-to-expire applicable licensed patent. Our royalty obligations are subject to specified reductions in the event that we are required to obtain additional licenses from third parties and to make payments to such third parties under such licenses.

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

Government Regulation and Product Approvals

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

Approval and Regulation of Drugs in the United States

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

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

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

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

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

Preclinical Studies

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

The IND and IRB Processes

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

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

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

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

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

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

Expanded Access to an Investigational Drug for Treatment Use

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

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

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

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

Human Clinical Studies in Support of an NDA

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

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

- *Phase 1:* The drug is initially introduced into healthy human subjects or, in certain indications such as cancer, patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.
- *Phase 2:* The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- *Phase 3:* The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.
- *Phase 4:* Post-approval studies, which are conducted following initial approval, are typically conducted to gain additional experience and data from treatment of patients in the intended therapeutic indication.

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

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

Pediatric Studies

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

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

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

The FDA Reauthorization Act of 2017 established new requirements to govern certain molecularly targeted cancer indications. Any company that submits an NDA three years after the date of enactment of that statute must submit pediatric assessments with the NDA if the drug is intended for the treatment of an adult cancer and is directed at a molecular target that FDA determines to be substantially relevant to the growth or progression of a pediatric cancer. The investigation must be designed to yield clinically meaningful pediatric study data regarding the dosing, safety and preliminary efficacy to inform pediatric labeling for the product.

Submission of an NDA to the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the drug product for one or more indications. Under federal law, the submission of most NDAs is additionally subject to an application user fee, which for federal fiscal year 2019 is $2,588,478, unless a partial or full fee waiver is granted as may occur for the first NDA of a small business or an NDA for drug intended to treat a rare, or "orphan" disease. The sponsor of an approved NDA may also be subject to an annual program fee, which for fiscal year 2019 is $309,915 per product, per approved indication up to 5 indications.

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

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

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

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

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

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

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

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

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

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

Accelerated Approval Pathway

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

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

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

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

The FDA's Decision on an NDA

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

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

Post-Approval Requirements

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

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

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

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

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

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

Abbreviated New Drug Applications for Generic Drugs

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

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

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

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

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

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

505(b)(2) NDAs

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

Hatch-Waxman Patent Certification and the 30-Month Stay

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

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

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

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

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

Pediatric Exclusivity

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

Orphan Drug Designation and Exclusivity

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

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

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

Patent Term Restoration and Extension

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

FDA Approval and Regulation of Companion Diagnostics

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

If FDA determines that a companion diagnostic device is essential to the safe and effective use of a novel therapeutic product or indication, FDA generally will not approve the therapeutic product or new therapeutic product indication if the companion diagnostic device is not approved or cleared for that indication. Approval or clearance of the companion diagnostic device will ensure that the device has been adequately evaluated and has adequate performance characteristics in the intended population. The review of *in vitro* companion diagnostics in conjunction with the review of our therapeutic treatments for cancer will, therefore, likely involve coordination of review by the FDA's Center for Drug Evaluation and Research and the FDA's Center for Devices and Radiological Health Office of In Vitro Diagnostics Device Evaluation and Safety.

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

The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, can take several years or longer. It involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications are subject to fees for medical device product review; for federal fiscal year 2018, the standard fee for review of a PMA is $310,764 and the small business fee is $77,691.

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

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

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

The 21st Century Cures Act

On December 13, 2016, the 21st Century Cures Act, or the Cures Act, was signed into law. The Cures Act is designed to modernize and personalize healthcare, spur innovation and research, and streamline the discovery and development of new therapies through increased federal funding of particular programs. It authorizes increased funding for the FDA to spend on innovation projects. The new law also amends the PHSA to reauthorize and expand funding for the NIH. The Cures Act establishes the NIH Innovation Fund to pay for the cost of development and implementation of a strategic plan, early stage investigators and research. It also charges NIH with leading and coordinating expanded pediatric research. Further, the Cures Act directs the Centers for Disease Control and Prevention to expand surveillance of neurological diseases.

With amendments to the FDCA and the PHSA, Title III of the Cures Act seeks to accelerate the discovery, development, and delivery of new medicines and medical technologies. To that end, and among other provisions, the Cures Act reauthorizes the existing priority review voucher program for certain drugs intended to treat rare pediatric diseases until 2020; creates a new priority review voucher program for drug applications determined to be material national security threat medical countermeasure applications; revises the FDCA to streamline review of combination product applications; requires FDA to evaluate the potential use of “real world evidence” to help support approval of new indications for approved drugs; provides a new “limited population” approval pathway for antibiotic and antifungal drugs intended to treat serious or life-threatening infections; and authorizes FDA to designate a drug as a “regenerative advanced therapy,” thereby making it eligible for certain expedited review and approval designations.

Regulation Outside the United States

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

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

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

In April 2014, the European Union passed a new Clinical Trials Regulation, (EU) No 536/2014, which will replace the current Clinical Trials Directive 2001/20/EC. To ensure that the rules for clinical trials are identical throughout the European Union, the new European Union clinical trials legislation was passed as a regulation that is directly applicable in all European Union member states without the need for implementation into the member states’ national laws. All clinical trials performed in the European Union are required to be conducted in accordance with the Clinical Trials Directive 2001/20/EC until the new Clinical Trials Regulation (EU) No 536/2014 becomes applicable. According to the current plans of the European Medicines Agency, or EMA, the new Clinical Trials Regulation is not expected to become applicable until later in 2019. The Clinical Trials Directive 2001/20/EC will, however, still apply three years from the date of entry into application of the Clinical Trials Regulation to (i) clinical trials applications submitted before the entry into application and (ii) clinical trials applications submitted within one year after the entry into application if the sponsor opts for old system.

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

PRIME Designation in the EU

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

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

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

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

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

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

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

Regulation 847/2000 sets out criteria and procedures governing designation of orphan drugs in the European Union. Specifically, an application for designation as an orphan product can be made any time prior to the filing of an application for approval to market the product. Marketing authorization for an orphan drug leads to a ten-year period of market exclusivity. During this market exclusivity period, the EMA or the member state competent authorities, cannot accept another application for a marketing authorization, or grant a marketing authorization, for a similar medicinal product for the same indication. The period of market exclusivity is extended by two years for medicines that have also complied with an agreed PIP.

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

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

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

Authorization to Market Companion Diagnostics in the European Union.

In the European Economic Area, or EEA, *in vitro* medical devices are currently required to conform with the essential requirements of the European Union Directive on *in vitro* diagnostic medical devices (Directive No 98/79/EC, as amended). To demonstrate compliance with the essential requirements, the manufacturer must undergo a conformity assessment procedure. The conformity assessment varies according to the type of medical device and its classification. The conformity assessment of *in vitro* diagnostic medical devices can require the intervention of an accredited EEA Notified Body. If successful, the conformity assessment concludes with the drawing up by the manufacturer of an EC Declaration of Conformity entitling the manufacturer to affix the CE mark to its products and to sell them throughout the EEA. On April 5, 2017, the European Parliament passed the In Vitro Device Regulation, or IVDR, which repeals and replaces Directive No 98/79/EC. Unlike directives, which must be implemented into the national laws of the EU member states, a regulation is directly applicable, i.e., without the need for adoption of EU member state laws implementing them, in all EEA member states. The IVDR, among other things, is intended to establish a uniform, transparent, predictable and sustainable regulatory framework across the EU for *in vitro* diagnostic medical devices and ensure a high level of safety and health while supporting innovation. The IVDR will not become fully applicable until five years following its entry into force. Once applicable, the IVDR will among other things:

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

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. The withdrawal of the United Kingdom from the European Union will take effect either on the effective date of the withdrawal agreement or, in the absence of agreement, two years after the United Kingdom provides a notice of withdrawal pursuant to the European Union Treaty. The United Kingdom communicated the notice of withdrawal to the EU on March 29, 2017. Since the regulatory framework for pharmaceutical products in the United Kingdom covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the United Kingdom. It remains to be seen how, if at all, Brexit will impact regulatory requirements for product candidates and products in the United Kingdom.

The United Kingdom has a period of a maximum of two years from the date of its formal notification to negotiate the terms of its withdrawal from, and future relationship with, the European Union. If no formal withdrawal agreement is reached between the United Kingdom and the European Union, then it is expected the United Kingdom's membership of the European Union will automatically terminate two years after the submission of the notification of the United Kingdom's intention to withdraw from the European Union. Discussions between the United Kingdom and the European Union focused on finalizing withdrawal issues and transition agreements are ongoing. However, limited progress to date in these negotiations and ongoing uncertainty within the UK Government and Parliament sustains the possibility of the United Kingdom leaving the European Union on March 29, 2019 without a withdrawal agreement and associated transition period in place, which is likely to cause significant market and economic disruption.

Pharmaceutical Coverage, Pricing and Reimbursement

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

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

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

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

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

Healthcare Law and Regulation

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

- the federal anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing any remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good, facility, item or service, for which payment may be made, in whole or in part, by a federal healthcare program such as Medicare and Medicaid;
- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government.
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the Affordable Care Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the U.S. Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, can apply to sales or marketing arrangements and claims involving healthcare items or services and are reimbursed by non-governmental third-party payors, including private insurers.

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

Pharmaceutical Insurance Coverage and Health Care Reform

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

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

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

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

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drug agents or biologic agents, which is apportioned among these entities according to their market share in certain government health care programs;
- an increase in the rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for branded and generic drugs, respectively;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts to negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations, unless the drug is subject to discounts under the 340B drug discount program;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements under the federal Physician Payments Sunshine Act for drug manufacturers to report information related to payments and other transfers of value made to physicians and teaching hospitals as well as ownership or investment interests held by physicians and their immediate family members;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- creation of the Independent Payment Advisory Board, which, if and when impaneled, will have authority to recommend certain changes to the Medicare program that could result in reduced payments for prescription drugs; and
- establishment of a Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation’s automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers up to 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments, will remain in effect through 2027 unless additional Congressional action is taken. 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. Since enactment of the ACA, there have been numerous legal challenges and Congressional actions to repeal and replace provisions of the ACA.

For example, with enactment of the Tax Cuts and Jobs Act of 2017, in December 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Additionally, on January 22, 2018, the President signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018, among other things, amends 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 current administration has also taken executive actions to undermine or delay implementation of the ACA. Since January 2017, the President has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. One Executive Order directs 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. The second Executive Order terminates the cost-sharing subsidies that reimburse insurers under the ACA. Several state Attorneys General filed suit to stop the current administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. In addition, CMS has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. The effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business, are not yet known.

Further, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. For example, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, Congress and the current administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs

For example, on May 11, 2018, the Trump Administration issued a plan to lower drug prices. Under this blueprint for action, the current administration indicated that the Department of Health and Human Services (HHS) will take steps to end the gaming of regulatory and patent processes by drug makers to unfairly protect monopolies; advance biosimilars and generics to boost price competition; evaluate the inclusion of prices in drug makers' ads to enhance price competition; speed access to and lower the cost of new drugs by clarifying policies for sharing information between insurers and drug makers; avoid excessive pricing by relying more on value-based pricing by expanding outcome-based payments in Medicare and Medicaid; work to give Part D plan sponsors more negotiation power with drug makers; examine which Medicare Part B drugs could be negotiated for a lower price by Part D plans, and improving the design of the Part B Competitive Acquisition Program; update Medicare's drug-pricing dashboard to increase transparency; prohibit Part D contracts that include "gag rules" that prevent pharmacists from informing patients when they could pay less out-of-pocket by not using insurance; and require that Part D plan members be provided with an annual statement of plan payments, out-of-pocket spending, and drug price increases. More recently, on January 31, 2019, the HHS Office of Inspector General proposed modifications to the federal Anti-Kickback Statute discount safe harbor for the purpose of reducing the cost of drug products to consumers which, among other things, if finalized, will affect discounts paid by manufacturers to Medicare Part D plans, Medicaid managed care organizations and pharmacy benefit managers working with these organizations.

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

Employees

As of December 31, 2018 we had 23 full-time employees, including a total of 10 employees with M.D. or Ph.D. degrees. Of these full-time employees, 16 employees are engaged in research and development and 7 employees are engaged in general and administrative activities. None of our employees are represented by labor unions or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

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 490 Arsenal Way, Suite 210, Watertown, MA 02472, and our telephone number is (617) 995-0900.

Information Available on the Internet

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

Item 1A. Risk Factors.

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

Risks Related to Our Financial Position and Need for Additional Capital

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

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

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

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

We believe that, based on our current operating plan, our cash, cash equivalents and investments of $20.7 million as of December 31, 2018 will enable us to fund our operating expenses and capital expenditure requirements into the third quarter of 2019. On March 28, 2019, we entered into a securities purchase agreement with certain accredited investors pursuant to which we agreed to issue and sell an aggregate of (i) 11,838,582 units, consisting of 11,838,582 shares of common stock and associated warrants to purchase an aggregate of 11,838,582 shares of common stock and (ii) 1,096,741 units, consisting of 1,096,741 pre-funded warrants to purchase 1,096,741 shares of common stock and associated warrants to purchase an aggregate of 1,096,741 shares of common stock in a private placement. The private placement is expected to close on April 2, 2019, subject to the satisfaction of customary closing conditions. We expect to receive aggregate gross proceeds of approximately $26 million, before deducting placement agent fees and offering expenses. We believe that with the proceeds of the private placement, our cash, cash equivalents and investments will enable us to fund our operating expenses into the fourth quarter of 2020. Our funding estimates are based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate. In any event, our cash, cash equivalents and investments will not be sufficient to fund all of the efforts that we plan to undertake or to fund the completion of development of any of our product candidates.

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

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

We do not believe that our cash, cash equivalents and investments as of the date of this Annual Report on Form 10-K will be sufficient to enable us to fund our current operations for at least 12 months from the date of issuance of the financial statements included in this Annual Report on Form 10-K and have therefore concluded that this circumstance raises substantial doubt about our ability to continue as a going concern. See Note 1 to our financial statements appearing elsewhere in this Annual Report on Form 10-K for additional information on our assessment. On March 28, 2019, we entered into a securities purchase agreement with certain accredited investors pursuant to which we agreed to issue and sell an aggregate of (i) 11,838,582 units, consisting of 11,838,582 shares of common stock and associated warrants to purchase an aggregate of 11,838,582 shares of common stock and (ii) 1,096,741 units, consisting of 1,096,741 pre-funded warrants to purchase 1,096,741 shares of common stock and associated warrants to purchase an aggregate of 1,096,741 shares of common stock in a private placement. The private placement is expected to close on April 2, 2019, subject to the satisfaction of customary closing conditions. We expect to receive aggregate gross proceeds of approximately $26.0 million, before deducting placement agent fees and offering expenses. We plan to address this condition through the sale of common stock in public offerings and/or private placements, through other capital sources, including collaborations with other companies or other strategic transactions, including the securities purchase agreement we entered into on March 28, 2019. If our private placement does not close on a timely basis or at all and we are otherwise unable to raise sufficient capital or otherwise when needed, our business, financial condition and results of operations will be materially and adversely affected, and we will need to significantly modify our operational plans to continue as a going concern. If we are unable to 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.

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

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

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

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

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

We were incorporated in 2001 and commenced principal operations in 2006. We are an early-stage company, and our operations to date have been limited to organizing and staffing our company, business planning, raising capital, developing our stabilized cell-permeating peptide platform, identifying potential product candidates, conducting preclinical studies of our product candidates and conducting clinical trials of our product candidates. All of our product candidates other than ALRN-6924 are in preclinical research. We have not yet demonstrated our ability to successfully complete any Phase 2 or Phase 3 clinical trials, including large-scale, pivotal clinical trials, obtain marketing approvals, manufacture a commercial-scale drug or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful drug commercialization. Typically, it takes about six to ten years to develop a new drug from the time it is in Phase 1 clinical trials to when it is approved for treating patients, but in many cases, it may take longer. Consequently, any predictions made about our future success or viability may not be as accurate as they could be if we had a longer operating history.

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

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

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

Since our inception, we have incurred significant losses on an aggregate basis. Our net loss was $31.6 million and $22.6 million for the years ended December 31, 2018 and 2017, respectively. We have not generated any revenue to date from sales of any drugs and have financed our operations principally through the sale of our common stock in our initial public offering, through private placements of our preferred stock, and, to a lesser extent, through a collaboration agreement. We have devoted substantially all of our efforts to research and development. Our lead product candidate, ALRN-6924, is in clinical development, and our other product candidates are in preclinical research. As a result, we expect that it will be several years, if ever, before we have any product candidates ready for commercialization. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if and as we:

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

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

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

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

Our future success is substantially dependent on our ability to timely obtain marketing approval for, and then successfully commercialize, ALRN-6924, our lead product candidate. We are investing a majority of our efforts and financial resources in the research and development of ALRN-6924. Our other product candidates are in earlier stages of development. Our business depends entirely on the successful development and commercialization of our product candidates. We currently generate no revenues from sales of any products, and we may never be able to develop a marketable product.

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

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

- successful and timely completion of our ongoing clinical trials of ALRN-6924;
- initiation and successful patient enrollment and completion of additional clinical trials on a timely basis;
- safety, tolerability and efficacy profiles that are satisfactory to the FDA or any comparable foreign regulatory authority for marketing approval;
- timely receipt of marketing approvals for both ALRN-6924 and any required companion diagnostic from applicable regulatory authorities;
- the performance of our current and future collaborators, if any;
- the extent of any required post-marketing approval commitments to applicable regulatory authorities;
- establishment of supply arrangements with third-party raw materials and drug product suppliers and manufacturers;
- establishment of scaled production arrangements with third-party manufacturers to obtain finished products that are appropriately packaged for sale;
- obtaining and maintaining patent protection, trade secret protection and regulatory exclusivity, both in the United States and internationally;
- protection of our rights in our intellectual property portfolio, including our licensed intellectual property;
- successful launch of commercial sales following any marketing approval;
- a continued acceptable safety profile following any marketing approval;
- commercial acceptance by patients, the medical community and third-party payors; and
- our ability to compete with other therapies.

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

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

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

Moreover, we believe our lead product candidate, ALRN-6924, reactivates p53 by disrupting the interactions between p53 and MDM2 and MDMX, thereby freeing p53 to transit to its DNA target in the nucleus and initiate apoptosis in cancerous cells. We believe that ALRN-6924 is the first and only product candidate in clinical development that can bind to and disrupt the interaction of MDM2 and MDMX with p53 with equivalent effectiveness, or equipotently. Although we have evaluated ALRN-6924 in preclinical studies and are aware of published literature supporting the role of MDM2 and MDMX in reactivating non-mutated or wild type, or WT, p53 as well as clinical results for small molecule inhibitors that act to disrupt the interaction of p53 and MDM2, we believe that we are the first to clinically test a molecule that binds directly to both MDM2 and MDMX. As such, the effect of binding to and simultaneously disrupting the interactions of MDM2 and MDMX with WT p53 in cancer patients has not been established in clinical trials. In addition, the role of factors other than MDM2 and MDMX in circumventing the p53 mechanism is still the subject of continued research. As a result, we do not know whether the mechanism of action of ALRN-6924 will have the expected effect on all target cancer indications and whether ALRN-6924 will succeed in demonstrating the safety and efficacy needed to advance in clinical development and obtain marketing approval.

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

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

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

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

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

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

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

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

From time to time, we may publish or report interim or preliminary data from our clinical trials. Interim or preliminary data from clinical trials that we may conduct may not be indicative of the final results of the trial and are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Interim or preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the interim or preliminary data. As a result, interim or preliminary data should be viewed with caution until the final data are available.

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

In some instances, there can be significant variability in safety and efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial protocols, differences in size and type of the patient populations, differences in and adherence to the dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. We do not know whether any clinical trials we may conduct will demonstrate consistent or adequate efficacy and safety sufficient to obtain marketing approval to market our product candidates. We may also determine to discontinue development of our product candidates for certain indications for a variety of other strategic reasons. For example, we have decided not to further develop ALRN-6924 for the treatment of PTCL.

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

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

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

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

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

We do not know whether ongoing clinical trials will be completed on schedule or at all, or whether future clinical trials will begin on time, need to be redesigned, enroll patients on time or be completed on schedule, if at all.

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

- obtaining marketing approval to commence a trial;
- reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- obtaining institutional review board approval at each clinical trial site;
- recruiting suitable patients to participate in a trial;
- developing and validating any companion diagnostic to be used in the trial, to the extent we are required to do so;
- patients failing to comply with trial protocol or dropping out of a trial;
- clinical trial sites deviating from trial protocol or dropping out of a trial;
- the need to add new clinical trial sites; or
- manufacturing sufficient quantities of product candidate for use in clinical trials.

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

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

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

- incur unplanned costs;
- be delayed in obtaining marketing approval for our product candidates or not obtain marketing approval at all;
- obtain marketing approval in some countries and not in others;
- obtain marketing approval for indications or patient populations that are not as broad as intended or desired;
- obtain marketing approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;
- be subject to additional post-marketing testing requirements; or
- have the drug removed from the market after obtaining marketing approval.

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

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

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or comparable foreign regulatory authorities. Patient enrollment is a significant factor in the timing of clinical trials. We do not yet know exactly how many patients will have the genetic profile that ALRN-6924 or other future product candidates are designed to address. In particular, because our clinical trials of ALRN-6924 are focused on indications with small patient populations and are targeted at a subset of patients in such indications with cancer cells that contain WT p53 or WT p53 with MDM2 amplifications, our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate.

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

- size and nature of the patient population;
- severity of the disease under investigation;
- availability and efficacy of approved drugs for the disease under investigation;
- patient eligibility criteria for the trial in question;
- perceived risks and benefits of the product candidate under study;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;

- the ability to monitor patients adequately during and after treatment;
- proximity and availability of clinical trial sites for prospective patients; and
- continued enrollment of prospective patients by clinical trial sites.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

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

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

In general, our clinical trials of ALRN-6924 include cancer patients who are very sick and whose health is deteriorating, and we expect that additional clinical trials of ALRN-6924 and our other product candidates will include similar patients with deteriorating health. It is possible that some of these patients might die prior to their completion of our clinical trial. Such deaths may be caused by the cancers from which such patients are suffering, or other causes, unrelated to ALRN-6924 or the other product candidates that may be the subject of the clinical trial. Even if the deaths are not related to our product candidate, the deaths could affect perceptions regarding the safety of our product candidate.

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. We have reported the death to the FDA, and after an evaluation of the probable cause of the death, dosed an additional four patients at the 2.7 mg/kg dose level as per trial protocol. We were cleared by the safety review committee to enroll our next patients at the 3.3 mg/kg dose level. However, we have determined to cease enrollment of patients in the trial. If any of our product candidates, either as a single agent or in combination, are associated with adverse events or undesirable side effects or have properties that are unexpected such as the death we observed in our Phase 1 trial of single agent ALRN-6924 for the treatment of AML and MDS, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. We, or any future collaborators, may abandon development or limit development of that product candidate to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, results of operations, financial condition and prospects significantly.

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

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

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

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

If we decide to seek marketing approval of ALRN-6924 with a label limited to WT p53 and/or MDM2-amplified cancer patients, the FDA may, under certain circumstances, require us to have a companion *in vitro* diagnostic approved for use with ALRN-6924. We may also be required to obtain similar approvals from comparable foreign regulatory authorities. In such cases, we would need to contract with a third party for the supply of a commercially available diagnostic to identify patients with WT p53 and/or MDM2-amplified status, or develop such a diagnostic ourselves, in each case requiring approval of the diagnostic by regulatory authorities. We are currently evaluating the likelihood of such a requirement, given recent FDA actions, as well as the risks and benefits of each approach. We currently rely upon commercially available third-party assays and employ a central laboratory to test both archived tumor tissue samples and fresh biopsy samples from patients taken prior to enrollment in clinical trials of ALRN-6924 to identify WT p53 and/or MDM2-amplified status. We do not have experience or capabilities in developing or commercializing companion diagnostics.

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

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

Because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable drugs. For instance, we have conducted clinical trials of ALRN-6924 for the treatment of PTCL, AML and MDS and, in part, due to commercial developments, have ceased clinical development of ALRN-6924 for those indications. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other strategic arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

The FDA may not approve an ANDA for a generic drug until any applicable period of non-patent exclusivity for the reference-listed drug has expired. The Federal Food, Drug, and Cosmetic Act, or FDCA, provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity, or NCE. Specifically, in cases where such exclusivity has been granted, an ANDA may not be filed with the FDA and the FDA may not approve the application until the expiration of five years unless the submission is accompanied by a Paragraph IV certification that a patent covering the reference-listed drug is either invalid or will not be infringed by the generic drug, in which case the applicant may submit its application four years following approval of the reference-listed drug. Manufacturers may seek to launch these generic drugs following the expiration of the marketing exclusivity period, even if we still have patent protection for our drug.

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

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

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

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

There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be reimbursed in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs, may be incorporated into existing payments for other services and may reflect budgetary constraints or imperfections in Medicare data. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement rates. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for new products that we develop and for which we obtain marketing approval could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

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

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

- decreased demand for any product candidates or drugs that we may develop;
- injury to our reputation and significant negative media attention;

- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any drugs that we may develop.

We currently hold clinical trial liability insurance coverage for up to $5.0 million, but that coverage may not be adequate to cover any and all liabilities that we may incur. We would need to increase our insurance coverage when we begin the commercialization of our product candidates, if ever. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

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

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

Risks Related to Our Dependence on Third Parties

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

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

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

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

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

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

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

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

- the possible failure of the third party to manufacture our product candidate according to our schedule, or at all, including if our third-party contractors give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of the agreements between us and them;
- the possible termination or nonrenewal of agreements by our third-party contractors at a time that is costly or inconvenient for us;
- the possible breach by the third-party contractors of our agreements with them;
- the failure of third-party contractors to comply with applicable regulatory requirements;
- the possible failure of the third party to manufacture our product candidates according to our specifications;
- the possible mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or active drug or placebo not being properly identified;

- the possibility of clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales; and
- the possible misappropriation of our proprietary information, including our trade secrets and know-how.

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

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

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

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

Although we currently plan to retain all commercial rights to ALRN-6924 and our other cell-permeating peptide product candidates, we may enter into strategic collaborations for the development, marketing and commercialization of ALRN-6924 and our other stabilized cell-permeating peptide product candidates. If those collaborations are not successful, the development, marketing and/or commercialization of our product candidates that are the subject of such collaborations would be harmed.

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

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

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

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

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

Our drug development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. As noted above, we may seek to selectively form collaborations to expand our capabilities, potentially accelerate research and development activities and provide for commercialization activities by third parties.

We would face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or comparable foreign regulatory authorities, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing drugs, the existence of uncertainty with respect to our ownership of intellectual property, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The potential collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate.

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

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

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

Risks Related to Our Intellectual Property

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

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

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

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

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

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

The licensing and acquisition of third-party intellectual property rights is a competitive practice, and companies that may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their larger size and cash resources or greater clinical development and commercialization capabilities. There can be no assurance that we will be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to acquire.

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

The patent position of pharmaceutical and biotechnology companies generally is highly uncertain and involves complex legal and factual questions for which many legal principles remain unresolved. In recent years patent rights have been the subject of significant litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued in the United States or in other jurisdictions which protect our technology or products or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. In addition, the U.S. Patent and Trademark Office, or USPTO, might require that the term of a patent issuing from a pending patent application be disclaimed and limited to the term of another patent that is commonly owned or names a common inventor. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain.

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

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

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

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

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

If any of our owned or in-licensed patents are found to be invalid or unenforceable, or if we are otherwise unable to adequately protect our rights, it could have a material adverse impact on our business and our ability to commercialize or license our technology and product candidates. Likewise, our current owned and in-licensed patents covering our proprietary technologies and our product candidates are expected to expire on various dates from 2020 through 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 2020 through 2037, without taking into account any possible patent term adjustments or extensions. However, we cannot be assured that the USPTO or relevant foreign patent offices will grant any of these patent applications.

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

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

In early 2016, Harvard asserted that we had not achieved one or more of the diligence milestones set forth in our license agreement with Harvard and DFCI within the time provided for in the agreement and that we were in material breach of the license agreement. In making this assertion, Harvard did not seek to terminate the license agreement or interfere with our ongoing p53 program, but instead proposed to convert our exclusive license with respect to certain of the patent families licensed under the license agreement to a non-exclusive license. DFCI did not join Harvard in making this assertion or proposal and has not expressed a similar position to us. Under Harvard’s proposal, we would have retained our rights to these patent families under the license agreement on a non-exclusive basis, and Harvard and DFCI would have been able to license these patent families to third parties so that we would be unable to prevent third parties from practicing the claims of those patents, but Harvard and DFCI would not have been able to license to third parties any of the other patent families licensed to us under the license agreement or any of our own patents or patent applications. As such, Harvard’s proposal would not have impeded our development of ALRN-6924 or our other ongoing programs. However, we rejected the proposal and provided Harvard with a response stating that we believe that we had fully satisfied the diligence milestones as required under the license agreement and that Harvard’s claim of breach is incorrect.

Since that time, we have continued to communicate with Harvard in the ordinary course under the license agreement and have paid a milestone payment to Harvard, and Harvard has not further asserted to us its claim of material breach or sought to terminate the license agreement. In addition, in May 2017, we received correspondence from Harvard, which indicated that Harvard is aware of a third party that is interested in developing a product that may require a license under certain of the patent families licensed to us under the license agreement. If Harvard were to assert in the future that we are in material breach of the license agreement and to seek to terminate the license agreement such that we lost our right to practice the claims of the patents licensed under the license agreement, we would not be able to commercialize ALRN-6924 until the applicable patents expired unless we were able to negotiate a new license arrangement with Harvard or DFCI with respect to the patent families owned by them respectively. Such loss of license rights under the license agreement with Harvard and DFCI or the loss of license rights under other of our license agreements if we were found not to be in compliance with such license agreements could materially adversely affect our business, results of operations, financial condition and prospects. We may enter into additional licenses in the future and if we fail to comply with obligations under those agreements, we could suffer similar consequences.

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

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

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

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

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

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

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

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

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

In addition, because some patent applications in the United States may be maintained in secrecy until the patents are issued, patent applications in the United States and many foreign jurisdictions are typically not published until 18 months after filing, and publications in the scientific literature often lag behind actual discoveries, we cannot be certain that others have not filed patent applications for technology covered by our owned and in-licensed issued patents or our pending applications, or that we or, if applicable, a licensor were the first to invent the technology. Our competitors may have filed, and may in the future file, patent applications covering our products or technology similar to ours. Any such patent application may have priority over our owned and in-licensed patent applications or patents, which could require us to obtain rights to issued patents covering such technologies. If another party has filed a U.S. patent application on inventions similar to those owned by or in-licensed to us, we or, in the case of in-licensed technology, the licensor may have to participate in an interference proceeding declared by the USPTO to determine priority of invention in the United States. If we or one of our licensors is a party to an interference proceeding involving a U.S. patent application on inventions owned by or in-licensed to us, we may incur substantial costs, divert management's time and expend other resources, even if we are successful.

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

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

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

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

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

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

Filing, prosecuting and defending patents on all of our product candidates throughout the world would be prohibitively expensive. Competitors may use our technology in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but where enforcement is not as strong as in the United States. These products may compete with our product candidates in jurisdictions where we do not have any issued patents and our patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so competing. Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products against third parties in violation of our proprietary rights generally. The initiation of proceedings by third parties to challenge the scope or validity of our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business.

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

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent prosecution process and following the issuance of a patent. Our failure to comply with such requirements could result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case if our patent were in force, which would have a material adverse effect on our business.

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

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

Risks Related to Marketing Approval and Other Legal Compliance Matters

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

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

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

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

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

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

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

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

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

In order to market and sell our drugs in the European Union and many other jurisdictions, we, and any collaborators we may have in the future, must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The marketing approval process outside 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 drug be approved for reimbursement before the drug can be approved for sale in that country. We, and any collaborators we may have in the future, may not obtain approvals from regulatory authorities outside of the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside of the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA.

Additionally, on June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. On March 29, 2017, the United Kingdom formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. Since a significant proportion of the regulatory framework in the United Kingdom is derived from European Union directives and regulations, the withdrawal could materially impact the regulatory regime with respect to the approval of our product candidates in the United Kingdom or the European Union. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for our product candidates, which could significantly and materially harm our business.

The United Kingdom has a period of a maximum of two years from the date of its formal notification to negotiate the terms of its withdrawal from, and future relationship with, the European Union. If no formal withdrawal agreement is reached between the United Kingdom and the European Union, then it is expected the United Kingdom's membership of the European Union will automatically terminate two years after the submission of the notification of the United Kingdom's intention to withdraw from the European Union. Discussions between the United Kingdom and the European Union focused on finalizing withdrawal issues and transition agreements are ongoing. However, limited progress to date in these negotiations and ongoing uncertainty within the UK Government and Parliament sustains the possibility of the United Kingdom leaving the European Union on March 29, 2019 without a withdrawal agreement and associated transition period in place, which is likely to cause significant market and economic disruption

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

Regulatory authorities in some jurisdictions, including the United States and the European Union, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In April 2017, the FDA granted orphan drug designation to ALRN-6924 for use in the treatment of AML. We may also seek orphan drug designations for ALRN-6924 for other indications, or for other of our product candidates. There can be no assurances that we will be able to obtain such designations.

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

Even if we, or any future collaborators, obtain orphan drug designation for a product candidate as we have obtained for ALRN-6924 for AML, we, or they, may not be able to obtain or maintain orphan drug exclusivity for that product candidate. We may not be the first to obtain marketing approval of any product candidate for which we have obtained orphan drug designation for the orphan-designated indication due to the uncertainties associated with developing pharmaceutical products. In addition, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan-designated indication or may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Further, even if we, or any future collaborators, obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties may be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug with the same active moiety for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care or the manufacturer of the product with orphan exclusivity is unable to maintain sufficient product quantity. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

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

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

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a drug. For example, the approval may be subject to limitations on the indicated uses for which the drug may be marketed or to the conditions of approval, including the requirement to implement a Risk Evaluation and Mitigation Strategy, which could include requirements for a restricted distribution system. Manufacturers of approved drugs and those manufacturers' facilities are also required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, our contract manufacturers, our future collaborators and their contract manufacturers could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMPs.

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

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

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

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

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the current administration may impact our business and industry. Namely, the current administration has taken several executive actions, including the issuance of a number of executive orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance and review and approval of marketing applications. Notably, on January 30, 2017, the President issued an executive order, applicable to all executive agencies, including the FDA, which requires that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the "two-for-one" provisions. This executive order includes a budget neutrality provision that required the total incremental cost of all new regulations in the 2017 fiscal year, including repealed regulations, to be no greater than zero, except in limited circumstances. For fiscal years 2018 and beyond, the executive order requires agencies to identify regulations to offset any incremental cost of a new regulation and approximate the total costs or savings associated with each new regulation or repealed regulation. In interim guidance issued by the Office of Information and Regulatory Affairs within Office of Management and Budget on February 2, 2017, the administration indicated that the "two-for-one" provisions may apply not only to agency regulations, but also to significant agency guidance documents. In addition, on February 24, 2017, the President issued an executive order directing each affected agency to designate an agency official as a "Regulatory Reform Officer" and establish a "Regulatory Reform Task Force" to implement the two-for-one provisions and other previously issued executive orders relating to the review of federal regulations; however, it is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

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

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

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

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

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

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

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability, or the ability of any future collaborators, to profitably sell any product candidates for which we, or they, obtain marketing approval. The pharmaceutical industry has been a particular focus of these efforts and have been significantly affected by legislative initiatives. 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 future collaborators, may receive for any FDA approved product.

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 Reconciliation Act of 2010, or collectively the Affordable Care Act, or ACA, which substantially changed the way healthcare is financed by both governmental and private insurers, was enacted. Among the provisions of the ACA of potential importance to our business, including, without limitation, our ability to commercialize and the prices we may obtain for any of our product candidates that are approved for sale, are the following:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of federal healthcare fraud and abuse laws, including the civil False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for non-compliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices (and 70% starting January 1, 2019);
- extension of manufacturers’ Medicaid rebate liability;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report certain financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 and, due to subsequent legislative amendments to the statute, will stay in effect through 2027 unless additional congressional action is taken, and the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Further, there have been several recent U.S. congressional inquiries and proposed state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products.

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 receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

With enactment of the Tax Cuts and Jobs Act of 2017, which was signed by the President 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, will become effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause an estimated 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Additionally, on January 22, 2018, the President signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called “Cadillac” tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018, among other things, amends the ACA, effective January 1, 2019, to increase from 50% to 70% 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”. Further, each chamber of the U.S. Congress has put forth multiple bills designed to repeal or repeal and replace portions of the ACA. Although none of these measures has been enacted by Congress to date, Congress may consider other legislation to repeal and replace elements of the ACA.

The current administration has also taken executive actions to undermine or delay implementation of the ACA. Since January 2017, the President has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. One Executive Order directs 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. The second Executive Order terminates the cost-sharing subsidies that reimburse insurers under the ACA. Several state Attorneys General filed suit to stop the current administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. In addition, CMS has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. The effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business, are not yet known.

The costs of prescription pharmaceuticals have also been the subject of considerable discussion in the United States, and members of Congress and the current administration have stated that they will address such costs through new legislative and administrative measures. To date, there have been several recent U.S. congressional inquiries and proposed and enacted state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, the current administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. While any proposed measures will require authorization through additional legislation to become effective, Congress and the current administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Specifically, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, Congress and the current administration have each indicated that they will continue to seek new legislative and/or administrative measures to control drug costs. For example, on May 11, 2018, the current administration issued a plan to lower drug prices. Under this blueprint for action, the current administration indicated that the Department of Health and Human Services (HHS) will: take steps to end the gaming of regulatory and patent processes by drug makers to unfairly protect monopolies; advance biosimilars and generics to boost price competition; evaluate the inclusion of prices in drug makers' ads to enhance price competition; speed access to and lower the cost of new drugs by clarifying policies for sharing information between insurers and drug makers; avoid excessive pricing by relying more on value-based pricing by expanding outcome-based payments in Medicare and Medicaid; work to give Part D plan sponsors more negotiation power with drug makers; examine which Medicare Part B drugs could be negotiated for a lower price by Part D plans, and improve the design of the Part B Competitive Acquisition Program; update Medicare's drug-pricing dashboard to increase transparency; prohibit Part D contracts that include "gag rules" that prevent pharmacists from informing patients when they could pay less out-of-pocket by not using insurance; and require that Part D plan members be provided with an annual statement of plan payments, out-of-pocket spending, and drug price increases. More recently, on January 31, 2019, the HHS Office of Inspector General proposed modifications to the federal Anti-Kickback Statute discount safe harbor for the purpose of reducing the cost of drug products to consumers which, among other things, if finalized, will affect discounts paid by manufacturers to Medicare Part D plans, Medicaid managed care organizations and pharmacy benefit managers working with these organizations.

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

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. Increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us and any future collaborators to more stringent product labeling and post-marketing testing and other requirements.

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

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

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

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

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

- *Anti-Kickback Statute*—the federal anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing any remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good, facility, item or service, for which payment may be made, in whole or in part, by a federal healthcare program, such as Medicare and Medicaid.
- *False Claims Act*—the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- *HIPAA*—the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- *HIPAA Privacy Provisions*—as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information
- *Transparency Requirements*—the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the Affordable Care Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the U.S. Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- *Analogous State and Foreign Laws*—analogous state and foreign fraud and abuse laws and regulations, such as state anti-kickback and false claims laws, can apply to sales or marketing arrangements and claims involving healthcare items or services and are reimbursed by non-governmental third-party payors, including private insurers.

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

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

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

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

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

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

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

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

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

If we expand our operations outside of the United States, we must comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The creation and implementation of international business practices compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required.

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

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

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

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

Risks Related to Employee Matters and Managing Growth

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

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

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

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

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

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

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

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

Risks Related to Our Common Stock

Our executive officers and directors and entities associated or affiliated with our executive officers and directors may have the ability to significantly influence all matters submitted to stockholders for approval.

As of March 23, 2019, our executive officers and directors and entities associated and affiliated with our executive officers and directors, in the aggregate, beneficially own shares representing approximately 21% of our outstanding common stock. As a result, if these stockholders were to choose to act together, they may have the ability to significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, could significantly influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of our company on terms that other stockholders may desire.

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

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

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

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

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

Our shares of common stock began trading on The Nasdaq Global Market June 29, 2017. 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 23, 2019, the closing price of our common stock ranged from a high of $14.91 per share to a low of $0.71 per share. The stock market in general and the market for pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, our stockholders may not be able to sell their shares at or above the price they paid for their shares. The market price for our common stock may be influenced by many factors, including:

- the timing and results of clinical trials of ALRN-6924 and any of our other product candidates;
- regulatory actions with respect to our product candidates or our competitors’ products and product candidates;
- the success of existing or new competitive products or technologies;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- establishment or termination of collaborations for our product candidates or development programs;
- failure or discontinuation of any of our development programs;
- results of clinical trials of product candidates of our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or development programs;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;
- actual or anticipated changes in estimates as to financial results or development timelines;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or other stockholders;

- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts, if any, that cover our stock;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this “Risk Factors” section.

We could be subject to securities class action litigation.

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

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

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

We are also a smaller reporting company, and we will remain a smaller reporting company until the fiscal year following the determination that our voting and non-voting common stock held by non-affiliates is more than $250 million measured on the last business day of our second fiscal quarter, or our annual revenues are less than $100 million during the most recently completed fiscal year and our voting and non-voting common stock held by non-affiliates is more than $700 million measured on the last business day of our second fiscal quarter. Similar to emerging growth companies, smaller reporting companies are able to provide simplified executive compensation disclosure, are exempt from the auditor attestation requirements of Section 404 and have certain other reduced disclosure obligations, including, among other things, being required to provide only two years of audited financial statements and not being required to provide selected financial data, supplemental financial information or risk factors.

We have elected to take advantage of certain of the reduced reporting obligations. Investors may find our common stock less attractive as a result of our reliance on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

We will incur increased costs as a result of operating as a public company, and our management is required to devote substantial time to new compliance initiatives. Any failure to maintain effective internal control over our financial reporting could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

As a public company, we incur, and particularly after we are no longer an "emerging growth company," 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.

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, 2018, we had federal net operating loss carryforwards of $157.6 million, of which $2.5 million will, if not utilized, begin to expire in 2029. As of December 31, 2018, we had state net operating carryforwards of $153.1 million, which will, if not utilized, begin to expire in 2030. Our federal and state research and development tax credit carryforwards of $2.4 million and $1.5 million, respectively, will, if not utilized, begin to expire in 2025. These net operating loss and tax credit carryforwards could expire unused and be unavailable to offset future income tax liabilities. Under the newly enacted federal income tax law, federal net operating losses incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such carryforwards is limited to 80% of our taxable income in the year in which such carryforwards are used.

In addition, under Section 382 of the Internal Revenue Code of 1986, as amended, 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 over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income may be limited. We have not conducted a study to assess whether we have experienced Section 382 ownership changes in the past and if a portion of our net operating loss and tax credit carryforwards are subject to an annual limitation under Section 382. In addition, we may experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which may be outside of our control. If we determine that an ownership change has occurred at any time since our inception and our ability to use our historical net operating loss and tax credit carryforwards is materially limited, it would harm our future operating results by effectively increasing our future tax obligations.

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 23, 2019, we had 14,867,868 shares of common stock outstanding. The holders of an aggregate of approximately 5,000,000 shares of our common stock have rights, subject to conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. In connection with the private placement, we entered into a registration rights agreement, pursuant to which we agreed to register for resale the shares to be purchased in the private placement and shares issuable upon exercise of warrants to be issued in the private placement. Under this agreement, we agreed to file a registration statement covering the resale of shares by the purchasers within 30 days following the closing of the private placement. We have 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. 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 18,768 square feet of office and laboratory space at our corporate headquarters in Watertown, Massachusetts. The lease commenced August 2018, and has an initial term of eight years. In addition, we have an option to extend the lease for one additional five-year period following the initial term. We believe that our existing facilities are adequate for our current needs

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 Global 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 23, 2019, there were approximately 47 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.

Use of Proceeds from Registered Securities

On July 5, 2017, we closed our initial public offering of 3,750,000 shares of our common stock at a public offering price of $15.00 per share for an aggregate offering of $56.3 million. The offer and sale of all of the shares in the offering were registered under the Securities Act pursuant to registration statement on Form S-1 (File No. 333-218474), which was declared effective by the SEC on June 28, 2017. Merrill Lynch, Pierce, Fenner & Smith Incorporated and Jefferies LLC acted as joint book-running managers for the offering and as representatives of the underwriters. William Blair & Company, L.L.C. and Canaccord Genuity Inc. acted as co-managers. The offering commenced on June 28, 2017 and did not terminate until the sale of all of the shares offered.

We received aggregate net proceeds from the offering of $50.0 million, after deducting underwriting discounts and commissions of $3.9 million and offering expenses of $2.4 million payable by us. None of the underwriting discounts and commissions or offering expenses were incurred or paid to directors or officers of ours or their associates or to persons owning 10% or more of our common stock or to any affiliates of ours.

As of December 31, 2018, we have used $29.3 million of the net proceeds from our initial public offering to fund ongoing clinical trials of ALRN-6924, including our Phase 1 All-comers trial, Phase 2a trial for the treatment of PTCL, Phase 1 trial for the treatment of AML/MDS as a single agent and Phase 1b trial for the treatment of AML/MDS in combination with Ara-C, and for working capital and other general corporate purposes. We have invested the net proceeds in a variety of capital preservation investments, including short-term, investment-grade, interest-bearing instruments. There has been no material change in our planned use of the net proceeds from the offering as described in our final prospectus filed with the SEC pursuant to Rule 424(b)(4) on June 29, 2017.

Item 6. Selected Financial Data.

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

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

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

Overview

We are a clinical-stage biopharmaceutical company that is focused on developing and commercializing a novel class of stabilized cell-permeating alpha-helical peptides to address intracellular targets in oncology and other therapeutic areas. Our lead product candidate, ALRN-6924, is a cell-permeating peptide that disrupts the interaction of p53 suppressors MDM2 and MDMX with tumor suppressor p53 to reactivate tumor suppression in non-mutant, or wild-type, p53 cancers. Based on preclinical data and preliminary evidence of safety and anti-tumor activity in our ongoing clinical trials, we believe that there may be a significant opportunity to develop ALRN-6924 in combination with other drugs for a wide variety of cancers.

Our clinical development program for ALRN-6924 is currently focused on our ongoing Phase 2a clinical trial of the combination of ALRN-6924 and palbociclib (Ibrance), marketed by Pfizer, Inc., for the treatment of MDM2-amplified advanced solid tumors and our planned Phase 1b/2 clinical trial to evaluate ALRN-6924 as a myelopreservative agent, to protect against chemotherapy-induced bone marrow toxicity. Our first planned clinical trial to assess the myelopreservation opportunity will be in small cell lung cancer patients who will be treated with the chemotherapy topotecan.

We have conducted other clinical trials of ALRN-6924 as a single agent and in combination with other therapies. For instance, we have conducted a single-agent Phase 2a trial for the treatment of peripheral T-cell lymphoma, or PTCL, a single-agent Phase 1 trial for the treatment of acute myeloid leukemia, or AML, and advanced high-risk myelodysplastic syndrome, or MDS, and a Phase 1b trial testing the combination of ALRN-6924 and cytarabine, or Ara-C, in patients with MDS. We have observed anticancer activity with ALRN-6924 in each of these trials. However, despite that activity, in light of our resources, and our assessment of the commercial opportunities in these indications, as well as the changed competitive landscape in myeloid cancers where seven drugs were approved for AML in the United States in the last two years, we have determined to cease enrollment in these trials and further clinical development for these indications at this time. We plan to present data from our AML/MDS trials in the fourth quarter of 2019.

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

On June 28, 2017, our registration statement on Form S-1 relating to our initial public offering of our common stock, or IPO, was declared effective by the SEC. The IPO closed on July 5, 2017 and we issued and sold 3,750,000 shares of common stock at a public offering price of $15.00 per share for net proceeds of $50.0 million after deducting underwriting discounts and commissions of $3.9 million and offering expenses of $2.3 million. Upon the closing of the IPO, all shares of redeemable convertible preferred stock then outstanding converted into an aggregate of 10,509,774 shares of common stock.

Prior to the IPO, we financed our operations through private placements of preferred stock and, to a lesser extent, from payments received under a collaboration agreement. From our inception through December 31, 2018, we had received $50.0 million in net proceeds from our IPO, $131.2 million from our sales of preferred stock and $34.9 million from the collaboration agreement.

Since our inception, we have incurred significant losses on an aggregate basis. Our net losses were $31.6 million and $22.6 million for the years ended December 31, 2018 and 2017, respectively. As of December 31, 2018, we had an accumulated deficit of $168.5 million. These losses have resulted primarily from costs incurred in connection with research and development activities, licensing and patent investment and general and administrative costs associated with our operations. We expect to continue to incur significant expenses and operating losses for at least the next several years.

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

Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate revenue from product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

As of December 31, 2018, we had cash, cash equivalents and investments of $20.7 million. We believe that, based on our current operating plan, our cash, cash equivalents and investments as of December 31, 2018 will enable us to fund our operating expenses and capital expenditure requirements into the third quarter of 2019. Accordingly, there is substantial doubt about our ability to continue as a going concern as we do not believe that our cash, cash equivalents and investments at December 31, 2018 will be sufficient to fund operations for at least twelve months from the date of issuance of the financial statements included in this Annual Report on Form 10-K.

On March 28, 2019, we entered into a securities purchase agreement with certain accredited investors pursuant to which we agreed to issue and sell an aggregate of (i) 11,838,582 units, consisting of 11,838,582 shares of common stock and associated warrants to purchase an aggregate of 11,838,582 shares of common stock and (ii) 1,096,741 units, consisting of 1,096,741 pre-funded warrants to purchase 1,096,741 shares of common stock and associated warrants to purchase an aggregate of 1,096,741 shares of common stock in a private placement. The private placement is expected to close on April 2, 2019, subject to the satisfaction of customary closing conditions. We expect to receive aggregate gross proceeds of approximately $26.0 million, before deducting placement agent fees and offering expenses. We plan to address the existence of substantial doubt through the sale of common stock in public offerings and/or private placements, through other capital sources, including collaborations with other companies or other strategic transactions, including the securities purchase agreement we entered into on March 28, 2019. We have based this estimate on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we expect. See “Liquidity and Capital Resources.” Our future viability is dependent on our ability to raise additional capital to finance our operations.

We entered into a lease agreement that became effective on April 4, 2018 for 18,768 square feet of office and laboratory space in Watertown, Massachusetts. We moved into this new facility in August 2018. The lease has an initial term of eight years and provides us with an option to extend the lease term for one additional five-year period.

Components of our Results of Operations

Revenue

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

Operating Expenses

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

Research and Development Expenses

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

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

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

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

The following table summarizes our research and development expenses by product candidate or development program:

	Year Ended December 31,	
	2018	2017
ALRN-6924 and p53 program	$ 10,730	$ 8,755
Other early-stage development programs	336	232
Employee, facility and other development expenses	7,382	5,252
Total research and development expenses	$ 18,448	$ 14,239

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect to incur significant research and development expenses in the foreseeable future as we continue our non-clinical research testing a variety of approved drugs in combination with ALRN-6924, initiate additional clinical trials of ALRN-6924, pursue later stages of clinical development of ALRN-6924, initiate clinical trials for product candidates other than ALRN-6924 and continue to discover and develop additional product candidates, including product candidates for targets in which we have made substantial investments in prior years for the treatment of a variety of disease indications.

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

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

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

We are currently conducting a Phase 2a clinical trial of the combination of ALRN-6924 and palbociclib (Ibrance), for the treatment of MDM2-amplified advanced solid tumors and expect to begin enrolling patients in a Phase 1b/2 clinical trial to evaluate ALRN-6924 as a myelopreservative agent in the third quarter of 2019. We have also determined to cease clinical development of ALRN-6924 for the treatment of PTCL, AML and MDS. At this time, we cannot reasonably estimate the cost for initiating and completing these and other clinical trials of ALRN-6924 and preclinical studies of ALRN-6924, as it will be highly dependent on the clinical data from ongoing clinical trials as well as any target disease subpopulations chosen for further evaluation.

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, corporate and business development 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.

Subject to obtaining the necessary funding, we expect that our general and administrative expenses will increase in the future as we increase our general and administrative personnel headcount to support personnel in research and development and to support our operations generally as we increase our research and development activities and activities related to the potential commercialization of our product candidates. We also expect to incur increased expenses associated with operating as a public company, including costs of accounting, audit, legal, regulatory and tax-related services associated with maintaining compliance with exchange listing and SEC requirements; director and officer insurance costs; and investor and public relations costs.

Interest Income, net

Interest income consists of interest income earned on our cash, cash equivalents and investments. Interest expense consists of imputed interest expense related to our construction financing liability associated with the build-out and tenant improvements to our leased office and laboratory facility. Prior to the IPO, our interest income had not been significant due to low investment balances and low interest earned on those balances. Our interest income increased following the IPO due to higher investment balances and interest carried on those balances.

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, 2018, we had federal and state net operating loss carryforwards of $157.6 million and $153.1 million, respectively, which begin to expire in 2029 and 2030, respectively. As of December 31, 2018, we also had federal and state research and development tax credit carryforwards of $2.4 million and $1.5 million, respectively, which begin to expire in 2025.

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

Critical Accounting Policies and Use of Estimates

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

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

Accrued Research and Development Expenses

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

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

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

Stock-Based Compensation

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

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

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

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

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

Determination of Fair Value of Common Stock

Due to the absence of a public market for our common stock, prior to June 28, 2017, the date our stock began publicly trading, the estimated fair value of our common stock was determined by our board of directors as of the date of each option grant, with input from management, considering our most recently available third-party valuations of common stock and our board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the grant. These third-party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. These common stock valuations were prepared using a hybrid method, which used market approaches to estimate our enterprise value. The hybrid method is a probability-weighed expected return method, or PWERM, where the equity value in one or more scenarios is calculated using an option-pricing method, or OPM. The OPM treats common stock and preferred stock as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. Under this method, the common stock has value only if the funds available for distribution to stockholders exceeded the value of the preferred stock liquidation preference at the time of the liquidity event, such as a strategic sale or a merger. The PWERM is a scenario-based methodology that estimates the fair value of common stock based upon an analysis of future values for the company, assuming various outcomes. The common stock value is based on the probability-weighted present value of expected future investment returns considering each of the possible outcomes available as well as the rights of each class of stock. The future value of the common stock under each outcome is discounted back to the valuation date at an appropriate risk-adjusted discount rate and probability weighted to arrive at an indication of value for the common stock.

For grants made after the date our stock began public trading, the fair value per share of our common stock on the date of grant is determined using the closing price of our common stock on The Nasdaq Global Market on the date of grant.

Emerging Growth Company Status

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

Results of Operations

Comparison of the Years Ended December 31, 2018 and 2017

The following table summarizes our results of operations for the years ended December 31, 2018 and 2017:

	Year Ended December 31, 2018	2017	Increase (Decrease)
	(in thousands)		
Revenue	$ —	$ —	$ —
Operating expenses:			
Research and development	18,448	14,239	4,209
General and administrative	13,454	8,769	4,685
Total operating expenses	31,902	23,008	8,894
Loss from operations	(31,902)	(23,008)	(8,894)
Interest income, net	355	404	(49)
Net loss	$ (31,547)	$ (22,604)	$ (8,943)

Research and Development Expenses

	Year Ended December 31, 2018	2017	Increase (Decrease)
	(in thousands)		
ALRN-6924 and p53 program	$ 10,730	$ 8,755	$ 1,975
Other early-stage development programs	336	232	104
Employee, facility and other development expenses	7,382	5,252	2,130
Total research and development expenses	$ 18,448	$ 14,239	$ 4,209

Research and development expenses for the year ended December 31, 2018 were $18.4 million, compared to $14.2 million for the year ended December 31, 2017. The increase of $4.2 million was primarily due to an increase of $2.0 million in research and development expenses associated with our ALRN-6924 and p53 program expenses and an increase of $2.1 million in employee, facility and other development expenses. The increase in our ALRN-6924 and p53 program expenses was primarily due to a $1.8 million increase in expenses for non-clinical research for the year ended December 31, 2018 associated with expanding our research to test a variety of approved drugs in combination with ALRN-6924, including cyclin-dependent kinase inhibitors, traditional chemotherapeutic agents and immuno-oncology agents. Also contributing to the increase was a $1.4 million increase in clinical expenses associated with increased data management and patient monitoring expenses. These increases were offset by a $1.2 million decrease in expenses associated with our manufacturing of ALRN-6924 for our clinical trials. This decrease resulted from the manufacture of sufficient quantities of ALRN-6924 during 2017 to supply our clinical trial needs for 2018. We expect to have more ALRN-6924 manufactured as our clinical trials advance. The increase in employees, facility and other development expenses was primarily due to increased wage and other personnel related costs resulting from personnel that we hired to support our ongoing trials. Subject to obtaining the necessary funding, we expect that our research and development expenses will continue to increase in the foreseeable future as we advance our non-clinical research to test a variety of approved drugs in combination with ALRN-6924, initiate additional clinical trials of ALRN-6924, pursue later stages of clinical development of ALRN-6924, initiate clinical trials for product candidates other than ALRN-6924 and continue to discover and develop additional product candidates, including product candidates for targets in which we have made substantial investments in prior years for the treatment of a variety of disease indications. We also expect that our research and development expenses will increase in the future as we hire research and development employees to support the increase in our research and development activities.

General and Administrative Expenses

General and administrative expenses were $13.5 million for the year ended December 31, 2018, compared to $8.8 million for the year ended December 31, 2017. Approximately $1.1 million of the $4.7 million increase was due to expenses incurred in connection with a separation agreement with our former Chief Executive Officer. Of this $1.1 million, approximately $0.5 million related to salary continuation payments and $0.6 million resulted from modifications to his stock options. The remaining increase of $3.6 million was primarily due to increases of $1.3 million in personnel-related costs, $1.3 million in external costs and $0.7 million in stock compensation expense. The increase in personnel-related costs was due to higher wages and recruiting fees associated with increased headcount. The increase in external costs was primarily due to increased legal fees related to lease negotiations for our move into our new office and laboratory facility in August 2018 and to support our intellectual property portfolio, increased external consulting fees and higher insurance fees associated with being a public company. The increase in stock compensation expense was related to employee stock option grants made in 2017 and 2018.

We expect that our general and administrative expenses will increase slightly as we support expanded research and development activities and the potential commercialization of our product candidates. We also expect to incur increased expenses associated with operating as a public company, including costs of accounting, audit, legal, regulatory and tax-related services associated with maintaining compliance with exchange listing and SEC requirements, director and officer insurance costs, and investor and public relations costs.

Interest Income

Interest income, net for the year ended December 31, 2018 was less than $0.1 million lower compared to the year ended December 31, 2017 due to the inclusion of interest expense related to our construction financing liability associated with the build-out and tenant improvements to our leased office and laboratory space at in Watertown, Massachusetts. We anticipate that our interest income will decrease in the future due to interest expense recorded on our lease and to the extent our cash, cash equivalents and investments are lower due to our use of cash to fund our operations.

Liquidity and Capital Resources

Since our inception, we have incurred significant losses on an aggregate basis. We have not yet commercialized any of our product candidates, which are in various phases of preclinical and clinical development, and we do not expect to generate revenue from sales of any products for several years, if at all. Prior to the IPO, we financed our operations through private placements of our preferred stock and, to a lesser extent, through payments received under a collaboration agreement. Since our inception through December 31, 2018, we had received $50.0 million in net proceeds from our IPO, $131.2 million from our sales of preferred stock and $34.9 million from the collaboration agreement. As of December 31, 2018, we had cash, cash equivalents and investments of $20.7 million.

On June 28, 2017, our registration statement on Form S-1 relating to our initial public offering of our common stock was declared effective by the SEC. The IPO closed on July 5, 2017 and we issued and sold 3,750,000 shares of common stock at a public offering price of $15.00 per share for net proceeds of $50.0 million after deducting underwriting discounts and commissions of $3.9 million and other offering expenses of $2.3 million. Upon the closing of the IPO, all shares of preferred stock then outstanding converted into an aggregate of 10,509,774 shares of common stock.

On March 28, 2019, we entered into a securities purchase agreement with certain accredited investors pursuant to which we agreed to issue and sell an aggregate of (i) 11,838,582 units, consisting of 11,838,582 shares of common stock and associated warrants to purchase an aggregate of 11,838,582 shares of common stock, for a combined unit price of $2.01 per unit and (ii) 1,096,741 units, consisting of 1,096,741 pre-funded warrants to purchase 1,096,741 shares of common stock and associated warrants to purchase an aggregate of 1,096,741 shares of common stock, for a combined unit price of $2.01 per unit in a private placement. The pre-funded warrants will be exercisable following closing of the private placement at an exercise price of $0.01 per share. The common warrants will be exercisable following closing of the private placement at an exercise price of $2.00 per share and will expire five years from the date of issuance. The private placement is expected to close on April 2, 2019, subject to the satisfaction of customary closing conditions. We expect to receive aggregate gross proceeds of approximately $26 million before deducting placement agent fees and offering expenses.

Cash Flows

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

	Year Ended December 31, 2018	Year Ended December 31, 2017
	(in thousands)	
Cash used in operating activities	$ (27,926)	$ (20,531)
Cash provided by (used in) investing activities	24,688	(38,912)
Cash provided by financing activities	2,515	50,591
Net increase (decrease) in cash, cash equivalents and restricted cash	$ (723)	$ (8,852)

Operating Activities. During the year ended December 31, 2018, operating activities used $27.9 million of cash, primarily resulting from our net loss of $31.6 million offset by non-cash charges of $3.2 million and a decrease in working capital of $0.4 million. Non-cash charges resulted primarily from stock-based compensation expense. The decrease in our working capital during the year ended December 31, 2018 consisted primarily of an increase of $0.5 million in accrued expenses and accounts payable partially offset by an increase of $0.1 million in prepaid expenses and other current assets. The increase in accrued expenses and other current liabilities was primarily due to the increase of clinical trial-related accruals and contract manufacturing costs. The increase in prepaid expenses and other current assets was primarily due to the timing of vendor invoicing and payments.

During the year ended December 31, 2017, operating activities used $20.5 million of cash, primarily resulting from our net loss of $22.6 million offset by net cash provided by non-cash charges of $1.7 million and changes in our operating assets and liabilities of $0.4 million. Non-cash charges resulted primarily from stock-based compensation expense. Net cash provided by changes in our operating assets and liabilities during the year ended December 31, 2017 consisted primarily of an increase of $1.2 million in accrued expenses and other current liabilities offset by an increase of $0.8 million in prepaid expenses and other current assets. The increase in accrued expenses and other current liabilities was primarily due to the increase of clinical trial-related accruals and contract manufacturing costs. The increase in prepaid expenses and other current assets was primarily due to the timing of vendor invoicing and payments.

Investing Activities. During the year ended December 31, 2018, investing activities provided $24.7 million of cash. Proceeds from sales or maturities of investments, net of purchases of investments were $29.1 million and were used to fund operating activities and capital purchases. During 2018, we used $4.4 million to purchase capital equipment, primarily related to the build out of our newly leased facility.

During the year ended December 31, 2017, investing activities used $38.9 million of cash, consisting of net purchases of investments of $71.1 million offset against proceeds from the sales or maturities of those investments of $32.3 million.

We expect that purchases of property and equipment will decrease over the next year as we completed the build-out of our new leased office and laboratory space in 2018 and thus do not expect to purchase similar levels of property and equipment in 2019.

Financing Activities. During the year ended December 31, 2018, net cash provided by financing activities was $2.5 million primarily due to the landlord reimbursement of construction costs incurred in the build out of our newly leased facility.

During the year ended December 31, 2017, net cash provided by financing activities was $50.6 million primarily due to the proceeds, less underwriting discounts, from our IPO in July 2017 of $52.3 million. These proceeds were offset by payments of initial public offering costs of $2.3 million.

Funding Requirements

Subject to obtaining the necessary funding, we expect our expenses to increase substantially in connection with our ongoing development activities related to ALRN-6924, which is still in the early stages of clinical development, and other product candidates and programs. In addition, we expect to incur additional costs associated with operating as a public company. We expect that our expenses will increase substantially if and as we:

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

As of December 31, 2018, we had cash, cash equivalents and investments of $20.7 million. We believe that, based on our current operating plan, our cash, cash equivalents and investments will enable us to fund our operating expenses and capital expenditure requirements into the third quarter of 2019. Accordingly, there is substantial doubt about our ability to continue as a going concern as we do not believe that our cash, cash equivalents and investments will be sufficient to fund operations for at least twelve months from the date of issuance of these financial statements

On March 28, 2019, we entered into a securities purchase agreement with certain accredited investors pursuant to which we agreed to issue and sell an aggregate of (i) 11,838,582 units, consisting of 11,838,582 shares of common stock and associated warrants to purchase an aggregate of 11,838,582 shares of common stock and (ii) 1,096,741 units, consisting of 1,096,741 pre-funded warrants to purchase 1,096,741 shares of common stock and associated warrants to purchase an aggregate of 1,096,741 shares of common stock in a private placement. The private placement is expected to close on April 2, 2019, subject to the satisfaction of customary closing conditions. We expect to receive aggregate gross proceeds of approximately $26 million, before deducting placement agent fees and offering expenses. We plan to address the existence of substantial doubt through the sale of common stock in public offerings and/or private placements, through other capital sources, including collaborations with other companies or other strategic transactions, including the securities purchase agreement we entered into on March 28, 2019. If our private placement does not close on a timely basis, or at all and we are otherwise unable to raise sufficient capital or otherwise when needed, our business, financial condition and results of operations will be materially and adversely affected, and we will need to significantly modify our operational plans to continue as a going concern.

In any event, our cash, cash equivalents and investments will not be sufficient to fund all of the efforts that we plan to undertake or to fund the completion of development of any of our product candidates. Accordingly, we will be required to obtain further funding through public or private equity offerings, collaborations and licensing arrangements, or other sources of capital. Adequate additional financing may not be available to us on acceptable terms, if at all. In addition, while we may seek one or more collaborators for future development of our product candidates for one or more indications, we may not be able to enter into a collaboration for any of our product candidate for such indications on suitable terms, on a timely basis or at all. Although we have been successful in raising capital in the past, there is no assurance that we will be successful in obtaining such additional financing and therefore it is not considered probable that we will be able to raise the necessary additional capital to alleviate the substantial doubt regarding our ability to continue as a going concern.

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

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

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

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

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

Contractual Obligations and Commitments

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

Off-Balance Sheet Arrangements

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

Recently Issued Accounting Pronouncements

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

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

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

Item 8. Financial Statements and Supplementary Data.

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

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

None

Item 9A. Controls and Procedures.

Limitations on Effectiveness of Controls and Procedures

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

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

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, evaluated, as of the end of the period covered by this Annual Report on Form 10-K, the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act of 1934). Based on that evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2018.

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, 2018. 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, 2018, 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 three months ended December 31, 2018 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

On March 27, 2019, our Board of Directors appointed Richard Wanstall as our principal accounting officer. Mr. Wanstall, age 50, has served as our Vice President, Finance and Operations since July 2018. From July 2014 to July 2018, Mr. Wanstall served as Vice President, Finance at Moderna Therapeutics, Inc., a biotechnology company focused on drug discovery and drug development based on messenger RNA. Prior to Moderna, Mr. Wanstall served as Senior Vice President, Global Finance at Stream Global Services, Inc., a multinational business process outsourcing company, from May 2010 to July 2014. Previously, Mr. Wanstall served in management roles in finance, accounting and SEC reporting for several technology and financial services companies. Mr. Wanstall began his career at Coopers & Lybrand, LLC. Mr. Wanstall received a B.A. from Salem State College, and a M.B.A. from Babson College.

Mr. Wanstall was not appointed as principal accounting officer pursuant to any arrangement or understanding between him and any other person. There are no family relationships between Mr. Wanstall and any director, executive officer or any person nominated or chosen by us to become a director or executive officer.

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 “Section 16(a) Beneficial Ownership Reporting Compliance” in our definitive proxy statement to be filed with the Securities and Exchange Commission, or SEC, with respect to our 2019 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, 2018 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 2019 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this Item 12 will be included under the captions “Security Ownership of Certain Beneficial Owners and Management” and “Securities Authorized for Issuance Under Equity Compensation Plans” in our definitive proxy statement to be filed with the SEC with respect to our 2019 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 2019 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 2019 Annual Meeting of Stockholders and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

The following documents are filed as part of this Report:

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

INDEX TO FINANCIAL STATEMENTS

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

(c) *Exhibits*.

Exhibit Number	Description	Incorporation by Reference			Filed Herewith
		Form	Date of Filing	Exhibit Number	
3.1	Restated Certificate of Incorporation of the Registrant	8-K	7/5/2017	3.1	
3.2	Amended and Restated By-laws of the Registrant	8-K	7/5/2017	3.2	
4.1	Specimen stock certificate evidencing shares of common stock	S-1^	6/19/2017	4.1	
4.2	Seventh Amended and Restated Investor Rights Agreement, dated as of December 23, 2016, among the Registrant and the other parties thereto	S-1^	6/2/2017	4.2	
10.1*	2006 Stock Incentive Plan, as amended	S-1^	6/2/2017	10.1	
10.2*	Form of Incentive Stock Option Agreement under 2006 Stock Incentive Plan	S-1^	6/2/2017	10.2	
10.3*	Form of Nonstatutory Stock Option Agreement under 2006 Stock Incentive Plan	S-1^	6/2/2017	10.3	
10.4*	2016 Stock Incentive Plan	S-1^	6/2/2017	10.4	
10.5*	Form of Incentive Stock Option Agreement under 2016 Stock Incentive Plan	S-1^	6/2/2017	10.5	
10.6*	Form of Nonstatutory Stock Option Agreement under 2016 Stock Incentive Plan	S-1^	6/2/2017	10.6	
10.7*	2017 Stock Incentive Plan	S-1^	6/19/2017	10.8	
10.8*	Form of Incentive Stock Option Agreement under 2017 Stock Incentive Plan	S-1^	6/19/2017	10.9	
10.9*	Form of Nonstatutory Stock Option Agreement under 2017 Stock Incentive Plan	S-1^	6/19/2017	10.10	
10.10*	2017 Employee Stock Purchase Plan	S-1^	6/19/2017	10.11	
10.11	Form of Director and Officer Indemnification Agreement	S-1^	6/19/2017	10.12	
10.12+	License Agreement, dated as of December 31, 2006, by and between the Registrant and Materia, Inc. (now Umicore Precious Metals Chemistry USA, LLC)	S-1^	6/2/2017	10.13	
10.13+	Amended and Restated License Agreement, dated as of February 19, 2010, by and among the Registrant, President and Fellows of Harvard College and Dana-Farber Cancer Institute, Inc.	S-1^	6/19/2017	10.14	

10.14	Lease Agreement, effective as of April 4, 2018, between the Registrant and 480 Arsenal Group LLC	10-Q	8/7/2018	10.1	
10.15	Amendment to Lease Agreement, dated as of August 23, 2018, between the Registrant and 480 Arsenal Group LLC	10-Q	11/7/2018	10.1	
10.16*	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	
10.17*	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	
10.18*	Employment Agreement, dated as of June 5, 2017, between the Registrant and Donald V. Dougherty	S-1^	6/19/2017	10.2	
10.19*	Severance Agreement, dated as of October 1, 2018, between the Registrant and Donald V. Dougherty				X
10.20*	Offer Letter and Severance Agreement, dated as of November 1, 2018, between the Registrant and Vojislav Vukovic, M.D., Ph.D.				X
10.21*	Offer Letter, dated as of November 15, 2007, between the Registrant and D. Allen Annis, Ph.D.				X
10.22*	Severance Agreement, dated as of November 5, 2018, between the Registrant and D. Allen Annis, Ph.D.				X
10.23*	Offer Letter and Severance Agreement, dated as of February 15, 2019, between the Registrant and Kathryn Gregory.				X
10.24*	Employment Agreement, dated as of May 15, 2018, between the Registrant and John P. Longenecker.	10-Q	8/7/2018	10.3	
10.25*	Consulting Agreement, dated as of September 30, 2018, between the Registrant and John P. Longenecker, as subsequently amended on December 17, 2018.				X
10.26*	Employment Agreement, dated as of March 1, 2008, between the Registrant and Joseph A. Yanchik III, as amended on December 31, 2008.	S-1^	6/2/2017	10.16	
10.27*	Separation and Release of Claims Agreement, dated as of May 15, 2018, between the Registrant and Joseph A. Yanchik III.	10-Q	8/7/2018	10.2	
23.1	Consent of PricewaterhouseCoopers LLP, independent registered public accounting firm.				X
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				X

31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	X
32.1	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	X
32.2	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	X
101.INS	XBRL Instance Document	
101.SCH	XBRL Taxonomy Extension Schema Document	
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document	
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document	
101.LAB	XBRL Taxonomy Extension Label Linkbase Document	
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document	
*	Indicates management contract or compensatory plan.	
+	Confidential treatment has been requested and/or granted as to certain portions, which portions have been omitted and filed separately with the U.S. Securities and Exchange Commission.	
^	SEC File No. 333-218474	

SIGNATURES

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

Aileron Therapeutics, Inc.

Date: March 29, 2019

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 29, 2019
/s/ Donald V. Dougherty **Donald V. Dougherty**	Senior Vice President, Chief Financial Officer (principal financial officer)	March 29, 2019
/s/ Richard J. Wanstall **Richard J. Wanstall**	Vice President, Finance & Operations (principal accounting officer)	March 29, 2019
/s/ Jeffrey A. Bailey **Jeffrey A. Bailey**	Chairman of the Board of Directors	March 29, 2019
/s/ Reinhard J. Ambros, Ph.D. **Reinhard J. Ambros, Ph.D.**	Director	March 29, 2019
/s/ John H. McArthur, D.B.A. **John H. McArthur, D.B.A.**	Director	March 29, 2019
/s/ Armen B. Shanafelt, Ph.D. **Armen B. Shanafelt, Ph.D.**	Director	March 29, 2019
/s/ Caleb Winder **Caleb Winder**	Director	March 29, 2019
/s/ Jodie P. Morrison **Jodie P. Morrison**	Director	March 29, 2019

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, 2018 and 2017, and the related statements of operations and comprehensive loss, of redeemable convertible preferred stock and stockholders' equity (deficit) and of cash flows for the years then ended, including the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2018 and 2017, 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 suffered recurring losses and negative cash flows from operations since its inception 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 audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

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

/s/ PricewaterhouseCoopers LLP
Boston, Massachusetts
March 29, 2019

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, 2018	December 31, 2017
Assets		
Current assets:		
Cash and cash equivalents	$ 10,635	$ 11,863
Investments	10,060	38,889
Prepaid expenses and other current assets	1,055	1,000
Restricted cash	25	88
Total current assets	21,775	51,840
Property and equipment, net	7,290	154
Restricted cash, non-current	568	—
Other assets	679	694
Total assets	$ 30,312	$ 52,688
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 1,731	$ 1,600
Accrued expenses and other current liabilities	3,639	3,291
Total current liabilities	5,370	4,891
Construction financing liability	5,342	—
Total liabilities	10,712	4,891
Commitments and contingencies (Note 9)		
Stockholders' equity:		
Preferred stock, $0.001 par value; 5,000,000 shares authorized at December 31, 2018 and December 31, 2017; no shares issued and outstanding at December 31, 2018 and December 31, 2017	—	—
Common stock, $0.001 par value; 150,000,000 shares authorized at December 31, 2018 and December 31, 2017; 14,748,475 and 14,723,818 shares issued and outstanding at December 31, 2018 and December 31, 2017, respectively	15	15
Additional paid-in capital	188,083	184,761
Accumulated other comprehensive loss	(5)	(33)
Accumulated deficit	(168,493)	(136,946)
Total stockholders' equity	19,600	47,797
Total liabilities and stockholders' equity	$ 30,312	$ 52,688

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, 2018	Year Ended December 31, 2017
Revenue	$ —	$ —
Operating expenses:		
Research and development	18,448	14,239
General and administrative	13,454	8,769
Total operating expenses	31,902	23,008
Loss from operations	(31,902)	(23,008)
Interest income, net	355	404
Net loss	(31,547)	(22,604)
Accretion of redeemable convertible preferred stock to redemption value	—	(41)
Net loss	$ (31,547)	$ (22,645)
Net loss per share—basic and diluted	$ (2.14)	$ (3.04)
Weighted average common shares outstanding—basic and diluted	14,738,193	7,443,078
Comprehensive loss:		
Net loss	$ (31,547)	$ (22,604)
Other comprehensive gain (loss):		
Unrealized gain (loss) on investments, net of tax of $0	28	(33)
Total other comprehensive gain (loss)	28	(33)
Total comprehensive loss	$ (31,519)	$ (22,637)

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

AILERON THERAPEUTICS, INC.
STATEMENT OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)

(In thousands, except share data)

	Redeemable Convertible Preferred Stock		Common Stock		Additional	Accumulated Other		Total
	Shares	Amount	Shares	Par Value	Paid-in Capital	Comprehensive Loss	Accumulated Deficit	Stockholders' Equity
Balances at December 31, 2016	105,631,019	129,745	432,413	—	2,536	—	(114,342)	(111,806)
Issuance of Series F redeemable convertible preferred stock, net of issuance costs of $32	483,501	626	—	—	—	—	—	—
Accretion of redeemable convertible preferred stock to redemption value	—	41	—	—	(41)	—	—	(41)
Conversion of redeemable convertible preferred stock to common stock	(106,114,520)	(130,412)	10,509,774	11	130,401	—	—	130,412
Issuance of common stock upon completion of initial public offering, net of commissions, underwriting discounts and offering costs	—	—	3,750,000	4	50,005	—	—	50,009
Exercise of stock options	—	—	31,631	—	111	—	—	111
Stock-based compensation expense	—	—	—	—	1,749	—	—	1,749
Unrealized loss on investments	—	—	—	—	—	(33)	—	(33)
Net loss	—	—	—	—	—	—	(22,604)	(22,604)
Balances at December 31, 2017	—	—	14,723,818	15	184,761	(33)	(136,946)	47,797
Exercise of stock options	—	—	24,657	—	42	—	—	42
Stock-based compensation expense	—	—	—	—	3,280	—	—	3,280
Unrealized gain on investments	—	—	—	—	—	28	—	28
Net loss	—	—	—	—	—	—	(31,547)	(31,547)
Balances at December 31, 2018	—	$ —	14,748,475	$ 15	$ 188,083	$ (5)	$ (168,493)	$ 19,600

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

AILERON THERAPEUTICS, INC.
STATEMENTS OF CASH FLOWS

(In thousands)

	Year Ended December 31, 2018	Year Ended December 31, 2017
Cash flows from operating activities:		
Net loss	$ (31,547)	$ (22,604)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	3,280	1,749
Depreciation and amortization expense	218	129
Net amortization of premiums and discounts on investments	(253)	(152)
Change in deferred rent	(11)	(11)
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(117)	(764)
Other assets	15	147
Accounts payable	130	(241)
Accrued expenses and other current liabilities	359	1,216
Net cash used in operating activities	(27,926)	(20,531)
Cash flows from investing activities:		
Purchases of property and equipment	(4,423)	(142)
Purchases of investments	(31,194)	(71,056)
Proceeds from sales or maturities of investments	60,305	32,286
Net cash provided by (used in) investing activities	24,688	(38,912)
Cash flows from financing activities:		
Proceeds from exercise of stock options	42	111
Construction financing liability borrowings	2,473	—
Proceeds from initial public offering of common stock, net of commissions and underwriting discounts	—	52,313
Payments of initial public offering costs	—	(2,304)
Proceeds from issuance of redeemable convertible preferred stock, net of issuance costs	—	471
Net cash provided by financing activities	2,515	50,591
Net increase (decrease) in cash, cash equivalents and restricted cash	(723)	(8,852)
Cash, cash equivalents and restricted cash at beginning of period	11,951	20,803
Cash, cash equivalents and restricted cash at end of period	$ 11,228	$ 11,951
Supplemental disclosure of non-cash financing activities:		
Accretion of redeemable convertible preferred stock to redemption value	$ —	$ 41
Capitalization of build-to-suit asset	$ 2,869	$ —

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

(Amounts in thousands, except share and per share data)

1. Nature of the Business and Basis of Presentation

Aileron Therapeutics, Inc. (“Aileron” or the “Company”) is a clinical-stage biopharmaceutical company that is focused on developing and commercializing a novel class of stabilized cell-permeating alpha-helical peptides to address intracellular targets in oncology and other therapeutic areas. The Company’s lead product candidate, ALRN-6924, targets the tumor suppressor p53 for the treatment of a wide variety of cancers. ALRN-6924 is a stabilized cell-permeating peptide that disrupts the interaction of the two primary p53 suppressor proteins, MDM2 and MDMX, with p53, thereby reactivating tumor suppression in wild-type p53 cancers. ALRN-6924 was in multiple clinical trials as of December 31, 2018.

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 and the need to obtain additional financing. Product candidates currently under development will require significant additional research and development efforts, including extensive preclinical and clinical testing and regulatory approval, prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel infrastructure, and extensive compliance-reporting capabilities.

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

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

Reverse Stock Split

On June 16, 2017, in connection with its initial public offering (“IPO”), the Company effected a one-for-9.937 reverse stock split of its issued and outstanding shares of common stock and a proportional adjustment to the existing conversion ratios for each series of the Company’s redeemable convertible preferred stock (see Note 7). Accordingly, all common share and per share amounts for all periods presented in the accompanying financial statements and notes thereto have been adjusted retroactively, where applicable, to reflect this reverse stock split and the associated adjustment of the preferred stock conversion ratios.

Initial Public Offering

On June 28, 2017, the Company’s registration statement on Form S-1 relating to its IPO was declared effective by the Securities and Exchange Commission (“SEC”). In the IPO, which closed on July 5, 2017, the Company issued and sold 3,750,000 shares of common stock at a public offering price of $15.00 per share for net proceeds of $50,009 after deducting underwriting discounts and commissions of $3,937 and offering expenses of $2,304. Upon the closing of the IPO, all 106,114,520 shares of redeemable convertible preferred stock then outstanding converted into an aggregate of 10,509,774 shares of common stock.

Liquidity

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

The Company's financial statements have been prepared on a going concern basis, which contemplates the continuity of operations, realization of assets and the satisfaction of liabilities in the ordinary course of business. Through December 31, 2018, the Company has funded its operations with net proceeds of $50,009 from its IPO, $131,211 from sales of preferred stock and $34,910 from a collaboration agreement. As of December 31, 2018, the Company had cash, cash equivalents and investments of $20,695. The Company has incurred losses and negative cash flows from operations and had an accumulated deficit of $168,493 as of December 31, 2018. The Company expects to continue to generate losses for the foreseeable future.

The Company believes that, based on its current operating plan, its cash, cash equivalents and investments of $20,695 as of December 31, 2018, will enable it to fund its operating expenses and capital expenditure requirements into the third quarter of 2019. Accordingly, there is substantial doubt about the Company's ability to continue as a going concern as the Company does not believe that its cash, cash equivalents and investments will be sufficient to fund operations for at least twelve months from the date of issuance of these financial statements. The Company plans to address this condition through the sale of common stock in public offerings and/or private placements, through other capital sources, including collaborations with other companies or other strategic transactions, including the securities purchase agreement it entered into on March 28, 2019 to sell an aggregate of (i) 11,838,582 units, consisting of 11,838,582 shares of common stock, and associated warrants to purchase an aggregate of 11,838,582 shares of common stock and (ii) 1,096,741 units, consisting of 1,096,741 pre-funded warrants to purchase 1,096,741 shares of common stock and associated warrants to purchase an aggregate of 1,096,741 shares of common stock in a private placement. The Company expects to receive aggregate gross proceeds of approximately $26,000, before deducting placement agent fees and offering expenses. However, receipt of the funds cannot be considered probable, as defined in accounting standards ASU No. 2014-15 (subtopic 205-40), until the closing occurs and the funds are received. The private placement is expected to close on April 2, 2019, subject to the satisfaction of customary closing conditions. Although the Company has been successful in raising capital in the past, there is no assurance that, if the closing does not occur and the Company does not receive the proceeds, it will be successful in obtaining any additional financing and therefore it is not considered probable that the Company will be able to raise the necessary additional capital to alleviate the substantial doubt regarding its ability to continue as a going concern.

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

2. Summary of Significant Accounting Policies

Use of Estimates

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

Cash Equivalents

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

Restricted Cash

As of December 31, 2018, current 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. As of December 31, 2017, current restricted cash consisted of $25 of cash deposited in a separate restricted bank account as a security deposit for the Company's corporate credit cards and $63 of cash deposited in a separate restricted bank account as a security deposit for the lease of the Company's facilities. As of December 31, 2018, non-current restricted cash consisted of $568 of cash deposited in a separate restricted bank account as a security deposit for the lease of the Company's new facility (see Note 12). The Company did not have any non-current restricted cash as of December 31, 2017.

Investments

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

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

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

Concentration of Credit Risk and of Significant Suppliers

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

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

Fair Value Measurements

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

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

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

Deferred Offering Costs

The Company capitalizes certain legal, professional accounting and other third-party fees that are directly associated with in-process equity financings as deferred offering costs until such financings are consummated. After consummation of the equity financing, these costs are recorded in stockholders' equity (deficit) as a reduction of additional paid-in capital generated as a result of the offering. Should the planned equity financing be abandoned, the deferred offering costs would be expensed immediately as a charge to operating expenses in the statement of operations and comprehensive loss.

Property and Equipment

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

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

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

Impairment of Long-Lived Assets

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

Research and Development Costs

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

Research Contract Costs and Accruals

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

Patent Costs

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

Accounting for Stock-Based Compensation

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

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

Effective October 1, 2018, the Company adopted Accounting Standards Update ("ASU") No. 2018-07, Compensation - Stock Compensation (Topic 718): Improvements to Non-employee Share-based Payment Accounting ("ASU 2018-07"), which sets out to simplify the accounting for non-employee share-based awards. The ASU expands the scope of Topic 718, Compensation-Stock Compensation, which currently only includes share-based payments issued to employees, to also include share-based payments issued to non-employees for goods and services. Consequently, the accounting for share-based payments to non-employees and employees is substantially aligned. ASU 2018-07 impacts the value at which share-based payments to non-employees is recognized.

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

After adoption of ASU 2018-07, the measurement date for non-employee awards is the date of the grant. The compensation expense for non-employees is recognized, without changes in the fair value of the award, over the requisite service period, which is the vesting period of the respective award. The compensation expense for non-employees was measured as of the adoption date of October 1, 2018, and this amount is the basis for prospective expense recognition. All of the Company's non-employee awards were previously measured as of September 30, 2018. Accordingly, no cumulative adjustment to beginning retained earnings was recorded as a result of the ASU 2018-07 adoption, as the measured value prior to adoption and the remeasured value on the date of adoption were materially the same.

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

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

Income Taxes

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

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

Segment Data

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

Comprehensive Loss

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

Net Income (Loss) per Share

The Company follows the two-class method when computing net income (loss) per share as the Company has issued shares that meet the definition of participating securities. The two-class method determines net income (loss) per share for each class of common and participating securities according to dividends declared or accumulated and participation rights in undistributed earnings. The two-class method requires income available to common stockholders for the period to be allocated between common and participating securities based upon their respective rights to receive dividends as if all income for the period had been distributed.

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

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

Recently Adopted Accounting Pronouncements

Effective January 1, 2018, the Company adopted ASU 2016-18, "Statement of Cash Flows (Topic 230): Restricted Cash," which requires entities to show the change in the total of cash, cash equivalents, restricted cash and restricted cash equivalents within the statement of cash flows. The guidance is effective retrospectively. As a result, the Company retrospectively included restricted cash in the beginning cash for the twelve months ended December 31, 2017 on the condensed statement of cash flows, and no longer separately presents transfers between unrestricted cash and restricted cash.

Effective January 1, 2018, the Company adopted ASU No. 2016-15, Statement of Cash Flows: Classification of Certain Cash Receipts and Cash Payments ("ASU 2016-15"), which addresses diversity in practice in how certain cash receipts and cash payments are presented and classified in the statement of cash flows. The adoption of this new guidance had no impact on the Company's financial position or operating results.

Recently Issued Accounting Pronouncements

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

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, 2018 using:			
	Level 1	Level 2	Level 3	Total
Cash equivalents:				
Money market funds	$ 6,041	$ —	$ —	$ 6,041
Corporate notes	—	998	—	998
Commercial paper	—	2,495	—	2,495
Investments:				
Corporate notes	—	3,644	—	3,644
Commercial paper	—	6,416	—	6,416
	$ 6,041	$ 13,553	$ —	$ 19,594

	Fair Value Measurements as of December 31, 2017 using:			
	Level 1	Level 2	Level 3	Total
Cash equivalents:				
Money market funds	$ 10,509	$ —	$ —	$ 10,509
Investments:				
Corporate notes	—	25,710	—	25,710
Commercial paper	—	13,179	—	13,179
	$ 10,509	$ 38,889	$ —	$ 49,398

As of December 31, 2018 and 2017, the Company's cash equivalents and investments were invested in money market funds, corporate notes and commercial paper and were valued based on Level 1 and Level 2 inputs. In determining the fair value of its corporate notes and commercial paper at each date presented above, the Company relied on quoted prices for similar securities in active markets or using other inputs that are observable or can be corroborated by observable market data. The Company's cash equivalents have original maturities of less than 90 days from the date of purchase. All available-for-sale investments have contractual maturities of less than one year. During the years ended December 31, 2018 and 2017, there were no transfers between Level 1, Level 2 and Level 3.

4. Investments

As of December 31, 2018 and 2017, the fair value of available-for-sale investments by type of security was as follows:

	December 31, 2018			
	Amortized Cost	Gross Unrealized Gain	Gross Unrealized Loss	Fair Value
Investments:				
Corporate notes	$ 3,647	$ —	$ (3)	$ 3,644
Commercial paper	6,418	—	(2)	6,416
	$ 10,065	$ —	$ (5)	$ 10,060

	December 31, 2017			
	Amortized Cost	Gross Unrealized Gain	Gross Unrealized Loss	Fair Value
Investments:				
Corporate notes	$ 25,733	$ —	$ (23)	$ 25,710
Commercial paper	13,189	—	(10)	13,179
	$ 38,922	$ —	$ (33)	$ 38,889

5. Property and Equipment, Net

Property and equipment, net consisted of the following:

	December 31,	
	2018	2017
Build-to-suit asset	$ 7,080	$ —
Laboratory equipment	1,047	1,308
Computer equipment and software	184	195
Furniture and fixtures	185	71
Leasehold improvements	—	559
	8,496	2,133
Less: Accumulated depreciation and amortization	(1,206)	(1,979)
	$ 7,290	$ 154

Depreciation and amortization expense for the years ended December 31, 2018 and 2017 was $218 and $129, respectively. During the year ended December 31, 2018, fully depreciated assets with a cost of $929 were disposed of for no proceeds, resulting in neither a gain nor a loss during the year ended December 31, 2018. During the year ended December 31, 2017, fully depreciated assets with a cost of $210 were disposed of for no proceeds, resulting in neither a gain nor a loss.

6. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following:

	December 31, 2018	December 31, 2017
External research and development services	$ 1,307	$ 1,284
Payroll and payroll-related costs	1,473	1,120
Professional fees	436	536
Other	423	351
	$ 3,639	$ 3,291

7. Redeemable Convertible Preferred Stock

Prior to the closing of the Company's IPO in July 2017, the Company had shares of redeemable convertible preferred stock outstanding, including shares of Series A, Series A-1, Series B, Series C-1 and Series C-2 redeemable convertible preferred stock (collectively, the "Junior Preferred Stock") and Series D, Series D-1, Series E, Series E-1, Series E-2, Series E-3 and Series F redeemable convertible preferred stock (collectively, the "Senior Preferred Stock" and, together with the Junior Preferred Stock, the "Redeemable Preferred Stock"). The Redeemable Preferred Stock was classified outside of stockholders' equity (deficit) because the shares contain redemption features that are not solely within the control of the Company.

In February 2017, the Company issued 483,501 shares of Series F redeemable convertible preferred stock (the "Series F preferred stock") at a price of $1.36 per share, resulting in proceeds of $626, net of issuance costs of $32. Pursuant to the amended Series F preferred stock purchase agreement, holders of 4,411,765 shares of Series E-1 preferred stock that participated in the February 2017 closing elected to convert their shares of Series E-1 preferred stock into 4,411,765 shares of Series E-3 preferred stock.

The Company determined that the conversion of shares of preferred stock that occurred in February 2017 represented modifications of these securities for accounting purposes; however, the modifications did not result in the recognition of a deemed dividend for accounting purposes because the modifications did not result in a transfer of value from common stockholders to preferred stockholders.

Pursuant to the terms of the amended Series F preferred stock purchase agreement, if the second tranche closing did not occur prior to the closing of the Company's initial public offering of common stock, then, immediately prior to such closing, the purchasers of the Series F preferred stock would be required to purchase a number of shares of the Company's common stock equal to $11,516 divided by the price per share paid by the public in the initial public offering in a concurrent private offering. This requirement to purchase shares immediately prior to the closing of the Company's initial public offering could be waived in whole or in part by the Company's board of directors. On June 15, 2017, the Company's board of directors waived in whole, effective immediately prior to the closing of the Company's IPO, the requirement of the purchasers of Series F preferred stock to purchase shares of the Company's common stock in a concurrent private offering in connection with the Company's initial public offering.

Upon the closing of the Company's IPO on July 5, 2017, all shares of the Redeemable Preferred Stock converted into an aggregate of 10,509,774 shares of common stock. As of December 31, 2018 and 2017, there were no shares of Redeemable Preferred Stock authorized, issued or outstanding.

8. Preferred Stock

On July 5, 2017, in connection with the closing of the Company's IPO, the Company filed its amended and restated certificate of incorporation, which authorizes the Company to issue up to 5,000,000 shares of preferred stock, $0.001 par value per share. As of December 31, 2018 and 2017, the Company had no shares of preferred stock issued or outstanding. The preferred stock was classified under stockholders' equity as of December 31, 2018.

9. Common Stock

As of December 31, 2016, the Company's certificate of incorporation, as amended and restated, authorized the Company to issue up to 143,500,000 shares of $0.001 par value common stock. On July 5, 2017, the Company filed the amended and restated certificate of incorporation which increased the authorized number of shares of common stock to 150,000,000 shares.

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, 2018 and 2017, no dividends had been declared.

As of December 31, 2018, the Company had reserved 3,678,575 shares for the exercise of outstanding stock options and grant of future awards under the Company's stock incentive plans (see Note 10).

10. Stock-Based Awards

2017 Stock Incentive Plan

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

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

The total number of shares of common stock that may be issued under the 2017 Plan was 2,442,249 as of December 31, 2018, of which 1,000,278 shares remained available for grant. The Company initially reserved 1,244,816 shares of common stock plus the number of shares equal to the sum of the number of shares of common stock then available for issuance under the 2016 Plan, which was 424,601 shares, and the number of shares of common stock subject to outstanding awards under the 2006 Plan and the 2016 Plan that expire, terminate or are otherwise surrendered, canceled, forfeited or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right. The number of shares of common stock that may be issued under the 2017 Plan will automatically increase on January 1 of each year, beginning with the fiscal year ending December 31, 2018 and continuing for each fiscal year until, and including, the fiscal year ending December 31, 2027, equal to the least of (i) 1,244,816 shares of common stock, (ii) 4% of the outstanding shares of common stock on such date and (iii) an amount determined by the Company's board of directors. For the year ended December 31, 2018, the Company's compensation committee of the board of directors authorized an increase of 588,953 shares that may be issued under the 2017 Plan.

During the year ended December 31, 2018, pursuant to the terms of the 2017 Plan, the Company granted options to employees and directors to purchase 947,914 shares of common stock at a weighted average exercise price of $4.16 per share.

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

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

2017 Employee Stock Purchase Plan

On June 16, 2017, the Company's stockholders approved the 2017 Employee Stock Purchase Plan (the "2017 ESPP"), which became effective on June 28, 2017. As of December 31, 2018, a total of 150,000 shares of common stock are reserved for issuance under the 2017 ESPP. The number of shares of common stock that may be issued under the 2017 ESPP automatically increase on each January 1 and continuing for each fiscal year until, and including, the fiscal year ending December 31, 2027, equal to the least of (i) 622,408 shares, (ii) 1% of the outstanding shares of common stock on such date and (iii) an amount determined by the Company's board of directors. The board of directors has not initiated any offerings under the ESPP.

2016 Stock Incentive Plan

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

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

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

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

2006 Stock Incentive Plan

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

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

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

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

Stock Option Valuation

The assumptions that the Company used to determine the grant-date fair value of the stock options granted to employees and directors during the year ended December 31, 2018 and 2017 were as follows, presented on a weighted average basis:

	Year Ended December 31,	
	2018	2017
Risk-free interest rate	2.93%	2.16%
Expected term (in years)	7.3	6.1
Expected volatility	74.8%	80.4%
Expected dividend yield	0%	0%

Stock Options

The following table summarizes the Company's stock option activity since January 1, 2018:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value
Outstanding at December 31, 2017	2,096,233	$ 8.02	8.0	$ 7,332
Granted	947,914	4.16		
Exercised	(24,657)	1.70		
Canceled	(23,020)	12.09		
Forfeited	(468,173)	9.60		
Outstanding at December 31, 2018	2,528,297	$ 6.31	6.7	$ —
Options exercisable at December 31, 2018	1,214,016	$ 6.29	3.9	$ —
Options vested and expected to vest at December 31, 2018	2,485,495	$ 6.31	6.6	$ —
Options exercisable at December 31, 2017	784,190	$ 4.71	6.0	$ 4,667
Options vested and expected to vest at December 31, 2017	2,030,629	$ 7.96	7.9	$ 7,198

The weighted average grant-date fair value of stock options granted during the year ended December 31, 2018 and 2017 was $2.57 and $7.49, respectively.

The aggregate fair value of stock options that vested during the year ended December 31, 2018 and 2017 was $2,889 and $1,268, 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, 2018 and 2017 was $105 and $165, respectively.

Stock-Based Compensation

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

	Year Ended December 31, 2018	Year Ended December 31, 2017
Research and development expenses	$ 851	$ 611
General and administrative expenses	2,429	1,138
	$ 3,280	$ 1,749

The Company used an estimated forfeiture rate of 2.43% to calculate its stock compensation expense for each of the years ended December 31, 2018 and 2017.

As of December 31, 2018, the Company had an aggregate of $5,364 of unrecognized stock-based compensation expense, which it expects to recognize over a weighted average period of 2.6 years. In May 2018, the Company modified certain equity awards in connection with a separation agreement with its former Chief Executive Officer. The modification included acceleration of vesting of stock options to purchase 80,822 shares of common stock and an extension of the post-termination exercise period for vested options from 90 days to up to two years. In connection with this modification, the Company recorded an incremental compensation charge of $612 during the year ended December 31, 2018.

11. Net Loss per Share

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

	Year Ended December 31, 2018	Year Ended December 31, 2017
Numerator:		
Net loss	$ (31,547)	$ (22,604)
Accretion of redeemable convertible preferred stock to redemption value	—	(41)
Net loss attributable to common stockholders	$ (31,547)	$ (22,645)
Denominator:		
Weighted average common shares outstanding—basic and diluted	14,738,193	7,443,078
Net loss per share attributable to common stockholders—basic and diluted	$ (2.14)	$ (3.04)

The Company's potential dilutive securities, which include stock options as of December 31, 2018 and 2017, 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, 2018	Year Ended December 31, 2017
Stock options to purchase common stock	2,528,297	2,096,233
	2,528,297	2,096,233

12. Commitments and Contingencies

Operating Leases

490 Arsenal Way

On April 4, 2018, a lease agreement (the "Lease") entered into between the Company and 480 Arsenal Group LLC became effective. The Lease is for approximately 18,768 square feet of office and laboratory space in Watertown, Massachusetts. The Lease has an initial term of eight years and provides the Company with an option to extend the Lease term for one additional five-year period. The future minimum rent commitment for the initial eight-year term is approximately $8,771. In addition to rent, the Lease requires the Company to pay additional amounts for taxes, insurance, maintenance and other operating expenses.

The Company was required to provide a $568 security deposit, which the Company provided in the form of a letter of credit in the favor of the landlord which is included as non-current restricted cash on the balance sheet as of December 31, 2018.

The Company is not the legal owner of the leased space. However, in accordance with ASC 840, *Leases*, because of the Company's expected level of direct financial and operational involvement in the substantial tenant improvements required, the Company is deemed to be the owner of the leased space for accounting purposes. As a result, during the year ended December 31, 2018, the Company capitalized a build-to-suit asset of $7,080 within property, plant and equipment, net and recognized a corresponding build-to-suit facility lease obligation within other liabilities and other non-current liabilities on its balance sheet as of December 31, 2018, equal to the estimated replacement cost of its leased portion of the building at the inception of the Lease.

Additionally, construction costs incurred as part of the build-out and tenant improvements were capitalized within property, plant and equipment, net. Rental payments made under the Lease will be allocated to imputed ground rent, interest expense and the build-to-suit facility lease obligation, based on the implicit rate of the build-to-suit facility lease obligation. The build-to-suit facility lease obligation was $5,342 as of December 31, 2018.

281 Albany Street

In February 2010, the Company entered into an operating lease agreement for office and laboratory space in Cambridge, Massachusetts, which, as amended, expired in August 2018.

Upon entering into the agreement, the Company was required to maintain a security deposit which was recorded as restricted cash on the Company's balance sheet.

The agreement requires no future minimum lease payments for the year ending December 31, 2018.

The Company recognizes rent expense on a straight-line basis over the lease period and has recorded deferred rent for rent expense incurred but not yet paid. Rental expense under operating leases totaled $560 and $494 for the years ended December 31, 2018 and 2017, respectively.

Intellectual Property Licenses

Harvard and Dana-Farber Agreement

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

In February 2010, the agreement was amended and restated (the "Harvard/DFCI agreement") under which additional patent rights were added to the scope of the license agreement and the annual license maintenance fees were increased. Under the Harvard/DFCI agreement, the Company is obligated to make aggregate milestones payments of up to $7,700 per licensed therapeutic product upon the Company's achievement of specified clinical, regulatory and sales milestones with respect to such product and up to $700 per licensed diagnostic product upon the Company's achievement of specified regulatory and sales milestones with respect to such product. In addition, the Company is obligated to pay royalties of low single-digit percentages on annual net sales of licensed products sold by the Company, its affiliates or its sublicensees. The royalties are payable on a product-by-product and country-by-country basis and may be reduced in specified circumstances. In addition, the agreement obligates the Company to pay a percentage, up to the mid-twenties, of fees received by the Company in connection with its sublicense of the licensed products. In accordance with the terms of the agreement, the Company's sublicense payment obligations may be subject to specified reductions.

The Harvard/DFCI agreement requires the Company to pay annual license maintenance fees of $145 each year. Any payments made in connection with the annual license maintenance fees will be credited against any royalties due.

The Company incurred license fees of $145 during each of the years ended December 31, 2018 and 2017. In addition, the Company did not make any milestone payments during the years ended December 31, 2018 and 2017. During the years ended December 31, 2018, no milestones were achieved and no liabilities for milestone payments were recorded in the Company's financial statements. From 2010 through December 31, 2018 and December 31, 2017, the Company had made non-refundable cash payments, consisting of license and maintenance fees, milestone payments and sublicense fees, totaling $4,573 and $4,428, respectively.

As of December 31, 2018, 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, 2018 and 2017. The Company did not make any milestone payments during the years ended December 31, 2018 or 2017. During the year ended December 31, 2018, 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.

Scripps Agreement

In October 2010, the Company entered into a patent license agreement (the “Scripps agreement”) with The Scripps Research Institute (“Scripps”) under which it was granted a license, with the right to sublicense, for the exclusive worldwide rights to utilize Scripps’ “Click” chemistry for therapeutics and non-exclusive worldwide rights for diagnostics with the Company’s stabilized peptide and protein technology platforms.

Under the agreement, the Company is obligated to make aggregate milestone payments to Scripps of up to $1,900 for each licensed peptide product and up to $950 for each licensed protein product upon achieving of specified clinical, regulatory and commercial milestones. 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. The Scripps 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, 2018 and 2017.

As of December 31, 2018, no milestones had been achieved and no liabilities for milestone payments had been recorded in the Company’s financial statements. As of December 31, 2018, the Company had not developed a commercial product using the licensed technologies and no royalties under the agreement had been paid or were due.

The agreement expires upon expiration of the last of any patent rights 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, 2018 or December 31, 2017.

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,	
	2018	2017
Federal statutory income tax rate	(21.0)%	(34.0)%
State taxes, net of federal benefit	(5.5)	(4.3)
Research and development tax credits	(2.1)	(1.6)
Write-off of deferred offering costs	—	—
Other permanent items	0.9	2.1
Change in tax rate	—	69.1
Change in deferred tax asset valuation allowance	27.7	(31.3)
Effective income tax rate	—%	—%

Net deferred tax assets as of December 31, 2018 and 2017 consisted of the following:

	December 31,	
	2018	2017
Deferred tax assets:		
Net operating loss carryforwards	$ 42,773	$ 35,162
Research and development tax credit carryforwards	3,602	2,925
Capitalized research and development expenses	68	74
Accrued expenses and reserves	396	396
Depreciation and amortization	(1,398)	88
Construction financing liability	1,454	—
Stock compensation	504	—
Total deferred tax assets	47,399	38,645
Valuation allowance	(47,399)	(38,645)
Net deferred tax assets	$ —	$ —

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, 2018, the Company had net operating loss carryforwards for federal and state purposes of $157,611 and $153,078, respectively. $129,596 of the U.S. federal tax operating loss carryforwards will begin to expire in 2029. Approximately $28,016 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, 2018, the Company also had available research and development tax credit carryforwards for federal and state income tax purposes of $2,421 and $1,495, respectively, which begin to expire in 2025.

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

The Company has evaluated the positive and negative evidence bearing upon its ability to realize the deferred tax assets. Management has considered the Company's cumulative net losses and its lack of commercialization of any products or generation of any revenue from product sales since inception and has concluded that it is more likely than not that the Company will not realize the benefits of the deferred tax assets. Accordingly, a full valuation allowance has been established against the net deferred tax assets as of December 31, 2018 and 2017. Management reevaluates the positive and negative evidence at each reporting period. The increase in the valuation allowance for deferred tax assets during the year ended December 31, 2018 related primarily to the increase in net operating loss carryforwards. The decrease in the valuation allowance for deferred tax assets during the year ended December 31, 2017 related primarily to the decrease in corporate tax rate from 34% to 21% starting on January 1, 2018 as described below. Changes in the valuation allowance were as follows:

	Year Ended December 31,	
	2018	**2017**
Valuation allowance at beginning of year	$ (38,645)	$ (45,676)
Increases recorded to income tax provision	(8,754)	(8,599)
Decreases recorded as a benefit to income tax provision	—	15,630
Valuation allowance at end of year	$ (47,399)	$ (38,645)

The Company has not recorded any amounts for unrecognized tax benefits as of December 31, 2018 or 2017.

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 2015 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, 2018 and 2017, 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.

On December 22, 2017, the President of the United States signed into law the Tax Cuts and Jobs Act, or TCJA, tax reform legislation. The TCJA makes significant changes in U.S. tax law including a reduction in the corporate tax rates, changes to net operating loss carryforwards and carrybacks, and a repeal of the corporate alternative minimum tax. The TCJA reduced the U.S. corporate tax rate from the current rate of 34 percent down to 21 percent starting on January 1, 2018. As a result of the TCJA, the Company was required to revalue deferred tax assets and liabilities at 21 percent. This revaluation resulted in a provision of $15,630 to income tax expense in continuing operations and a corresponding reduction in the valuation allowance in 2017. As a result, there was no impact to the statements of comprehensive loss as a result of the reduction in tax rates. The other provisions of the TCJA did not have a material impact on the Company's financial statements. In December 2017, the SEC staff issued Staff Accounting Bulletin, or SAB, No. 118 to address the application of GAAP in situations when a registrant does not have the necessary information available, prepared, or analyzed (including computations) in reasonable detail to complete the accounting for certain income tax effects of TCJA. As of December 31, 2017, the effects of the TCJA were recorded on a provisional basis. As of December 31, 2018, the Company finalized its accounting for the TCJA and no measurement adjustments were recorded.

14. 401(k) Plan

The Company has a 401(k) plan available for participating employees who meet certain eligibility requirements. Eligible employees may defer a portion of their salary as defined by the plan. Company contributions to the plan may be made at the discretion of the Company's board of directors. The Company has not elected to make any employer contributions for the years ended December 31, 2018 or 2017.

15. Selected Quarterly Financial Data (unaudited)

The following table contains selected quarterly financial information for 2018 and 2017. The Company believes that the following information reflects all normal recurring adjustments necessary for a fair statement of the information for the periods presented. The operating results for any quarter are not necessarily indicative of results for any future period.

	Three Months Ended			
	March 31, 2018	June 30, 2018	September 30, 2018	December 31, 2018
Revenue	$ —	$ —	$ —	$ —
Operating expenses:				
Research and development	4,846	5,320	4,321	3,961
General and administrative	2,917	4,339	3,177	3,021
Total operating expenses	7,763	9,659	7,498	6,982
Loss from operations	(7,763)	(9,659)	(7,498)	(6,982)
Interest income	175	168	64	(52)
Net loss	(7,588)	(9,491)	(7,434)	(7,034)
Net loss per share—basic and diluted	$ (0.52)	$ (0.64)	$ (0.50)	$ (0.48)
Weighted average common shares outstanding—basic and diluted	14,732,287	14,737,236	14,737,402	14,745,707
Comprehensive loss:				
Net loss	$ (7,588)	$ (9,491)	$ (7,434)	$ (7,034)
Other comprehensive gain (loss):				
Unrealized gain (loss) on investments, net of tax of $0	(17)	38	9	(2)
Total other comprehensive gain (loss)	(17)	38	9	(2)
Total comprehensive loss	$ (7,605)	$ (9,453)	$ (7,425)	$ (7,036)

	Three Months Ended			
	March 31, 2017	June 30, 2017	September 30, 2017	December 31, 2017
Revenue	$ —	$ —	$ —	$ —
Operating expenses:				
Research and development	2,942	3,161	3,825	4,311
General and administrative	1,647	1,791	2,601	2,730
Total operating expenses	4,589	4,952	6,426	7,041
Loss from operations	(4,589)	(4,952)	(6,426)	(7,041)
Interest income	32	29	167	176
Net loss	(4,557)	(4,923)	(6,259)	(6,865)
Accretion of redeemable convertible preferred stock to redemption value	(20)	(21)	—	—
Net loss	$ (4,577)	$ (4,944)	$ (6,259)	$ (6,865)
Net loss per share attributable to common stockholders—basic and diluted	$ (10.58)	$ (10.98)	$ (0.45)	$ (0.47)
Weighted average common shares outstanding—basic and diluted	432,728	450,495	13,939,950	14,720,734
Comprehensive loss:				
Net loss	$ (4,557)	$ (4,923)	$ (6,259)	$ (6,865)
Other comprehensive loss:				
Unrealized loss on investments, net of tax of $0	—	—	(6)	(27)
Total other comprehensive loss	—	—	(6)	(27)
Total comprehensive loss	$ (4,557)	$ (4,923)	$ (6,265)	$ (6,892)

16. Subsequent Event (unaudited)

On March 28, 2019, the Company entered into a securities purchase agreement with certain accredited investors pursuant to which the Company agreed to issue and sell an aggregate of (i) 11,838,582 units, consisting of 11,838,582 shares of common stock, and associated warrants to purchase an aggregate of 11,838,582 shares of common stock and (ii) 1,096,741 units, consisting of 1,096,741 pre-funded warrants to purchase 1,096,741 shares of common stock and associated warrants to purchase an aggregate of 1,096,741 shares of common stock in a private placement. The private placement is expected to close on April 2, 2019, subject to the satisfaction of customary closing conditions. The Company expects to receive aggregate gross proceeds of approximately $26,000 before deducting placement agent fees and offering expenses.

Exhibit 10.19

SEVERANCE AGREEMENT

This SEVERANCE AGREEMENT (this "Agreement") is made and entered into as of October 1, 2018 by and between Donald Dougherty ("Executive") and Aileron Therapeutics, Inc. (the "Company").

WHEREAS, Executive is employed as a senior executive of the Company, and the Company desires to continue to retain the services of Executive; and

WHEREAS, the Company is entering into this Agreement in order to provide certain compensation and benefits to Executive in the event Executive's employment with the Company is terminated under certain circumstances.

NOW, THEREFORE, for good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the Company and Executive agree as follows:

1. Definitions.

1.1 "Affiliated Entity" means any corporation, partnership, trust or other entity of which the Company and/or any of its Affiliated Entities directly or indirectly owns a majority of the outstanding shares of any class of equity security thereof and any corporation, partnership, trust or other entity which directly or indirectly owns a majority of the outstanding shares of any class of any equity security of the Company or any of its Affiliated Entities.

1.2 "Cause" shall mean a finding by the Board that Executive: (i) materially breached Executive's Confidentiality, Inventions, Non-Competition and Non-Solicitation Agreement or any similar agreement between Executive and the Company (a "Confidentiality Agreement"); (ii) engaged in fraud, or embezzlement; (iii) engaged in willful misconduct or gross negligence with regard to the Company that the Board determines in good faith is, or is reasonably likely to be, materially injurious to the Company and its reputation; (iv) materially violated the Company's published policies, including those prohibiting unlawful harassment and discrimination, as in effect from time to time; or (v) was convicted of, or pleaded guilty or nolo contendere to any felony (other than traffic-related offenses).

1.3 "Change in Control Event" means

1.3.1 the acquisition by an individual, entity or group (within the meaning of Section 13(d)(3) or 14(d)(2) of the Securities Exchange Act of 1934, as amended) (a "Person") of beneficial ownership of any capital stock of the Company if, after such acquisition, such Person beneficially owns (within the meaning of Rule 13d-3 under the Securities Exchange Act of 1934, as amended) 50% or more of either (x) the then-outstanding shares of common stock of the Company (the "Outstanding Company Common Stock") or (y) the combined voting power of the then-outstanding securities of the Company entitled to vote generally in the election of directors (the "Outstanding Company Voting Securities"); provided, however, that for purposes of this Subsection 1.3.1, the following acquisitions shall not constitute a Change in Control Event: (A) any acquisition directly from the Company or (B) any acquisition by any corporation pursuant to a Business Combination (as defined below) which complies with clauses (x) and (y) of Subsection 1.3.2 of this definition;

1.3.2 the consummation of a merger, consolidation, reorganization, recapitalization or share exchange involving the Company or a sale or other disposition of all or substantially all of the assets of the Company (a "Business Combination"), unless, immediately following such Business Combination, each of the following two conditions is satisfied: (x) the Outstanding Company Common Stock and Outstanding Company Voting Securities immediately prior to such Business Combination represent more than 50% of the then-outstanding shares of common stock or other common equity and the combined voting power of the then-outstanding securities entitled to vote generally in the election of directors or other governing body, respectively, of the resulting or acquiring entity in such Business Combination (which shall include, without limitation, an entity which as a result of such transaction owns the Company or substantially all of the Company's assets either directly or through one or more subsidiaries) (such resulting or acquiring corporation is referred to herein as the "Acquiring Entity") and (y) no Person (excluding any employee benefit plan (or related trust) maintained or sponsored by the Company or by the Acquiring Entity) beneficially owns, directly or indirectly, 50% or more of the then-outstanding shares of common stock of the Acquiring Entity, or of the combined voting power of the then-outstanding securities of such entity entitled to vote generally in the election of directors or other governing body (except to the extent that such ownership existed prior to the Business Combination); or

1.3.3 the liquidation or dissolution of the Company;

provided that such Change in Control Event also satisfies Treasury Regulation Section 1.409A-3(i)(5) where required for compliance with Section 409A of the Internal Revenue Code and the guidance issued thereunder ("Section 409A").

1.4 "Date of Termination" means: (i) if Executive's employment ends other than for death, Executive's last day of employment with the Company and, (ii) if Executive's employment is terminated by reason of death, the date of Executive's death.

1.5 "Disability" shall mean any long-term disability or incapacity due to physical or mental illness that renders Executive unable to substantially perform his duties for at least ninety (90) consecutive days or one hundred twenty (120) total days during any twelve (12) month period, provided that it may occur in a shorter period if, after its commencement, it is determined to be total and permanent by a physician selected by the Company and its insurers and such determination is acceptable to Executive or to Executive's legal representative (with such agreement on acceptability not to be unreasonably withheld).

1.6 "Good Reason" means (i) a material diminution in the nature or scope of Executive's duties, responsibilities, or authority; (ii) a material reduction in Executive's base salary then in effect; (iii) a material reduction by the Company in the kind or level of employee benefits to which Executive is entitled immediately prior to such reduction with the result that the overall benefits package is materially reduced, other than a reduction comparable to reductions generally applicable to similarly situated employees of the Company; or (iv) the Company's requiring Executive's ongoing and regular services to be performed at a location more than fifty (50) miles from the geographic location at which Executive was providing services before such requirement. In order to terminate Executive's employment for Good Reason, Executive must (w) give notice to the Company of Executive's intention to resign for Good Reason within ninety (90) days after the occurrence of the event (or series of events) that Executive asserts entitles Executive to resign for Good Reason, (x) state in that notice the event that Executive considers to provide Executive with Good Reason to resign, (y) provide the Company with at least thirty (30) days after Executive's notice to cure the event, and (z) if the event is not cured within such thirty-day cure period, resign for Good Reason within thirty (30) days after the end of the thirty-day cure period.

2. Obligations of the Company upon Termination.

2.1 Termination for Any Reason or No Reason. In the event of the termination of Executive's employment for any reason or for no reason, the Company will pay to Executive (or to his estate) (i) the portion of his annualized base salary that has accrued prior to such termination and has not yet been paid and, to the extent consistent with general Company policy, accrued but unused paid time off through and including the Date of Termination, (ii) any bonus amount not yet paid that was earned by and approved for payment to Executive by the Board during or with respect to the calendar year preceding the Date of Termination; (iii) reimbursement for expenses properly incurred by Executive on behalf of the Company prior to such termination and properly documented in accordance with Company policy, and (iv) to the extent not theretofore paid or provided, any other amounts or benefits required to be paid or provided or which Executive is eligible to receive under any plan or agreement of or with the Company through the Date of Termination (all such amounts, collectively, the "Accrued Obligations"). The Accrued Obligations will be paid as required by law but in any event promptly after termination or as provided by any applicable policy, plan or agreement.

2.2 Termination by the Company Other Than for Cause or by Reason of Executive's Death or Disability; By Executive for Good Reason; and Other than Upon or within Twelve Months following a Change in Control Event. Subject to the satisfaction of the Severance Conditions (as defined below), if Executive's employment is terminated (i) by the Company other than (x) for Cause or (y) by reason of Executive's death or Disability, or (ii) by Executive for Good Reason, and, in each case, other than upon or within twelve (12) months following a Change in Control Event (the "CIC Period"), then in addition to the Accrued Obligations, the Company shall:

2.2.1 Pay to Executive a sum equal to nine (9) months of base salary at Executive's most recent base salary rate, such payment to be made in approximately equal installments according to the Company's then-current payroll practices.

2.2.2 Provided that Executive is eligible for and elects to continue receiving medical insurance pursuant to the federal "COBRA" law, 29 U.S.C. § 1161 et seq., continue to pay on Executive's behalf the share of the monthly premiums for such coverage that it pays for active and similarly situated employees receiving the same type of coverage for a period of up to nine (9) months following the Date of Termination. The remaining balance of the premium costs and all premium costs after such nine (9) month period shall be paid by Executive on a monthly basis for as long as, and to the extent that, he remains eligible for and elects to continue receiving continued coverage under COBRA; provided, however, that notwithstanding the foregoing, in the event Executive becomes eligible during the nine (9) month period for the same or substantially similar group health insurance coverage through another employer, Executive shall immediately notify the Company in writing of the date of eligibility for such coverage (the "Eligibility Date"), and the Company's obligation to make monthly premium payments pursuant to this Subsection 2.2.2 shall end on the Eligibility Date. Notwithstanding the foregoing, payments by the Company under this Subsection 2.2.2 (but not eligibility for COBRA) shall end early if the Company determines that the continued payments are reasonably likely to result in penalties on the Company, taxation of any other employee, or taxation of Executive on income other than the payment of the premiums; provided, however, that if the Company is able to reasonably conclude that making a taxable lump sum payment to Executive in the amount of and in lieu of any remaining COBRA premiums that would otherwise be paid by the Company on Executive's behalf under this Subsection 2.2.2 would not result in any such penalties or taxation, the Company will make such lump sum payment no later than the last day of the nine (9) month period following the Date of Termination.

2.3 Termination By the Company for Cause; By Reason of Executive's Death or Disability; Or By Executive Other than for Good Reason. If Executive's employment is terminated by the Company for Cause, or by reason of Executive's death or Disability, or by Executive for any reason other than for Good Reason, this Agreement shall terminate without further obligations to Executive or Executive's legal representatives under this Agreement, other than for payment of the Accrued Obligations.

2.4 Effect of Termination on Other Positions. If, on the Date of Termination, Executive is a member of the Company's Board of Directors (the "Board") or the board of directors of any Affiliated Entity, or holds any other office or position with the Company or any Affiliated Entity, Executive shall, unless otherwise requested by the Company, be deemed to have resigned from all such offices and positions as of the Date of Termination. Executive agrees to execute such documents and take such other actions as the Company may request to reflect such resignation.

2.5 Conditions to Payment of Post-Separation Benefits. As a condition of Executive's receipt of the post-separation benefits in Section 2.2 and Section 3.1, Executive must execute and return to the Company a severance and release of claims agreement provided by and satisfactory to the Company (the "Release Agreement"), and such Release Agreement must become binding, enforceable and irrevocable within sixty (60) calendar days after Executive's termination of employment (the "Severance Conditions"). Payments will begin in the first pay period beginning after the Severance Conditions have been satisfied or as promptly as practicable thereafter, provided that if the foregoing sixty (60) day period would end in a calendar year subsequent to the year in which Executive's employment ends, payments will not be made before the first payroll period of the subsequent year (the "Payment Date"). Notwithstanding the foregoing, the acceleration of vesting of the Equity Awards contemplated by Subsection 3.1.4 below shall take immediate effect upon the Date of Termination; provided, however, that Executive agrees that the portion of such Equity Awards that shall have been accelerated pursuant to Subsection 3.1.4 (the "Accelerated Portion") shall not be exercised prior to the date on which the Severance Conditions have been satisfied, that any shares to be issued or retained under other Equity Awards will not be issued or retained prior to the date on which the Severance Conditions have been satisfied and that if the Severance Conditions have not been satisfied within the prescribed time period, than, as of such date, the Accelerated Portion shall be cancelled and cease to be exercisable, forfeited, or not issued, as applicable on the basis of the type of Equity Award.

3. Change in Control.

3.1 Subject to the satisfaction of the Severance Conditions, if, during the CIC Period, Executive's employment is terminated by the Company without Cause and not for death or Disability, or if Executive resigns his employment for Good Reason, then, in addition to the Accrued Obligations, the Company shall:

3.1.1 Pay to Executive a sum equal to twelve (12) months of base salary at Executive's most recent base salary rate, such payment to be made in approximately equal installments according to the Company's then-current payroll practices.

3.1.2 Provided that Executive is eligible for and elects to continue receiving medical insurance under COBRA, continue to pay on Executive's behalf the share of the monthly premiums for such coverage that it pays for active and similarly situated employees receiving the same type of coverage for a period of up to twelve (12) months following the Date of Termination. The remaining balance of the premium costs and all premium costs after such twelve (12) month period shall be paid by Executive on a monthly basis for as long as, and to the extent that, he remains eligible for and elects to continue receiving continued coverage under COBRA; provided, however, that notwithstanding the foregoing, in the event Executive becomes eligible during the twelve (12) month period for the same or substantially similar group health insurance coverage through another employer, Executive shall immediately notify the Company in writing of the Eligibility Date, and the Company's obligation to make monthly premium payments pursuant to this Subsection 3.1.2 shall end on the Eligibility Date. Notwithstanding the foregoing, payments by the Company under this Subsection 3.1.2 (but not eligibility for COBRA) shall end early if the Company determines that the continued payments are reasonably likely to result in penalties on the Company, taxation of any other employee, or taxation of Executive on income other than the payment of the premiums; provided, however that if the Company is able to reasonably conclude that making a taxable lump sum payment to Executive in the amount of and in lieu of any remaining COBRA premiums that would otherwise be paid by the Company on Executive's behalf under this Subsection 3.1.2 would not result in any such penalties or taxation, the Company will make such lump sum payment no later than the last day of the twelve (12) month period following the Date of Termination.

3.1.3 Pay to Executive, on the Payment Date, a lump sum equal to one times (1 x) Executive's target bonus award for the year in which the Date of Termination occurs without regard to whether the performance goals applicable to such target bonus had been established or satisfied at the Date of Termination.

3.1.4 Notwithstanding the terms of any stock option agreement, restricted stock agreement or other stock award ("Equity Award"), other than terms more favorable to Executive, effective as of the Termination Date, accelerate the vesting of all Equity Awards held by Executive at the Termination Date (other than Equity Awards that vest on the basis of performance and do not provide solely for time-based vesting), such that such Equity Awards shall become 100% vested.

3.2 280G. Notwithstanding any other provision of this Agreement to the contrary, if payments made hereunder or otherwise are considered "excess parachute payments" under Section 280G of the Internal Revenue Code of 1986, as amended (the "Code"), then such excess parachute payments plus any other payments made by the Company and its affiliates that Executive is entitled to receive that are considered excess parachute payments shall be limited to the greatest amount that may be paid to Executive under Section 280G of the Code without causing any loss of deduction to the Company under such Code Section, but only if, by reason of such reduction, the "Net After Tax Benefit" (as defined below) to Executive exceeds the net after tax benefit if such reduction was not made. "Net After Tax Benefit" for purposes of this Agreement shall mean the sum of (i) the total amounts payable to Executive that would constitute an "excess parachute payment" within the meaning of Section 280G of the Code, less (ii) the amount of federal, state and other income taxes payable with respect to the foregoing calculated at the maximum marginal tax rate for each year in which the foregoing shall be paid to Executive (based upon the rate in effect for such year as set forth in the Code at the time of termination of Executive's employment or the change in control), less (iii) the amount of excise taxes imposed with respect to the payments and benefits described above by Section 4999 of the Code. The determination of whether payments would be considered excess parachute payments and the calculation of all the amounts referred to in this section shall be made reasonably and in good faith by the parties, *provided*, that if the parties cannot agree, then such determination (and supporting calculations) shall be made by attorneys, accountants, or an executive compensation consulting firm each as selected by the Company at the expense of the Company (the "280G Service Providers"). Any determination by the 280G Service Providers made in good faith shall be binding upon the Company and Executive.

4. No Mitigation. In no event, except as set forth expressly in this or another agreement signed by Executive, shall Executive be obligated to seek other employment or take any other action by way of mitigation of the amounts payable to Executive under any of the provisions of this Agreement and, subject to the aforesaid exception, such amounts shall not be reduced whether or not Executive obtains other employment.

5. Restrictive Covenants. As a condition of the effectiveness of this Agreement, Executive shall have previously, or contemporaneously with the execution of this Agreement, executed and delivered to the Company a Confidentiality Agreement in form and substance reasonably acceptable to the Company and Executive.

6. Payments Subject to Section 409A. Subject to the provisions in this Section 6, any severance payments or benefits under this Agreement shall begin only upon the date of Executive's "separation from service" (determined as set forth below) which occurs on or after the date of termination of employment. The following rules shall apply with respect to distribution of the payments and benefits, if any, to be provided to Executive under this Agreement:

6.1 It is intended that each installment of the severance payments and benefits provided under this Agreement shall be treated as a separate "payment" for purposes of Section 409A. Neither Executive nor the Company shall have the right to accelerate or defer the delivery of any such payments or benefits except to the extent specifically permitted or required by Section 409A.

6.2 If, as of the date of Executive's "separation from service" from the Company, Executive is not a "specified employee" (within the meaning of Section 409A), then each installment of the severance payments and benefits shall be made on the dates and terms set forth in this Agreement

6.3 If, as of the date of Executive's "separation from service" from the Company, Executive is a "specified employee" (within the meaning of Section 409A), then:

6.3.1 Each installment of the severance payments and benefits due under this Agreement that, in accordance with the dates and terms set forth herein, will in all circumstances, regardless of when the separation from service occurs, be paid within the short-term deferral period (as defined under Section 409A) shall be treated as a short-term deferral within the meaning of Treasury Regulation Section 1.409A-1(b)(4) to the maximum extent permissible under Section 409A and shall be paid at the time and in the matter set forth in this Agreement; and

6.3.2 Each installment of the severance payments and benefits due under this Agreement that is not described in Subsection 6.3.1 above and that would, absent this subsection, be paid within the six-month period following Executive's "separation from service" from the Company shall not be paid until the date that is six months and one day after such separation from service (or, if earlier, Executive's death), with any such installments that are required to be delayed being accumulated during the six-month period and paid in a lump sum on the date that is six months and one day following Executive's separation from service and any subsequent installments, if any, being paid in accordance with the dates and terms set forth herein; provided, however, that the preceding provisions of this sentence shall not apply to any installment of severance payments and benefits if and to the maximum extent that such installment is deemed to be paid under a separation pay plan that does not provide for a deferral of compensation by reason of the application of Treasury Regulation 1.409A-1(b)(9)(iii) (relating to separation pay upon an involuntary separation from service). Any installments that qualify for the exception under Treasury Regulation Section 1.409A-1(b)(9)(iii) must be paid no later than the last day of Executive's second taxable year following the taxable year in which the separation from service occurs.

6.4 The determination of whether and when Executive's separation from service from the Company has occurred shall be made in a manner consistent with, and based on the presumptions set forth in, Treasury Regulation Section 1.409A-1(h). Solely for purposes of this Section 6.4, "Company" shall include all persons with whom the Company would be considered a single employer as determined under Treasury Regulation Section 1.409A-(h)(3).

6.5 All reimbursements and in-kind benefits provided under this Agreement shall be made or provided in accordance with the requirements of Section 409A to the extent that such reimbursements or in-kind benefits are subject to Section 409A, including, where applicable, the requirement that (i) any reimbursement is for expenses incurred during Executive's lifetime (or during a shorter period of time specified in this Agreement), (ii) the amount of expenses eligible for reimbursement during a calendar year may not affect the expenses eligible for reimbursement in any other calendar year, (iii) the reimbursement of an eligible expense will be made on or before the last day of the calendar year following the year in which the expense is incurred, and (iv) the right to reimbursement is not subject to set off or liquidation or exchange for any other benefit.

7. Return of Company Property. Upon termination of employment for any reason, Executive shall promptly return to the Company any keys, credit cards, passes, confidential documents or material, computer equipment, or other property belonging to the Company, and Executive shall also return all writings, files, records, correspondence, notebooks, notes and other documents and things (including any copies thereof) containing confidential information or relating to the business or proposed business of the Company or the Affiliated Entities or containing any trade secrets relating to the Company or the Affiliated Entities. For purposes of the preceding sentence, the term "trade secrets" shall have the meaning ascribed to it under the Uniform Trade Secrets Act. Executive agrees to represent in writing to the Company upon termination of employment that he has complied with the foregoing provisions of this Section.

8. Assistance with Claims. Executive agrees that, consistent with Executive's business and personal affairs, during and after his employment by the Company he will assist the Company and the Affiliated Entities in the defense of any claims, or potential claims that may be made or are threatened to be made against any of them in any action, suit or proceeding, whether civil, criminal, administrative or investigative (a "Proceeding"), and will assist the Company and the Affiliated Entities in the prosecution of any claims that may be made by the Company or the Affiliated Entities in any Proceeding, to the extent that such claims may relate to Executive's employment or the period of Executive's employment by the Company. The Company agrees to (i) reimburse Executive for all of Executive's reasonable out-of-pocket expenses associated with such assistance, including travel expenses and (ii) with respect to assistance provided after Executive's employment, compensate Executive on an hourly basis, based on a rate commensurate with Executive's base salary (assuming a forty (40) hour work week) in effect on the Date of Termination, for time Executive spends in excess of ten (10) hours in any calendar quarter providing such assistance to the Company, provided that such time shall not include any time spent testifying in any arbitration, trial, administrative hearing or other proceeding. Any amounts to be paid to Executive pursuant to this Section 8 shall be paid by the Company no later than thirty (30) days of the date on which Executive provides documentation to the Company that such expenses were incurred.

9. Successors. This Agreement is personal to Executive and shall not be assignable by Executive without the prior written consent of the Company. This Agreement and any rights and benefits hereunder shall inure to the benefit of and be enforceable by Executive's legal representatives, heirs or legatees. This Agreement and any rights and benefits hereunder shall inure to the benefit of and be binding upon the Company and its successors and assigns, including any corporation with which or into which the Company may be merged or which may succeed to its assets or business.

10. Miscellaneous.

10.1 Entire Agreement/Modification/Choice of Law/Enforceability/Jury Waiver. Both Executive and the Company acknowledge that this Agreement is the entire agreement of the parties, and supersedes any prior or contemporaneous discussions, understandings, or agreements, with respect to the subject matter hereof. For the avoidance of doubt and without limiting the foregoing, (a) Executive shall not be eligible to receive severance or similar post-employment payments or benefits under any severance plan, program or policy now or hereafter maintained by the Company, and (b) any employment offer letter or employment agreement between Executive and the Company (such offer letter or employment agreement, the "Employment Agreement") shall survive the execution and delivery of this Agreement and remain in full force and effect in accordance with its original terms; provided, however, that any provisions of the Employment Agreement relating to severance and post-employment payments and benefits shall be superseded hereby in their entirety and shall hereafter cease to be of any force or effect. This Agreement may be amended only in a written agreement duly executed by the parties hereto. This Agreement shall be deemed to have been made in the Commonwealth of Massachusetts and shall be governed by and construed in accordance with the laws of such Commonwealth, without giving effect to conflict of law principles. Both parties agree that any action, demand, claim or counterclaim relating to the terms and provisions of this Agreement, or to its formation or breach, or to Executive's employment or the termination thereof, shall be commenced only in Massachusetts in a court of competent jurisdiction, and further acknowledge that venue for such actions shall lie exclusively in Massachusetts. Both parties hereby waive and renounce in advance any right to a trial by jury in connection with such legal action.

10.2 Withholding. The Company may withhold from any amounts payable under this Agreement such Federal, state, local or foreign taxes as shall be required to be withheld pursuant to any applicable law or regulation.

10.3 No Guarantee of any Tax Consequences. The Company makes no guarantee of any tax consequences with respect to any payment hereunder including, without limitation, under Section 409A.

10.4 Severability. The invalidity or unenforceability of any provision of this Agreement will not affect the validity or enforceability of any other provision of this Agreement, and this Agreement will be construed as if such invalid or unenforceable provision were omitted (but only to the extent that such provision cannot be appropriately reformed or modified).

10.5 Waiver of Breach. No waiver by any party hereto of a breach of any provision of this Agreement by any other party, or of compliance with any condition or provision of this Agreement to be performed by such other party, will operate or be construed as a waiver of any subsequent breach by such other party of any similar or dissimilar provisions and conditions at the same or any prior or subsequent time.

10.6 Notices. Notices and all other communications provided for in this Agreement shall be in writing and shall be delivered personally or sent by registered or certified mail, return receipt requested, postage prepaid, or prepaid overnight courier to the parties at the addresses set forth below (or such other addresses as shall be specified by the parties by like notice):

to the Company:

Aileron Therapeutics, Inc.
490 Arsenal Way
Watertown, MA 02472
Attention: Chief Executive Officer

with a copy to:

Wilmer Cutler Pickering Hale and Dorr, LP
60 State Street
Boston, MA 02109
Attention: Stuart Falber

or to Executive:

At the most recent address maintained
by the Company in its personnel records

10.7 Each party, by written notice furnished to the other party, may modify the applicable delivery address, except that notice of change of address shall be effective only upon receipt. Such notices, demands, claims and other communications shall be deemed given in the case of delivery by overnight service with guaranteed next day delivery, the next day or the day designated for delivery; or in the case of certified or registered U.S. mail, five days after deposit in the U.S. mail; provided, however, that in no event shall any such communications be deemed to be given later than the date they are actually received.

10.8 Not Employment Contract. Executive acknowledges that this Agreement does not constitute a contract of employment, does not imply that the Company will continue his employment for any period of time and does not change the at-will nature of his employment.

10.9 Survivorship. Upon the expiration or other termination of this Agreement, the respective rights and obligations of the parties hereto shall survive such expiration or other termination to the extent necessary to carry out the intentions of the parties under this Agreement.

10.10 Counterparts. This Agreement may be executed in separate facsimile or electronic counterparts, each of which is deemed to be an original and all of which taken together constitute one and the same agreement.

10.11 Representations. Executive hereby acknowledges that he understands this Agreement and enters into this Agreement voluntarily.

IN WITNESS THEREOF, Executive has hereunto set his hand, and the Company has caused this Agreement to be executed in its name and on its behalf, all as of the day and year first above written.

AILERON THERAPEUTICS, INC.	DONALD DOUGHERTY
/s/ Manuel Aivado	/s/ Donald Dougherty
Name: Manuel Aivado Title: President and CEO	

November 1, 2018

Vojislav Vukovic, MD, PhD
23 David Drive
Newtown, PA 18940

Dear Vojo**:**

It is my great pleasure to extend to you this offer of employment with Aileron Therapeutics, Inc. (the "Company"). The purpose of this letter is to summarize the terms of your employment with the Company, should you accept our offer:

1. **Employment.** You will be employed to serve on a full-time basis as Senior Vice President, Chief Medical Officer, responsible for leading the clinical development function at the Company and reporting to the Company's chief executive officer, effective November 5, 2018 (the "Effective Date"). You agree to devote your best efforts, skill, knowledge, attention and energies to the advancement of the Company's business and interests and to the performance of your duties and responsibilities as an employee of the Company. Notwithstanding the foregoing, you will be entitled to participate on scientific advisory boards and boards of directors for other companies, provided that such activities do not present a conflict of interest with your duties and responsibilities as an employee of the Company and the Company's chief executive officer consents to such activities.

2. **Base Salary and Bonus.** Your base salary will be at the rate of $16,875.00 per semi-monthly pay period (equivalent to $405,000 annualized) less all applicable taxes and withholdings, to be paid in installments in accordance with the Company's regular payroll practices. Your base salary may be adjusted in the sole discretion of the Company from time to time in accordance with normal business practices. Following the end of each calendar year in which you are employed by the Company, you may be eligible for a discretionary performance bonus of up to 35% of your then current annualized base salary, as may be determined by the Company's Board of Directors ("Board") in its sole discretion. Any such bonus shall be based on the achievement of performance milestones for that calendar year as may be determined by the Board in its sole discretion. Any such discretionary bonus shall be paid to you in the subsequent calendar year in accordance with the Company's customary practices. You must be an active employee of the Company on the date the bonus is distributed in order to be eligible for and to earn any bonus award, as it also serves as an incentive to remain employed by the Company. You will be eligible for this annual bonus award beginning with 2018 calendar year performance and your 2018 bonus will be pro-rated. All compensation payable to you will be subject to applicable taxes and withholdings.

3. **<u>Equity</u>.** Subject to approval by the Board, you will receive options to purchase up to 150,000 shares of the Company's Common Stock under the Company's 2017 Stock Incentive Plan (the "Plan") for a price per share equal to the fair market value of one share of the Common Stock on the date of the option grant as determined by the Board and pursuant and subject to the terms of the Company's option agreement (which must be executed to receive the grant) and the Plan. The stock options will vest (become exercisable) as follows: 25% of the shares underlying the options shall vest upon the twelve (12) month anniversary of the Effective Date and 1/36th of the remainder of such shares will vest on a monthly basis in thirty-six (36) equal monthly installments with the first such installment vesting on the thirteenth month anniversary of the Effective Date, subject to your continued employment with the Company through each vesting date. You may also be eligible for other grants of stock or stock options as determined by and in the sole discretion of the Board. Any grant of options is subject to all of the terms and conditions of the relevant stock plan and option agreement.

4. **<u>Location and Relocation Expenses</u>.**

(a) From the Effective Date until the earliest of (i) the six-month anniversary of the Effective Date, (ii) the Company's completion of a fundraising transaction which the Company believes will enable it to fund its operations into at least May 2020 and (iii) your relocation to Massachusetts (the "Initial Employment Period"), you will be required to work a minimum of four business days per week in the Company's headquarters. During the Initial Employment Period, upon presentation of appropriate documentation, you will be reimbursed up to a total of $22,500 for expenses to be applied to travel and living accommodations reasonably incurred by you in order for you while working at the Company's headquarters. Your schedule will be agreed upon between you and the chief executive officer. In addition to managing the Company's clinical activities, it is expected that you will play a leadership role in the Company. As such, it is understood that working in the Company's headquarters for a minimum of four business days and interacting with employees is a necessary component of your employment. When you are working outside of the Company's headquarters, you will be available for calls and to participate in meetings telephonically during regular business hours and as required by business needs. It is further understood that the needs of the Company may from time-to-time require you to spend more than four business days in the Company's headquarters during the Initial Employment Period, and by accepting this offer of employment you hereby agree to do so as reasonably required in consultation with the chief executive officer and to travel as required by the Company's business needs.

(b) You will be required to relocate and work full time from the Company's headquarters prior to the date that is six months following the end of the Initial Employment Period. Upon presentation of appropriate documentation, you will be reimbursed up to a total of $50,000 for expenses reasonably incurred by you in connection with your relocation. Notwithstanding the foregoing, you agree that if, prior to the second anniversary of your relocation, you terminate your employment with the Company other than for Good Reason or the Company terminates your employment for Cause (as such terms are defined in the Severance Agreement (as defined below)), you shall pay to the Company within 15 days of such termination an amount determined by multiplying $50,000 by a fraction, the numerator of which equals the number of days in such two-year period that you are not an employee of the Company and the denominator of which equals the total number of days in such two-year period.

5. **Benefit Programs**. You may choose to participate in any and all benefit programs that the Company establishes and makes available to its employees from time to time, provided you are eligible under (and subject to all provisions of) the plan documents governing those programs. This presently includes (among other benefits) health and dental insurance, paid holidays, and a 401(k) savings program. Our benefits also include four (4) weeks of paid vacation per calendar year to be taken at such times as may be approved in advance by the Company, which approval will not be unreasonably withheld. The number of vacation days for which you are eligible shall accrue at the rate of 1.67 days per month that you are employed during such calendar year. You will also be entitled to sick leave and all Company holidays as determined by the Company, on the same terms as similarly situated senior executives. Where a particular benefit is subject to a formal plan, eligibility to participate in and receive any particular benefit is governed solely by the applicable plan document. Benefits are subject to change at any time in the Company's sole discretion.

6. **Business Expenses.** The Company will reimburse you for all documented, reasonable and necessary business expenses in accordance with the Company's expense reimbursement policy.

7. **Termination Benefits**. Concurrently with the execution of this Agreement, the Company and you shall sign the Severance Agreement attached hereto as Exhibit A (the "Severance Agreement").

8. **Indemnification and Insurance.** In connection with your employment with the Company, you will be entitled to indemnification to the fullest extent permitted by the Company's By-Laws and will be entitled to coverage under the Company's directors' and officers' liability insurance policy to the same extent as other senior executives of the Company.

9. **Confidentiality, Inventions and Non-Solicitation Agreement.** In order to protect the Company's substantial investment of time and money in the creation and maintaining of its Confidential Information and good-will, employees are required as a condition of employment, and continued employment, to execute the Proprietary Rights, Non-Disclosure, and Non-Solicitation Agreement (the "NSA") between you and the Company . The terms and conditions of the NSA will apply, regardless of any change in the nature of your duties, compensation or employment with any entity related to the Company.

   Just as the Company regards the protection of our confidential information as a matter of great importance, we also respect that you may have an obligation to your prior employers to safeguard the confidential information of those companies. The Company respects these obligations, and expects you to honor them as well. To that end, you hereby represent that you have disclosed and provided copies of any agreement that you have with a prior employer that relates to any obligations of the type and nature reflected in our NSA. We also expect that you have not taken any documents or other confidential information from your employer, and that you will make certain that you do not maintain any information that you may have received electronically. Further, we want to make it perfectly clear that you should not bring with you to the Company, or use in the performance of your responsibilities for the Company, any proprietary business or technical information, materials or documents of a former employer, or otherwise disclose or use any former employer's confidential information.

10. **<u>Company Policies and Procedures.</u>** As an employee of the Company, you will be required to comply with all Company policies and procedures, as in effect from time to time. Violations of the Company's policies may lead to immediate termination of your employment. Further, the Company's premises, including all workspaces, furniture, documents and other tangible materials, and all information technology resources of the Company (including computers, data and other electronic files, and all Internet and e-mail usage) are subject to oversight and inspection by the Company at any time. Company employees should have no expectation of privacy with regard to any Company premises, materials, resources or information, including any personal emails or other communications that are delivered into or out of a Company system.

11. **<u>Proof of Legal Right to Work.</u>** For purposes of federal immigration law, you will be required to provide the Company with documentary evidence of your identity and eligibility for employment in the United States. Such documentation must be provided to the Company within three (3) business days of your date of hire, or our employment relationship with you may be terminated. You may need to obtain a work visa in order to be eligible to work in the United States. If that is the case, your employment with the Company will be conditioned upon your obtaining a work visa in a timely manner as determined by the Company.

12. **<u>Nature of the Relationship</u>.** While we obviously are hopeful and confident that our relationship will be mutually rewarding, satisfactory and sustaining, this letter shall not be construed as an agreement, either express or implied, to employ you for any stated term, and shall in no way alter the Company's policy of employment at will, under which both you and the Company remain free to end the employment relationship. Similarly, nothing in this letter shall be construed as an agreement, either express or implied, to pay you any compensation of any kind, or grant you any benefit beyond the end of your employment with the Company. Also, this letter and the exhibits attached to this letter constitutes our entire offer regarding the terms and conditions of your employment by the Company, it supersedes any prior agreements, or other promises or statements (whether oral or written) regarding the offered terms of employment. Your employment with the Company shall be governed by and construed under the internal laws of the Commonwealth of Massachusetts, without giving effect to conflict of law principles.

[Remainder of Page Intentionally Left Blank]

This offer is contingent on your authorization and completion of reference checks, all being completed to the satisfaction of the Company. Such activities shall be completed prior to the Effective Date.

We are excited about the prospect of having you join the Company. We look forward to receiving your response acknowledging, by signing below, that you have accepted this offer of employment.

Very truly yours,

By: /s/ Manuel Aivado, MD, PhD
Manuel Aivado, MD, PhD
President and Chief Executive Officer

Accepted and Agreed To:

/s/ Vojislav Vukovic, MD, PhD
Name: Vojislav Vukovic, MD, PhD

Date: November 1, 2018

EXHIBIT A

Severance Agreement

SEVERANCE AGREEMENT

This SEVERANCE AGREEMENT (this "Agreement") is made and entered into as of November 1, 2018 by and between Vojislav Vukovic, MD, PhD ("Executive") and Aileron Therapeutics, Inc. (the "Company").

WHEREAS, Executive is employed as a senior executive of the Company, and the Company desires to retain the services of Executive; and

WHEREAS, the Company is entering into this Agreement in order to provide certain compensation and benefits to Executive in the event Executive's employment with the Company is terminated under certain circumstances.

NOW, THEREFORE, for good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the Company and Executive agree as follows:

1. Definitions.

1.1 "Affiliated Entity" means any corporation, partnership, trust or other entity of which the Company and/or any of its Affiliated Entities directly or indirectly owns a majority of the outstanding shares of any class of equity security thereof and any corporation, partnership, trust or other entity which directly or indirectly owns a majority of the outstanding shares of any class of any equity security of the Company or any of its Affiliated Entities.

1.2 "Cause" shall mean a finding by the Board that Executive: (i) materially breached Executive's Confidentiality, Inventions, Non-Competition and Non-Solicitation Agreement or any similar agreement between Executive and the Company (a "Confidentiality Agreement"); (ii) engaged in fraud, or embezzlement; (iii) engaged in willful misconduct or gross negligence with regard to the Company that the Board determines in good faith is, or is reasonably likely to be, materially injurious to the Company and its reputation; (iv) materially violated the Company's published policies, including those prohibiting unlawful harassment and discrimination, as in effect from time to time; or (v) was convicted of, or pleaded guilty or nolo contendere to any felony (other than traffic-related offenses).

1.3 "Change in Control Event" means

1.3.1 the acquisition by an individual, entity or group (within the meaning of Section 13(d)(3) or 14(d)(2) of the Securities Exchange Act of 1934, as amended) (a "Person") of beneficial ownership of any capital stock of the Company if, after such acquisition, such Person beneficially owns (within the meaning of Rule 13d-3 under the Securities Exchange Act of 1934, as amended) 50% or more of either (x) the then-outstanding shares of common stock of the Company (the "Outstanding Company Common Stock") or (y) the combined voting power of the then-outstanding securities of the Company entitled to vote generally in the election of directors (the "Outstanding Company Voting Securities"); provided, however, that for purposes of this Subsection 1.3.1, the following acquisitions shall not constitute a Change in Control Event: (A) any acquisition directly from the Company or (B) any acquisition by any corporation pursuant to a Business Combination (as defined below) which complies with clauses (x) and (y) of Subsection 1.3.2 of this definition;

1.3.2 the consummation of a merger, consolidation, reorganization, recapitalization or share exchange involving the Company or a sale or other disposition of all or substantially all of the assets of the Company (a "Business Combination"), unless, immediately following such Business Combination, each of the following two conditions is satisfied: (x) the Outstanding Company Common Stock and Outstanding Company Voting Securities immediately prior to such Business Combination represent more than 50% of the then-outstanding shares of common stock or other common equity and the combined voting power of the then-outstanding securities entitled to vote generally in the election of directors or other governing body, respectively, of the resulting or acquiring entity in such Business Combination (which shall include, without limitation, an entity which as a result of such transaction owns the Company or substantially all of the Company's assets either directly or through one or more subsidiaries) (such resulting or acquiring corporation is referred to herein as the "Acquiring Entity") and (y) no Person (excluding any employee benefit plan (or related trust) maintained or sponsored by the Company or by the Acquiring Entity) beneficially owns, directly or indirectly, 50% or more of the then-outstanding shares of common stock of the Acquiring Entity, or of the combined voting power of the then-outstanding securities of such entity entitled to vote generally in the election of directors or other governing body (except to the extent that such ownership existed prior to the Business Combination); or

1.3.3 the liquidation or dissolution of the Company;

provided that such Change in Control Event also satisfies Treasury Regulation Section 1.409A-3(i)(5) where required for compliance with Section 409A of the Internal Revenue Code and the guidance issued thereunder ("Section 409A").

1.4 "Date of Termination" means: (i) if Executive's employment ends other than for death, Executive's last day of employment with the Company and, (ii) if Executive's employment is terminated by reason of death, the date of Executive's death.

1.5 "Disability" shall mean any long-term disability or incapacity due to physical or mental illness that renders Executive unable to substantially perform his duties for at least ninety (90) consecutive days or one hundred twenty (120) total days during any twelve (12) month period, provided that it may occur in a shorter period if, after its commencement, it is determined to be total and permanent by a physician selected by the Company and its insurers and such determination is acceptable to Executive or to Executive's legal representative (with such agreement on acceptability not to be unreasonably withheld).

1.6 "Good Reason" means (i) a material diminution in the nature or scope of Executive's duties, responsibilities, or authority; (ii) a material reduction in Executive's base salary then in effect; or (iii) the Company's requiring Executive's ongoing and regular services to be performed at a location more than fifty (50) miles from the geographic location at which Executive was providing services before such requirement. In order to terminate Executive's employment for Good Reason, Executive must (w) give notice to the Company of Executive's intention to resign for Good Reason within ninety (90) days after the occurrence of the event (or series of events) that Executive asserts entitles Executive to resign for Good Reason, (x) state in that notice the event that Executive considers to provide Executive with Good Reason to resign, (y) provide the Company with at least thirty (30) days after Executive's notice to cure the event, and (z) if the event is not cured within such thirty-day cure period, resign for Good Reason within thirty (30) days after the end of the thirty-day cure period.

2. Obligations of the Company upon Termination.

2.1 Termination for Any Reason or No Reason. In the event of the termination of Executive's employment for any reason or for no reason, the Company will pay to Executive (or to his estate) (i) the portion of his annualized base salary that has accrued prior to such termination and has not yet been paid and, to the extent consistent with general Company policy, accrued but unused paid time off through and including the Date of Termination, (ii) any bonus amount not yet paid that was earned by and approved for payment to Executive by the Board during or with respect to the calendar year preceding the Date of Termination; (iii) reimbursement for expenses properly incurred by Executive on behalf of the Company prior to such termination and properly documented in accordance with Company policy, and (iv) to the extent not theretofore paid or provided, any other amounts or benefits required to be paid or provided or which Executive is eligible to receive under any plan or agreement of or with the Company through the Date of Termination (all such amounts, collectively, the "Accrued Obligations"). The Accrued Obligations will be paid as required by law but in any event promptly after termination or as provided by any applicable policy, plan or agreement.

2.2 Termination by the Company Other Than for Cause or by Reason of Executive's Death or Disability; By Executive for Good Reason; and Other than Upon or within Twelve Months following a Change in Control Event. Subject to the satisfaction of the Severance Conditions (as defined below), if Executive's employment is terminated (i) by the Company other than (x) for Cause or (y) by reason of Executive's death or Disability, or (ii) by Executive for Good Reason, and, in each case, other than upon or within twelve (12) months following a Change in Control Event (the "CIC Period"), then in addition to the Accrued Obligations, the Company shall:

2.2.1 Pay to Executive a sum equal to nine (9) months of base salary at Executive's most recent base salary rate, such payment to be made in approximately equal installments according to the Company's then-current payroll practices.

2.2.2 Provided that Executive is eligible for and elects to continue receiving medical insurance pursuant to the federal "COBRA" law, 29 U.S.C. § 1161 et seq., continue to pay on Executive's behalf the share of the monthly premiums for such coverage that it pays for active and similarly situated employees receiving the same type of coverage for a period of up to nine (9) months following the Date of Termination. The remaining balance of the premium costs and all premium costs after such nine (9)-month period shall be paid by Executive on a monthly basis for as long as, and to the extent that, he remains eligible for and elects to continue receiving continued coverage under COBRA; provided, however, that notwithstanding the foregoing, in the event Executive becomes eligible during the nine (9)-month period for the same or substantially similar group health insurance coverage through another employer, Executive shall immediately notify the Company in writing of the date of eligibility for such coverage (the "Eligibility Date"), and the Company's obligation to make monthly premium payments pursuant to this Subsection 2.2.2 shall end on the Eligibility Date. Notwithstanding the foregoing, payments by the Company under this Subsection 2.2.2 (but not eligibility for COBRA) shall end early if the Company determines that the continued payments are reasonably likely to result in penalties on the Company, taxation of any other employee, or taxation of Executive on income other than the payment of the premiums; provided, however, that if the Company is able to reasonably conclude that making a taxable lump sum payment to Executive in the amount of and in lieu of any remaining COBRA premiums that would otherwise be paid by the Company on Executive's behalf under this Subsection 2.2.2 would not result in any such penalties or taxation, the Company will make such lump sum payment no later than the last day of the nine (9)-month period following the Date of Termination.

2.3 Termination By the Company for Cause; By Reason of Executive's Death or Disability; Or By Executive Other than for Good Reason. If Executive's employment is terminated by the Company for Cause, or by reason of Executive's death or Disability, or by Executive for any reason other than for Good Reason, this Agreement shall terminate without further obligations to Executive or Executive's legal representatives under this Agreement, other than for payment of the Accrued Obligations.

2.4 Effect of Termination on Other Positions. If, on the Date of Termination, Executive is a member of the Company's Board of Directors (the "Board") or the board of directors of any Affiliated Entity, or holds any other office or position with the Company or any Affiliated Entity, Executive shall, unless otherwise requested by the Company, be deemed to have resigned from all such offices and positions as of the Date of Termination. Executive agrees to execute such documents and take such other actions as the Company may request to reflect such resignation.

2.5 Conditions to Payment of Post-Separation Benefits. As a condition of Executive's receipt of the post-separation benefits in Section 2.2 and Section 3.1, Executive must execute and return to the Company a severance and release of claims agreement provided by and satisfactory to the Company (the "Release Agreement"), and such Release Agreement must become binding, enforceable and irrevocable within sixty (60) calendar days after Executive's termination of employment (the "Severance Conditions"). Payments will begin in the first pay period beginning after the Severance Conditions have been satisfied or as promptly as practicable thereafter, provided that if the foregoing sixty (60) day period would end in a calendar year subsequent to the year in which Executive's employment ends, payments will not be made before the first payroll period of the subsequent year (the "Payment Date"). Notwithstanding the foregoing, the acceleration of vesting of the Equity Awards contemplated by Subsection 3.1.4 below shall take immediate effect upon the Date of Termination; provided, however, that Executive agrees that the portion of such Equity Awards that shall have been accelerated pursuant to Subsection 3.1.4 (the "Accelerated Portion") shall not be exercised prior to the date on which the Severance Conditions have been satisfied, that any shares to be issued or retained under other Equity Awards will not be issued or retained prior to the date on which the Severance Conditions have been satisfied and that if the Severance Conditions have not been satisfied within the prescribed time period, than, as of such date, the Accelerated Portion shall be cancelled and cease to be exercisable, forfeited, or not issued, as applicable on the basis of the type of Equity Award.

3. Change in Control.

3.1 Subject to the satisfaction of the Severance Conditions, if, during the CIC Period, Executive's employment is terminated by the Company without Cause and not for death or Disability, or if Executive resigns his employment for Good Reason, then, in addition to the Accrued Obligations, the Company shall:

3.1.1 Pay to Executive a sum equal to twelve (12) months of base salary at Executive's most recent base salary rate, such payment to be made in approximately equal installments according to the Company's then-current payroll practices.

3.1.2 Provided that Executive is eligible for and elects to continue receiving medical insurance under COBRA, continue to pay on Executive's behalf the share of the monthly premiums for such coverage that it pays for active and similarly situated employees receiving the same type of coverage for a period of up to twelve (12) months following the Date of Termination. The remaining balance of the premium costs and all premium costs after such twelve (12)-month period shall be paid by Executive on a monthly basis for as long as, and to the extent that, he remains eligible for and elects to continue receiving continued coverage under COBRA; provided, however, that notwithstanding the foregoing, in the event Executive becomes eligible during the twelve (12)-month period for the same or substantially similar group health insurance coverage through another employer, Executive shall immediately notify the Company in writing of the Eligibility Date, and the Company's obligation to make monthly premium payments pursuant to this Subsection 3.1.2 shall end on the Eligibility Date. Notwithstanding the foregoing, payments by the Company under this Subsection 3.1.2 (but not eligibility for COBRA) shall end early if the Company determines that the continued payments are reasonably likely to result in penalties on the Company, taxation of any other employee, or taxation of Executive on income other than the payment of the premiums; provided, however that if the Company is able to reasonably conclude that making a taxable lump sum payment to Executive in the amount of and in lieu of any remaining COBRA premiums that would otherwise be paid by the Company on Executive's behalf under this Subsection 3.1.2 would not result in any such penalties or taxation, the Company will make such lump sum payment no later than the last day of the twelve (12)-month period following the Date of Termination.

3.1.3 Pay to Executive, on the Payment Date, a lump sum equal to one times (1x) Executive's target bonus award for the year in which the Date of Termination occurs without regard to whether the performance goals applicable to such target bonus had been established or satisfied at the Date of Termination.

3.1.4 Notwithstanding the terms of any stock option agreement, restricted stock agreement or other stock award ("Equity Award"), other than terms more favorable to Executive, effective as of the Termination Date, accelerate the vesting of all Equity Awards held by Executive at the Termination Date (other than Equity Awards that vest on the basis of performance and do not provide solely for time-based vesting), such that such Equity Awards shall become 100% vested.

3.2 280G. Notwithstanding any other provision of this Agreement to the contrary, if payments made hereunder or otherwise are considered "excess parachute payments" under Section 280G of the Internal Revenue Code of 1986, as amended (the "Code"), then such excess parachute payments plus any other payments made by the Company and its affiliates that Executive is entitled to receive that are considered excess parachute payments shall be limited to the greatest amount that may be paid to Executive under Section 280G of the Code without causing any loss of deduction to the Company under such Code Section, but only if, by reason of such reduction, the "Net After Tax Benefit" (as defined below) to Executive exceeds the net after tax benefit if such reduction was not made. "Net After Tax Benefit" for purposes of this Agreement shall mean the sum of (i) the total amounts payable to Executive that would constitute an "excess parachute payment" within the meaning of Section 280G of the Code, less (ii) the amount of federal, state and other income taxes payable with respect to the foregoing calculated at the maximum marginal tax rate for each year in which the foregoing shall be paid to Executive (based upon the rate in effect for such year as set forth in the Code at the time of termination of Executive's employment or the change in control), less (iii) the amount of excise taxes imposed with respect to the payments and benefits described above by Section 4999 of the Code. The determination of whether payments would be considered excess parachute payments and the calculation of all the amounts referred to in this section shall be made reasonably and in good faith by the parties, *provided*, that if the parties cannot agree, then such determination (and supporting calculations) shall be made by attorneys, accountants, or an executive compensation consulting firm each as selected by the Company at the expense of the Company (the "280G Service Providers"). Any determination by the 280G Service Providers made in good faith shall be binding upon the Company and Executive.

4. No Mitigation. In no event, except as set forth expressly in this or another agreement signed by Executive, shall Executive be obligated to seek other employment or take any other action by way of mitigation of the amounts payable to Executive under any of the provisions of this Agreement and, subject to the aforesaid exception, such amounts shall not be reduced whether or not Executive obtains other employment.

5. Restrictive Covenants. As a condition of the effectiveness of this Agreement, Executive shall have previously, or contemporaneously with the execution of this Agreement, executed and delivered to the Company a Confidentiality Agreement in form and substance reasonably acceptable to the Company and Executive.

6. Payments Subject to Section 409A. Subject to the provisions in this Section 6, any severance payments or benefits under this Agreement shall begin only upon the date of Executive's "separation from service" (determined as set forth below) which occurs on or after the date of termination of employment. The following rules shall apply with respect to distribution of the payments and benefits, if any, to be provided to Executive under this Agreement:

6.1 It is intended that each installment of the severance payments and benefits provided under this Agreement shall be treated as a separate "payment" for purposes of Section 409A. Neither Executive nor the Company shall have the right to accelerate or defer the delivery of any such payments or benefits except to the extent specifically permitted or required by Section 409A.

6.2 If, as of the date of Executive's "separation from service" from the Company, Executive is not a "specified employee" (within the meaning of Section 409A), then each installment of the severance payments and benefits shall be made on the dates and terms set forth in this Agreement

6.3 If, as of the date of Executive's "separation from service" from the Company, Executive is a "specified employee" (within the meaning of Section 409A), then:

6.3.1 Each installment of the severance payments and benefits due under this Agreement that, in accordance with the dates and terms set forth herein, will in all circumstances, regardless of when the separation from service occurs, be paid within the short-term deferral period (as defined under Section 409A) shall be treated as a short-term deferral within the meaning of Treasury Regulation Section 1.409A-1(b)(4) to the maximum extent permissible under Section 409A and shall be paid at the time and in the matter set forth in this Agreement; and

6.3.2 Each installment of the severance payments and benefits due under this Agreement that is not described in Subsection 6.3.1 above and that would, absent this subsection, be paid within the six-month period following Executive's "separation from service" from the Company shall not be paid until the date that is six months and one day after such separation from service (or, if earlier, Executive's death), with any such installments that are required to be delayed being accumulated during the six-month period and paid in a lump sum on the date that is six months and one day following Executive's separation from service and any subsequent installments, if any, being paid in accordance with the dates and terms set forth herein; provided, however, that the preceding provisions of this sentence shall not apply to any installment of severance payments and benefits if and to the maximum extent that such installment is deemed to be paid under a separation pay plan that does not provide for a deferral of compensation by reason of the application of Treasury Regulation 1.409A-1(b)(9)(iii) (relating to separation pay upon an involuntary separation from service). Any installments that qualify for the exception under Treasury Regulation Section 1.409A-1(b)(9)(iii) must be paid no later than the last day of Executive's second taxable year following the taxable year in which the separation from service occurs.

6.4 The determination of whether and when Executive's separation from service from the Company has occurred shall be made in a manner consistent with, and based on the presumptions set forth in, Treasury Regulation Section 1.409A-1(h). Solely for purposes of this Section 6.4, "Company" shall include all persons with whom the Company would be considered a single employer as determined under Treasury Regulation Section 1.409A-(h)(3).

6.5 All reimbursements and in-kind benefits provided under this Agreement shall be made or provided in accordance with the requirements of Section 409A to the extent that such reimbursements or in-kind benefits are subject to Section 409A, including, where applicable, the requirement that (i) any reimbursement is for expenses incurred during Executive's lifetime (or during a shorter period of time specified in this Agreement), (ii) the amount of expenses eligible for reimbursement during a calendar year may not affect the expenses eligible for reimbursement in any other calendar year, (iii) the reimbursement of an eligible expense will be made on or before the last day of the calendar year following the year in which the expense is incurred, and (iv) the right to reimbursement is not subject to set off or liquidation or exchange for any other benefit.

7. Return of Company Property. Upon termination of employment for any reason, Executive shall promptly return to the Company any keys, credit cards, passes, confidential documents or material, computer equipment, or other property belonging to the Company, and Executive shall also return all writings, files, records, correspondence, notebooks, notes and other documents and things (including any copies thereof) containing confidential information or relating to the business or proposed business of the Company or the Affiliated Entities or containing any trade secrets relating to the Company or the Affiliated Entities. For purposes of the preceding sentence, the term "trade secrets" shall have the meaning ascribed to it under the Uniform Trade Secrets Act. Executive agrees to represent in writing to the Company upon termination of employment that he has complied with the foregoing provisions of this Section.

8. Assistance with Claims. Executive agrees that, consistent with Executive's business and personal affairs, during and after his employment by the Company he will assist the Company and the Affiliated Entities in the defense of any claims, or potential claims that may be made or are threatened to be made against any of them in any action, suit or proceeding, whether civil, criminal, administrative or investigative (a "Proceeding"), and will assist the Company and the Affiliated Entities in the prosecution of any claims that may be made by the Company or the Affiliated Entities in any Proceeding, to the extent that such claims may relate to Executive's employment or the period of Executive's employment by the Company. The Company agrees to (i) reimburse Executive for all of Executive's reasonable out-of-pocket expenses associated with such assistance, including travel expenses and (ii) with respect to assistance provided after Executive's employment, compensate Executive on an hourly basis, based on a rate commensurate with Executive's base salary (assuming a forty (40) hour work week) in effect on the Date of Termination, for time Executive spends in excess of ten (10) hours in any calendar quarter providing such assistance to the Company, provided that such time shall not include any time spent testifying in any arbitration, trial, administrative hearing or other proceeding. Any amounts to be paid to Executive pursuant to this Section 8 shall be paid by the Company no later than thirty (30) days of the date on which Executive provides documentation to the Company that such expenses were incurred.

9. Successors. This Agreement is personal to Executive and shall not be assignable by Executive without the prior written consent of the Company. This Agreement and any rights and benefits hereunder shall inure to the benefit of and be enforceable by Executive's legal representatives, heirs or legatees. This Agreement and any rights and benefits hereunder shall inure to the benefit of and be binding upon the Company and its successors and assigns, including any corporation with which or into which the Company may be merged or which may succeed to its assets or business.

10. Miscellaneous.

10.1 Entire Agreement/Modification/Choice of Law/Enforceability/Jury Waiver. Both Executive and the Company acknowledge that this Agreement is the entire agreement of the parties, and supersedes any prior or contemporaneous discussions, understandings, or agreements, with respect to the subject matter hereof. For the avoidance of doubt and without limiting the foregoing, (a) Executive shall not be eligible to receive severance or similar post-employment payments or benefits under any severance plan, program or policy now or hereafter maintained by the Company, and (b) any employment offer letter or employment agreement between Executive and the Company (such offer letter or employment agreement, the "Employment Agreement") shall survive the execution and delivery of this Agreement and remain in full force and effect in accordance with its original terms; provided, however, that any provisions of the Employment Agreement relating to severance and post-employment payments and benefits shall be superseded hereby in their entirety and shall hereafter cease to be of any force or effect. This Agreement may be amended only in a written agreement duly executed by the parties hereto. This Agreement shall be deemed to have been made in the Commonwealth of Massachusetts and shall be governed by and construed in accordance with the laws of such Commonwealth, without giving effect to conflict of law principles. Both parties agree that any action, demand, claim or counterclaim relating to the terms and provisions of this Agreement, or to its formation or breach, or to Executive's employment or the termination thereof, shall be commenced only in Massachusetts in a court of competent jurisdiction, and further acknowledge that venue for such actions shall lie exclusively in Massachusetts. Both parties hereby waive and renounce in advance any right to a trial by jury in connection with such legal action.

10.2 Withholding. The Company may withhold from any amounts payable under this Agreement such Federal, state, local or foreign taxes as shall be required to be withheld pursuant to any applicable law or regulation.

10.3 No Guarantee of any Tax Consequences. The Company makes no guarantee of any tax consequences with respect to any payment hereunder including, without limitation, under Section 409A.

10.4 Severability. The invalidity or unenforceability of any provision of this Agreement will not affect the validity or enforceability of any other provision of this Agreement, and this Agreement will be construed as if such invalid or unenforceable provision were omitted (but only to the extent that such provision cannot be appropriately reformed or modified).

10.5 Waiver of Breach. No waiver by any party hereto of a breach of any provision of this Agreement by any other party, or of compliance with any condition or provision of this Agreement to be performed by such other party, will operate or be construed as a waiver of any subsequent breach by such other party of any similar or dissimilar provisions and conditions at the same or any prior or subsequent time.

10.6 Notices. Notices and all other communications provided for in this Agreement shall be in writing and shall be delivered personally or sent by registered or certified mail, return receipt requested, postage prepaid, or prepaid overnight courier to the parties at the addresses set forth below (or such other addresses as shall be specified by the parties by like notice):

to the Company:

Aileron Therapeutics, Inc.
490 Arsenal Way
Watertown, MA 02472
Attention: Chief Executive Officer

with a copy to:

Wilmer Cutler Pickering Hale and Dorr, LP
60 State Street
Boston, MA 02109
Attention: Stuart Falber

or to Executive:

At the most recent address maintained
by the Company in its personnel records

10.7 Each party, by written notice furnished to the other party, may modify the applicable delivery address, except that notice of change of address shall be effective only upon receipt. Such notices, demands, claims and other communications shall be deemed given in the case of delivery by overnight service with guaranteed next day delivery, the next day or the day designated for delivery; or in the case of certified or registered U.S. mail, five days after deposit in the U.S. mail; provided, however, that in no event shall any such communications be deemed to be given later than the date they are actually received.

10.8 Not Employment Contract. Executive acknowledges that this Agreement does not constitute a contract of employment, does not imply that the Company will continue his employment for any period of time and does not change the at-will nature of his employment.

10.9 Survivorship. Upon the expiration or other termination of this Agreement, the respective rights and obligations of the parties hereto shall survive such expiration or other termination to the extent necessary to carry out the intentions of the parties under this Agreement.

10.10 Counterparts. This Agreement may be executed in separate facsimile or electronic counterparts, each of which is deemed to be an original and all of which taken together constitute one and the same agreement.

10.11 Representations. Executive hereby acknowledges that he understands this Agreement and enters into this Agreement voluntarily.

IN WITNESS THEREOF, Executive has hereunto set his hand, and the Company has caused this Agreement to be executed in its name and on its behalf, all as of the day and year first above written.

AILERON THERAPEUTICS, INC.	VOJISLAV VUKOVIC, MD, PHD
/s/ Manuel Aivado	/s/ Vojislav Vukovic, M.D., Ph.D.
Name: Manuel Aivado	
Title: President & CEO	

Exhibit 10.21

AILERON THERAPEUTICS

November 15, 2007

D. Allen Annis, Ph.D.
508 Green Street, No. 3
Cambridge, MA 02139

Dear Allen:

It is my pleasure to extend to you this offer of employment with Aileron Therapeutics, Inc. (the "Company"). The purpose of this letter is to summarize the terms of your employment with the Company, should you accept our offer:

1. **Employment.** You will be employed to serve as Senior Director of Biophysical and Analytical Technologies, effective November 19, 2007. As Senior Director of Biophysical and Analytical Technologies, you will be responsible for all internal and external pre-clinical and clinical development activities relating to the Company's technologies, building the team and overall capabilities for the Company to successfully run clinical trials and assisting with the development of the Company's strategic product direction, plus such other duties as may from time to time be assigned to you by the Company. You shall report directly to the Chief Scientific Officer of the Company and you agree to devote your full business time, best efforts, skill, knowledge, attention and energies to the advancement of the Company' s business and interests and to the performance of your duties and responsibilities as an employee of the Company.

2. **Base Salary and Bonus.** Your base salary will be at the rate of $14,583.33 per monthly pay period (which if annualized equals $175,000), less all applicable federal, state and local taxes and withholdings, to be paid in installments in accordance with the Company's regular payroll practices (which shall not be less than twice per month). Your base salary may be adjusted in the sole discretion of the Company from time to time in accordance with normal business practices. Following the end of any calendar year in which you are employed by the Company, and subject to the approval of the Company's Board of Directors (the "Board"), you may from time to time be eligible for a discretionary annual bonus award of up to 20% of your base salary. Any such bonus award would be based on both you and the Company achieving certain performance objectives, as determined by the Company in its sole discretion.

3. **Benefit Programs.** You may choose to participate in any and all benefit programs that the Company establishes and makes available to its employees from time to time, provided you are eligible under (and subject to all provisions of) the plan documents governing those programs. The Company reserves the right to change, add, or cease any particular benefit without notice, in its sole discretion. At present, the Company offers eligible employees health insurance, dental insurance, and a 401(k) savings program.

4. **Business Expenses.** The Company will reimburse you for all reasonable and documented business expenses. Expenses in excess of $500 will require pre-approval by the Chief Scientific Officer or his/her designate.

5. **Vacation.** You will be eligible for a maximum of three (3) weeks of paid vacation per calendar year to be taken at such times as may be approved in advance by the Company, which approval will not be unreasonably withheld. The number of vacation days for which you are eligible shall accrue at the rate of 1.25 days per month that you are employed during such calendar year. Pursuant to Company policy, vacation time cannot be carried over from year to year.

6. **Equity.** Subject to approval by the Board, you will receive stock options to purchase 75,000 shares of the Company's Common Stock for a price per share equal to the fair market value of one share of the Common Stock on the date of the option grant as determined by the Board and pursuant and subject to the terms of the Company's Option Agreement (which must be executed to receive the grant). The stock options will vest (become exercisable) as follows: 12.5% of the shares underlying the options shall vest upon the six (6) month anniversary of your employment commencement date and 1/42nd of the remainder of such shares will vest on a monthly basis in forty-two (42) equal monthly installments with the first such installment vesting on the seven (7) month anniversary of your employment commencement date, subject to your continued employment with the Company through each vesting date.

You may also be eligible for other grants of stock or stock options as determined by and in the sole discretion of the Board. Nothing in this section shall affect your status as an employee at will, as set forth below.

7. **Confidentiality, Inventions, Non-Solicitation and Non-Competition Agreement.** As a condition of employment, you will be required to execute the Confidentiality, Inventions, Non-Solicitation and Non-Competition Agreement enclosed herewith as Exhibit A.

8. **Company Policies and Procedures.** As an employee of the Company, you will be required to comply with all Company policies and procedures. Violations of the Company's policies may lead to immediate termination of your employment. Further, the Company's premises, including all workspaces, furniture, documents and other tangible materials, and all information technology resources of the Company (including computers, data and other electronic files, and all Internet and e-mail usage) are subject to oversight and inspection by the Company at any time. Company employees should have no expectation of privacy with regard to any Company premises, materials, resources or information.

9. **Proof of Legal Right to Work.** For purposes of federal immigration law, you will be required to provide the Company with documentary evidence of your identity and eligibility for employment in the United States. Such documentation must be provided to the Company within three (3) business days of your date of hire, or our employment relationship with you may be terminated. You may need to obtain a work visa in order to be eligible to work in the United States. If that is the case, your employment with the Company will be conditioned upon your obtaining a work visa in a timely manner as determined by the Company.

10. **At-Will Employment.** This letter shall not be construed as an agreement, either express or implied, to employ you for any stated term, and shall in no way alter the Company's policy of employment at will, under which both you and the Company remain free to end the employment relationship for any reason, at any time, with or without cause or notice. Although your job duties, title, compensation and benefits, as well as the Company's personnel policies and procedures, may change from time to time, the "at will" nature of your employment may only be changed by a written agreement signed by you and the Chief Executive Officer of the Company which expressly states the intention to modify the at-will nature of your employment. Similarly, nothing in this letter shall be construed as an agreement, either express or implied, to pay you any compensation or grant you any benefit beyond the end of your employment with the Company. This letter supersedes any prior understandings, whether written or oral, relating to the terms of your employment with the Company.

11. **Other Agreements and Governing Law.** You represent that you are not bound by any employment contract, restrictive covenant or other restriction preventing you from entering into employment with or carrying out your responsibilities for the Company, or which is in any way inconsistent with the terms of this letter. Please note that this offer letter is your formal offer of employment and supersedes any and all prior or contemporaneous agreements, discussions and/or understandings, whether written or oral, relating to the subject matter of this letter or your employment with the Company. The resolution of any disputes under this letter will be governed by Massachusetts law.

If this letter correctly sets forth the initial terms under which you will be employed by the Company, please sign the enclosed duplicate of this letter in the space provided below, along with the enclosed Confidentiality, Inventions, Non-Solicitation and Non-Competition Agreement, and return them to me. If you do not accept this offer by November 22, 2007, the offer will be deemed withdrawn. This offer is contingent on satisfactory reference checks.

Very truly yours,

By: /s/ Joseph A. Yanchik III
Name: Joseph A. Yanchik III
Title: Chief Executive Ifficer

The foregoing correctly sets forth the terms of my at-will employment with Aileron Therapeutics, Inc. I am not relying on any representations other than as set forth above.

/s/ D. Allen Annis		Date:	11/15/2007
Name:			

EXHIBIT A

AILERON THERAPEUTICS, INC.

CONFIDENTIALITY, INVENTIONS, NON-SOLICITATION AND NON-COMPETITION AGREEMENT

In consideration of my employment by Aileron Therapeutics, Inc. or any of its predecessors, successors or subsidiaries (collectively , the "Company"), and for other valuable consideration, the receipt and sufficiency of which is hereby acknowledged, I, intending to be legally bound, hereby agree as follows:

Confidentiality

I understand that the Company continually obtains and develops valuable proprietary and confidential information concerning its business, business relationships and financial affairs (the "Confidential Information") and valuable Biological and Biochemical Materials (as hereafter defined) which may become known to me in connection with my employment by the Company. By way of illustration, but not limitation, Confidential Information may include Inventions (as hereafter defined), trade secrets, technical information, know-how, research and development activities of the Company, product and marketing plans, customer and supplier information and information disclosed to the Company or to me by third parties of a proprietary or confidential nature or under an obligation of confidence. Confidential Information is contained in various documents and media, including without limitation, patent applications, computer programs in object and/or source code, flow charts and other program documentation, manuals, plans, drawings, designs, technical specifications, laboratory notebooks, supplier and customer lists, internal financial data and other documents and records of the Company. As used herein, "Biological and Biochemical Materials" means all biological and biochemical materials, including, without limitation, any and all reagents, substances, chemical compounds, subcellular constituents, cells or cell lines, organisms and progeny, mutants, derivatives or replications thereof or therefrom.

I hereby acknowledge that all Biological and Biochemical Materials and all Confidential Information, whether or not in writing and whether or not labeled or identified as confidential or proprietary, is and shall remain the exclusive property of the Company or the third party providing such information to me or the Company. I agree that I shall not, during the term of my employment by the Company and thereafter, publish, disclose or otherwise make available to any third party, other than employees, advisors and consultants of the Company, any Confidential Information or Biological and Biochemical Materials except as expressly authorized in writing by the Company. I agree that I shall use such Confidential Information and Biological and Biochemical Materials only in the performance of my employment duties to the Company and in accordance with Company policy with respect to the protection of Confidential Information and Biological and Biochemical Materials. I agree not to use such Confidential Information or Biological and Biochemical Materials for my own benefit or for the benefit of any other person or business entity.

I agree to exercise all reasonable precautions to protect the confidentiality of Confidential Information and Biological and Biochemical Materials in my possession. Upon the termination of my employment by the Company, or at any time upon the Company's request, I shall return immediately to the Company any and all materials containing any Confidential Information or any Biological or Biochemical Materials then in my possession or under my control.

Neither Confidential Information nor Biological and Biochemical Materials shall include information which (a) is or becomes generally known within the Company's industry through no fault of mine; (b) was known to me at the time it was disclosed as evidenced by my written records at the time of disclosure; (c) is lawfully and in good faith made available to me by a third party who did not derive it from the Company and who imposes no obligation of confidence on me; or (d) is required to be disclosed by a governmental authority or by order of a court of competent jurisdiction, provided that such disclosure is subject to all applicable governmental or judicial protection available for like material and reasonable advance notice is given to the Company. However, information shall not be deemed to be publicly available merely because it is embraced by general disclosures or because individual features or combinations thereof are publicly available.

Assignment of Inventions

I agree promptly to disclose to the Company any and all ideas, concepts, discoveries, inventions, developments, original works of authorship, software programs, software and systems documentation, trade secrets, technical data, know-how and Biological and Biochemical Materials that are conceived, devised, invented, developed or reduced to practice or tangible medium by me, under my direction or jointly with others during any period that I am employed or engaged by the Company, whether or not during normal working hours or on the premises of the Company, which relate to the business of the Company and arise out of my employment by the Company (collectively, "Inventions").

I hereby assign to the Company all of my right, title and interest to any and all Inventions and any and all related patent rights, copyrights and applications and registrations therefor which relate to the business of the Company and arise out of my employment by the Company. During and after my employment by the Company, I shall cooperate with the Company, at the Company's expense, in obtaining proprietary protection for any such Inventions and I shall, upon the Company's request, execute all documents necessary or advisable in order to perfect the Company's rights in such Inventions. In order to protect the Company in the event that I should fail or refuse to execute all such documents within a reasonable period following the Company's request, I hereby appoint the Company my agent and attorney-in-fact to execute and deliver any such documents on my behalf.

Notwithstanding the foregoing, any discoveries, improvements and inventions, made or conceived by me prior to my employment by the Company, or not otherwise covered by the foregoing, are expressly reserved and excerpted from the provisions of this Agreement.

I acknowledge that all original works of authorship created or developed by me within the scope of my employment by the Company which are protectable by copyright are intended to be "works made for hire", as that term is defined in Section 101 of the United States Copyright Act of 1976 (the "Act"), and shall be the property of the Company and the Company shall be the sole author within the meaning of the Act. If the copyright to any such copyrightable work shall not be the property of the Company by operation of law, then, without further consideration, I hereby assign to the Company all of my right, title and interest in such copyrightable work and I will cooperate with the Company and its designees, at the Company's expense, to secure, maintain and defend for the Company's benefit copyrights and any extensions and renewals thereof on any and all such work. I hereby waive all claims to moral rights in any Inventions.

Non-competition

I agree that while I am an employee of the Company and for a period of one (1) year after the termination or cessation of such employment for any reason, I shall not, without the Company's prior written consent, directly or indirectly, as a principal, employee, consultant, partner or stockholder of, or in any other capacity with, any business enterprise engaged in the Field of Interest (as defined on the attached Schedule A) (other than in my capacity as a holder of not more than 1% of the combined voting power of the outstanding stock of a publicly held company) develop, design, produce, market, sell or render (or assist any other person or entity in developing, designing, producing, marketing, selling or rendering) products or services competitive with those developed, designed, produced, marketed, sold or rendered by the Company during the period of my employment by the Company.

Non-Solicitation and Non-Interference

I agree that while I am an employee of the Company and for a period of one (1) year after the termination or cessation of such employment for any reason, I will not directly or indirectly induce or attempt to induce any employee or independent contractor of the Company or any of its affiliates to leave the employ of or cease providing services to the Company or such affiliate, or in any way interfere with the relationship between the Company or any of its affiliates and any employee or independent contractor thereof.

I agree that while I am an employee of the Company and for a period of one (1) year after the termination or cessation of such employment for any reason, I will not directly or indirectly hire, engage, send any work to, place orders with, or in any manner be associated with any supplier, contractor, subcontractor or other business relation of the Company or any of its affiliates if such could reasonably be expected to have a material adverse effect on the business, assets or financial condition of the Company or any of its affiliates or materially interfere with the relationship between any such person or entity and the Company or any of its affiliates.

<u>Other Agreements</u>

Except as identified on the attached <u>Schedule A</u>, I am not bound by any agreement with any person or company to disclose and assign inventions or refrain from competing with or using or disclosing any confidential or proprietary information in the Field of Interest (as defined on <u>Schedule A</u>) of that person or company. I will not disclose to the Company any confidential or proprietary information belonging to any other person or company. I will not perform any employment duties for the Company which could result in claims by any other person or company of rights in any Inventions without the express prior agreement of the Company and any such person or company.

<u>General</u>

In the event that any one or more of the provisions contained herein shall, for any reason, be held to be invalid, illegal, or unenforceable in any respect, such invalidity, illegality, or unenforceability shall not affect any other provisions of this Agreement, and all other provisions shall remain in full force and effect. If any of the provisions of this Agreement is held to be excessively broad, it shall be reformed and construed by limiting and reducing it so as to be enforceable to the maximum extent permitted by law.

No delay or omission by the Company in exercising any right under this agreement will operate as a waiver of that or any other right. No waiver or consent given by the Company on any occasion will be construed as a bar to or continuing waiver of any right on any other occasion.

I acknowledge that the restrictions contained in this agreement are necessary for the protection of the business and goodwill of the Company and are reasonable for such purpose. I agree that any breach of this agreement by me will cause irreparable damage to the Company and that in the event of such breach the Company will have, in addition to any and all remedies of law, the right to an injunction, specific performance, or other equitable relief, to prevent the violation of my obligations hereunder.

This Agreement shall be construed as a sealed instrument and shall in all events and for all purposes be governed by, and construed in accordance with the laws of the Commonwealth of Massachusetts without regard to any choice of law principle that would dictate the application of the laws of another jurisdiction. This Agreement supersedes all prior agreements, written or oral, with respect to the subject matter hereof.

I HAVE READ ALL OF THE PROVISIONS OF THIS AGREEMENT AND I UNDERSTAND, AND AGREE TO, EACH OF SUCH PROVISIONS.

11/15/2007 /s/ D. Allen Annis
Date (Signature)

Print Name: /s/ D. Allen Annis

Acknowledged and Agreed:

AILERON THERAPEUTICS, INC.

By: /s/ Joseph A. Yanchik III
Name: JOSEPH A. YANCHIK III
Title: President and CEO

Schedule A

"Field of Interest" shall mean those indications and compounds that, to your knowledge, the Company is developing or plans to develop.

Other Agreements

I am bound by agreements with the following entities:

/s/ Schering-Plough

SEVERANCE AGREEMENT

This SEVERANCE AGREEMENT (this "Agreement") is made and entered into as of November 5, 2018 by and between Allen Annis ("Executive") and Aileron Therapeutics, Inc. (the "Company").

WHEREAS, Executive is employed as a senior executive of the Company, and the Company desires to continue to retain the services of Executive; and

WHEREAS, the Company is entering into this Agreement in order to provide certain compensation and benefits to Executive in the event Executive's employment with the Company is terminated under certain circumstances.

NOW, THEREFORE, for good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the Company and Executive agree as follows:

1. Definitions.

1.1 "Affiliated Entity" means any corporation, partnership, trust or other entity of which the Company and/or any of its Affiliated Entities directly or indirectly owns a majority of the outstanding shares of any class of equity security thereof and any corporation, partnership, trust or other entity which directly or indirectly owns a majority of the outstanding shares of any class of any equity security of the Company or any of its Affiliated Entities.

1.2 "Cause" shall mean a finding by the Board that Executive: (i) materially breached Executive's Confidentiality, Inventions, Non-Competition and Non-Solicitation Agreement or any similar agreement between Executive and the Company (a "Confidentiality Agreement"); (ii) engaged in fraud, or embezzlement; (iii) engaged in willful misconduct or gross negligence with regard to the Company that the Board determines in good faith is, or is reasonably likely to be, materially injurious to the Company and its reputation; (iv) materially violated the Company's published policies, including those prohibiting unlawful harassment and discrimination, as in effect from time to time; or (v) was convicted of, or pleaded guilty or nolo contendere to any felony (other than traffic-related offenses).

1.3 "Change in Control Event" means

1.3.1 the acquisition by an individual, entity or group (within the meaning of Section 13(d)(3) or 14(d)(2) of the Securities Exchange Act of 1934, as amended) (a "Person") of beneficial ownership of any capital stock of the Company if, after such acquisition, such Person beneficially owns (within the meaning of Rule 13d-3 under the Securities Exchange Act of 1934, as amended) 50% or more of either (x) the then-outstanding shares of common stock of the Company (the "Outstanding Company Common Stock") or (y) the combined voting power of the then-outstanding securities of the Company entitled to vote generally in the election of directors (the "Outstanding Company Voting Securities"); provided, however, that for purposes of this Subsection 1.3.1, the following acquisitions shall not constitute a Change in Control Event: (A) any acquisition directly from the Company or (B) any acquisition by any corporation pursuant to a Business Combination (as defined below) which complies with clauses (x) and (y) of Subsection 1.3.2 of this definition;

1.3.2 the consummation of a merger, consolidation, reorganization, recapitalization or share exchange involving the Company or a sale or other disposition of all or substantially all of the assets of the Company (a "Business Combination"), unless, immediately following such Business Combination, each of the following two conditions is satisfied: (x) the Outstanding Company Common Stock and Outstanding Company Voting Securities immediately prior to such Business Combination represent more than 50% of the then-outstanding shares of common stock or other common equity and the combined voting power of the then-outstanding securities entitled to vote generally in the election of directors or other governing body, respectively, of the resulting or acquiring entity in such Business Combination (which shall include, without limitation, an entity which as a result of such transaction owns the Company or substantially all of the Company's assets either directly or through one or more subsidiaries) (such resulting or acquiring corporation is referred to herein as the "Acquiring Entity") and (y) no Person (excluding any employee benefit plan (or related trust) maintained or sponsored by the Company or by the Acquiring Entity) beneficially owns, directly or indirectly, 50% or more of the then-outstanding shares of common stock of the Acquiring Entity, or of the combined voting power of the then-outstanding securities of such entity entitled to vote generally in the election of directors or other governing body (except to the extent that such ownership existed prior to the Business Combination); or

1.3.3 the liquidation or dissolution of the Company;

provided that such Change in Control Event also satisfies Treasury Regulation Section 1.409A-3(i)(5) where required for compliance with Section 409A of the Internal Revenue Code and the guidance issued thereunder ("Section 409A").

1.4 "Date of Termination" means: (i) if Executive's employment ends other than for death, Executive's last day of employment with the Company and, (ii) if Executive's employment is terminated by reason of death, the date of Executive's death.

1.5 "Disability" shall mean any long-term disability or incapacity due to physical or mental illness that renders Executive unable to substantially perform his duties for at least ninety (90) consecutive days or one hundred twenty (120) total days during any twelve (12) month period, provided that it may occur in a shorter period if, after its commencement, it is determined to be total and permanent by a physician selected by the Company and its insurers and such determination is acceptable to Executive or to Executive's legal representative (with such agreement on acceptability not to be unreasonably withheld).

1.6 "Good Reason" means (i) a material diminution in the nature or scope of Executive's duties, responsibilities, or authority; (ii) a material reduction in Executive's base salary then in effect; (iii) a material reduction by the Company in the kind or level of employee benefits to which Executive is entitled immediately prior to such reduction with the result that the overall benefits package is materially reduced, other than a reduction comparable to reductions generally applicable to similarly situated employees of the Company; or (iv) the Company's requiring Executive's ongoing and regular services to be performed at a location more than fifty (50) miles from the geographic location at which Executive was providing services before such requirement. In order to terminate Executive's employment for Good Reason, Executive must (w) give notice to the Company of Executive's intention to resign for Good Reason within ninety (90) days after the occurrence of the event (or series of events) that Executive asserts entitles Executive to resign for Good Reason, (x) state in that notice the event that Executive considers to provide Executive with Good Reason to resign, (y) provide the Company with at least thirty (30) days after Executive's notice to cure the event, and (z) if the event is not cured within such thirty-day cure period, resign for Good Reason within thirty (30) days after the end of the thirty-day cure period.

2. Obligations of the Company upon Termination.

2.1 Termination for Any Reason or No Reason. In the event of the termination of Executive's employment for any reason or for no reason, the Company will pay to Executive (or to his estate) (i) the portion of his annualized base salary that has accrued prior to such termination and has not yet been paid and, to the extent consistent with general Company policy, accrued but unused paid time off through and including the Date of Termination, (ii) any bonus amount not yet paid that was earned by and approved for payment to Executive by the Board during or with respect to the calendar year preceding the Date of Termination; (iii) reimbursement for expenses properly incurred by Executive on behalf of the Company prior to such termination and properly documented in accordance with Company policy, and (iv) to the extent not theretofore paid or provided, any other amounts or benefits required to be paid or provided or which Executive is eligible to receive under any plan or agreement of or with the Company through the Date of Termination (all such amounts, collectively, the "Accrued Obligations"). The Accrued Obligations will be paid as required by law but in any event promptly after termination or as provided by any applicable policy, plan or agreement.

2.2 Termination by the Company Other Than for Cause or by Reason of Executive's Death or Disability; By Executive for Good Reason; and Other than Upon or within Twelve Months following a Change in Control Event. Subject to the satisfaction of the Severance Conditions (as defined below), if Executive's employment is terminated (i) by the Company other than (x) for Cause or (y) by reason of Executive's death or Disability, or (ii) by Executive for Good Reason, and, in each case, other than upon or within twelve (12) months following a Change in Control Event (the "CIC Period"), then in addition to the Accrued Obligations, the Company shall:

2.2.1 Pay to Executive a sum equal to nine (9) months of base salary at Executive’s most recent base salary rate, such payment to be made in approximately equal installments according to the Company’s then-current payroll practices.

2.2.2 Provided that Executive is eligible for and elects to continue receiving medical insurance pursuant to the federal “COBRA” law, 29 U.S.C. § 1161 et seq., continue to pay on Executive’s behalf the share of the monthly premiums for such coverage that it pays for active and similarly situated employees receiving the same type of coverage for a period of up to nine (9) months following the Date of Termination. The remaining balance of the premium costs and all premium costs after such nine (9) month period shall be paid by Executive on a monthly basis for as long as, and to the extent that, he remains eligible for and elects to continue receiving continued coverage under COBRA; provided, however, that notwithstanding the foregoing, in the event Executive becomes eligible during the nine (9) month period for the same or substantially similar group health insurance coverage through another employer, Executive shall immediately notify the Company in writing of the date of eligibility for such coverage (the “Eligibility Date”), and the Company’s obligation to make monthly premium payments pursuant to this Subsection 2.2.2 shall end on the Eligibility Date. Notwithstanding the foregoing, payments by the Company under this Subsection 2.2.2 (but not eligibility for COBRA) shall end early if the Company determines that the continued payments are reasonably likely to result in penalties on the Company, taxation of any other employee, or taxation of Executive on income other than the payment of the premiums; provided, however, that if the Company is able to reasonably conclude that making a taxable lump sum payment to Executive in the amount of and in lieu of any remaining COBRA premiums that would otherwise be paid by the Company on Executive’s behalf under this Subsection 2.2.2 would not result in any such penalties or taxation, the Company will make such lump sum payment no later than the last day of the nine (9) month period following the Date of Termination.

2.3 Termination By the Company for Cause; By Reason of Executive’s Death or Disability; Or By Executive Other than for Good Reason. If Executive’s employment is terminated by the Company for Cause, or by reason of Executive’s death or Disability, or by Executive for any reason other than for Good Reason, this Agreement shall terminate without further obligations to Executive or Executive’s legal representatives under this Agreement, other than for payment of the Accrued Obligations.

2.4 Effect of Termination on Other Positions. If, on the Date of Termination, Executive is a member of the Company’s Board of Directors (the “Board”) or the board of directors of any Affiliated Entity, or holds any other office or position with the Company or any Affiliated Entity, Executive shall, unless otherwise requested by the Company, be deemed to have resigned from all such offices and positions as of the Date of Termination. Executive agrees to execute such documents and take such other actions as the Company may request to reflect such resignation.

2.5 Conditions to Payment of Post-Separation Benefits. As a condition of Executive's receipt of the post-separation benefits in Section 2.2 and Section 3.1, Executive must execute and return to the Company a severance and release of claims agreement provided by and satisfactory to the Company (the "Release Agreement"), and such Release Agreement must become binding, enforceable and irrevocable within sixty (60) calendar days after Executive's termination of employment (the "Severance Conditions"). Payments will begin in the first pay period beginning after the Severance Conditions have been satisfied or as promptly as practicable thereafter, provided that if the foregoing sixty (60) day period would end in a calendar year subsequent to the year in which Executive's employment ends, payments will not be made before the first payroll period of the subsequent year (the "Payment Date"). Notwithstanding the foregoing, the acceleration of vesting of the Equity Awards contemplated by Subsection 3.1.4 below shall take immediate effect upon the Date of Termination; provided, however, that Executive agrees that the portion of such Equity Awards that shall have been accelerated pursuant to Subsection 3.1.4 (the "Accelerated Portion") shall not be exercised prior to the date on which the Severance Conditions have been satisfied, that any shares to be issued or retained under other Equity Awards will not be issued or retained prior to the date on which the Severance Conditions have been satisfied and that if the Severance Conditions have not been satisfied within the prescribed time period, than, as of such date, the Accelerated Portion shall be cancelled and cease to be exercisable, forfeited, or not issued, as applicable on the basis of the type of Equity Award.

3. Change in Control.

3.1 Subject to the satisfaction of the Severance Conditions, if, during the CIC Period, Executive's employment is terminated by the Company without Cause and not for death or Disability, or if Executive resigns his employment for Good Reason, then, in addition to the Accrued Obligations, the Company shall:

3.1.1 Pay to Executive a sum equal to twelve (12) months of base salary at Executive's most recent base salary rate, such payment to be made in approximately equal installments according to the Company's then-current payroll practices.

3.1.2 Provided that Executive is eligible for and elects to continue receiving medical insurance under COBRA, continue to pay on Executive's behalf the share of the monthly premiums for such coverage that it pays for active and similarly situated employees receiving the same type of coverage for a period of up to twelve (12) months following the Date of Termination. The remaining balance of the premium costs and all premium costs after such twelve (12) month period shall be paid by Executive on a monthly basis for as long as, and to the extent that, he remains eligible for and elects to continue receiving continued coverage under COBRA; provided, however, that notwithstanding the foregoing, in the event Executive becomes eligible during the twelve (12) month period for the same or substantially similar group health insurance coverage through another employer, Executive shall immediately notify the Company in writing of the Eligibility Date, and the Company's obligation to make monthly premium payments pursuant to this Subsection 3.1.2 shall end on the Eligibility Date. Notwithstanding the foregoing, payments by the Company under this Subsection 3.1.2 (but not eligibility for COBRA) shall end early if the Company determines that the continued payments are reasonably likely to result in penalties on the Company, taxation of any other employee, or taxation of Executive on income other than the payment of the premiums; provided, however that if the Company is able to reasonably conclude that making a taxable lump sum payment to Executive in the amount of and in lieu of any remaining COBRA premiums that would otherwise be paid by the Company on Executive's behalf under this Subsection 3.1.2 would not result in any such penalties or taxation, the Company will make such lump sum payment no later than the last day of the twelve (12) month period following the Date of Termination.

3.1.3 Pay to Executive, on the Payment Date, a lump sum equal to one times (1 x) Executive's target bonus award for the year in which the Date of Termination occurs without regard to whether the performance goals applicable to such target bonus had been established or satisfied at the Date of Termination.

3.1.4 Notwithstanding the terms of any stock option agreement, restricted stock agreement or other stock award ("Equity Award"), other than terms more favorable to Executive, effective as of the Termination Date, accelerate the vesting of all Equity Awards held by Executive at the Termination Date (other than Equity Awards that vest on the basis of performance and do not provide solely for time-based vesting), such that such Equity Awards shall become 100% vested.

3.2 280G. Notwithstanding any other provision of this Agreement to the contrary, if payments made hereunder or otherwise are considered "excess parachute payments" under Section 280G of the Internal Revenue Code of 1986, as amended (the "Code"), then such excess parachute payments plus any other payments made by the Company and its affiliates that Executive is entitled to receive that are considered excess parachute payments shall be limited to the greatest amount that may be paid to Executive under Section 280G of the Code without causing any loss of deduction to the Company under such Code Section, but only if, by reason of such reduction, the "Net After Tax Benefit" (as defined below) to Executive exceeds the net after tax benefit if such reduction was not made. "Net After Tax Benefit" for purposes of this Agreement shall mean the sum of (i) the total amounts payable to Executive that would constitute an "excess parachute payment" within the meaning of Section 280G of the Code, less (ii) the amount of federal, state and other income taxes payable with respect to the foregoing calculated at the maximum marginal tax rate for each year in which the foregoing shall be paid to Executive (based upon the rate in effect for such year as set forth in the Code at the time of termination of Executive's employment or the change in control), less (iii) the amount of excise taxes imposed with respect to the payments and benefits described above by Section 4999 of the Code. The determination of whether payments would be considered excess parachute payments and the calculation of all the amounts referred to in this section shall be made reasonably and in good faith by the parties, *provided*, that if the parties cannot agree, then such determination (and supporting calculations) shall be made by attorneys, accountants, or an executive compensation consulting firm each as selected by the Company at the expense of the Company (the "280G Service Providers"). Any determination by the 280G Service Providers made in good faith shall be binding upon the Company and Executive.

4. No Mitigation. In no event, except as set forth expressly in this or another agreement signed by Executive, shall Executive be obligated to seek other employment or take any other action by way of mitigation of the amounts payable to Executive under any of the provisions of this Agreement and, subject to the aforesaid exception, such amounts shall not be reduced whether or not Executive obtains other employment.

5. Restrictive Covenants. As a condition of the effectiveness of this Agreement, Executive shall have previously, or contemporaneously with the execution of this Agreement, executed and delivered to the Company a Confidentiality Agreement in form and substance reasonably acceptable to the Company and Executive.

6. Payments Subject to Section 409A. Subject to the provisions in this Section 6, any severance payments or benefits under this Agreement shall begin only upon the date of Executive's "separation from service" (determined as set forth below) which occurs on or after the date of termination of employment. The following rules shall apply with respect to distribution of the payments and benefits, if any, to be provided to Executive under this Agreement:

6.1 It is intended that each installment of the severance payments and benefits provided under this Agreement shall be treated as a separate "payment" for purposes of Section 409A. Neither Executive nor the Company shall have the right to accelerate or defer the delivery of any such payments or benefits except to the extent specifically permitted or required by Section 409A.

6.2 If, as of the date of Executive's "separation from service" from the Company, Executive is not a "specified employee" (within the meaning of Section 409A), then each installment of the severance payments and benefits shall be made on the dates and terms set forth in this Agreement

6.3 If, as of the date of Executive's "separation from service" from the Company, Executive is a "specified employee" (within the meaning of Section 409A), then:

6.3.1 Each installment of the severance payments and benefits due under this Agreement that, in accordance with the dates and terms set forth herein, will in all circumstances, regardless of when the separation from service occurs, be paid within the short-term deferral period (as defined under Section 409A) shall be treated as a short-term deferral within the meaning of Treasury Regulation Section 1.409A-1(b)(4) to the maximum extent permissible under Section 409A and shall be paid at the time and in the matter set forth in this Agreement; and

6.3.2 Each installment of the severance payments and benefits due under this Agreement that is not described in Subsection 6.3.1 above and that would, absent this subsection, be paid within the six-month period following Executive's "separation from service" from the Company shall not be paid until the date that is six months and one day after such separation from service (or, if earlier, Executive's death), with any such installments that are required to be delayed being accumulated during the six-month period and paid in a lump sum on the date that is six months and one day following Executive's separation from service and any subsequent installments, if any, being paid in accordance with the dates and terms set forth herein; provided, however, that the preceding provisions of this sentence shall not apply to any installment of severance payments and benefits if and to the maximum extent that such installment is deemed to be paid under a separation pay plan that does not provide for a deferral of compensation by reason of the application of Treasury Regulation 1.409A-1(b)(9)(iii) (relating to separation pay upon an involuntary separation from service). Any installments that qualify for the exception under Treasury Regulation Section 1.409A-1(b)(9)(iii) must be paid no later than the last day of Executive's second taxable year following the taxable year in which the separation from service occurs.

6.4 The determination of whether and when Executive's separation from service from the Company has occurred shall be made in a manner consistent with, and based on the presumptions set forth in, Treasury Regulation Section 1.409A-1(h). Solely for purposes of this Section 6.4, "Company" shall include all persons with whom the Company would be considered a single employer as determined under Treasury Regulation Section 1.409A-(h)(3).

6.5 All reimbursements and in-kind benefits provided under this Agreement shall be made or provided in accordance with the requirements of Section 409A to the extent that such reimbursements or in-kind benefits are subject to Section 409A, including, where applicable, the requirement that (i) any reimbursement is for expenses incurred during Executive's lifetime (or during a shorter period of time specified in this Agreement), (ii) the amount of expenses eligible for reimbursement during a calendar year may not affect the expenses eligible for reimbursement in any other calendar year, (iii) the reimbursement of an eligible expense will be made on or before the last day of the calendar year following the year in which the expense is incurred, and (iv) the right to reimbursement is not subject to set off or liquidation or exchange for any other benefit.

7. Return of Company Property. Upon termination of employment for any reason, Executive shall promptly return to the Company any keys, credit cards, passes, confidential documents or material, computer equipment, or other property belonging to the Company, and Executive shall also return all writings, files, records, correspondence, notebooks, notes and other documents and things (including any copies thereof) containing confidential information or relating to the business or proposed business of the Company or the Affiliated Entities or containing any trade secrets relating to the Company or the Affiliated Entities. For purposes of the preceding sentence, the term "trade secrets" shall have the meaning ascribed to it under the Uniform Trade Secrets Act. Executive agrees to represent in writing to the Company upon termination of employment that he has complied with the foregoing provisions of this Section.

8. Assistance with Claims. Executive agrees that, consistent with Executive's business and personal affairs, during and after his employment by the Company he will assist the Company and the Affiliated Entities in the defense of any claims, or potential claims that may be made or are threatened to be made against any of them in any action, suit or proceeding, whether civil, criminal, administrative or investigative (a "Proceeding"), and will assist the Company and the Affiliated Entities in the prosecution of any claims that may be made by the Company or the Affiliated Entities in any Proceeding, to the extent that such claims may relate to Executive's employment or the period of Executive's employment by the Company. The Company agrees to (i) reimburse Executive for all of Executive's reasonable out-of-pocket expenses associated with such assistance, including travel expenses and (ii) with respect to assistance provided after Executive's employment, compensate Executive on an hourly basis, based on a rate commensurate with Executive's base salary (assuming a forty (40) hour work week) in effect on the Date of Termination, for time Executive spends in excess of ten (10) hours in any calendar quarter providing such assistance to the Company, provided that such time shall not include any time spent testifying in any arbitration, trial, administrative hearing or other proceeding. Any amounts to be paid to Executive pursuant to this Section 8 shall be paid by the Company no later than thirty (30) days of the date on which Executive provides documentation to the Company that such expenses were incurred.

9. Successors. This Agreement is personal to Executive and shall not be assignable by Executive without the prior written consent of the Company. This Agreement and any rights and benefits hereunder shall inure to the benefit of and be enforceable by Executive's legal representatives, heirs or legatees. This Agreement and any rights and benefits hereunder shall inure to the benefit of and be binding upon the Company and its successors and assigns, including any corporation with which or into which the Company may be merged or which may succeed to its assets or business.

10. Miscellaneous.

10.1 Entire Agreement/Modification/Choice of Law/Enforceability/Jury Waiver. Both Executive and the Company acknowledge that this Agreement is the entire agreement of the parties, and supersedes any prior or contemporaneous discussions, understandings, or agreements, with respect to the subject matter hereof. For the avoidance of doubt and without limiting the foregoing, (a)

Executive shall not be eligible to receive severance or similar post-employment payments or benefits under any severance plan, program or policy now or hereafter maintained by the Company, and (b) any employment offer letter or employment agreement between Executive and the Company (such offer letter or employment agreement, the "Employment Agreement") shall survive the execution and delivery of this Agreement and remain in full force and effect in accordance with its original terms; provided, however, that any provisions of the Employment Agreement relating to severance and post-employment payments and benefits shall be superseded hereby in their entirety and shall hereafter cease to be of any force or effect. This Agreement may be amended only in a written agreement duly executed by the parties hereto. This Agreement shall be deemed to have been made in the Commonwealth of Massachusetts and shall be governed by and construed in accordance with the laws of such Commonwealth, without giving effect to conflict of law principles. Both parties agree that any action, demand, claim or counterclaim relating to the terms and provisions of this Agreement, or to its formation or breach, or to Executive's employment or the termination thereof, shall be commenced only in Massachusetts in a court of competent jurisdiction, and further acknowledge that venue for such actions shall lie exclusively in Massachusetts. Both parties hereby waive and renounce in advance any right to a trial by jury in connection with such legal action.

10.2 Withholding. The Company may withhold from any amounts payable under this Agreement such Federal, state, local or foreign taxes as shall be required to be withheld pursuant to any applicable law or regulation.

10.3 No Guarantee of any Tax Consequences. The Company makes no guarantee of any tax consequences with respect to any payment hereunder including, without limitation, under Section 409A.

10.4 Severability. The invalidity or unenforceability of any provision of this Agreement will not affect the validity or enforceability of any other provision of this Agreement, and this Agreement will be construed as if such invalid or unenforceable provision were omitted (but only to the extent that such provision cannot be appropriately reformed or modified).

10.5 Waiver of Breach. No waiver by any party hereto of a breach of any provision of this Agreement by any other party, or of compliance with any condition or provision of this Agreement to be performed by such other party, will operate or be construed as a waiver of any subsequent breach by such other party of any similar or dissimilar provisions and conditions at the same or any prior or subsequent time.

10.6 Notices. Notices and all other communications provided for in this Agreement shall be in writing and shall be delivered personally or sent by registered or certified mail, return receipt requested, postage prepaid, or prepaid overnight courier to the parties at the addresses set forth below (or such other addresses as shall be specified by the parties by like notice):

to the Company:

Aileron Therapeutics, Inc.
490 Arsenal Way
Watertown, MA 02472
Attention: Chief Executive Officer

with a copy to:

Wilmer Cutler Pickering Hale and Dorr, LP
60 State Street
Boston, MA 02109
Attention: Stuart Falber

or to Executive:

At the most recent address maintained
by the Company in its personnel records

10.7 Each party, by written notice furnished to the other party, may modify the applicable delivery address, except that notice of change of address shall be effective only upon receipt. Such notices, demands, claims and other communications shall be deemed given in the case of delivery by overnight service with guaranteed next day delivery, the next day or the day designated for delivery; or in the case of certified or registered U.S. mail, five days after deposit in the U.S. mail; provided, however, that in no event shall any such communications be deemed to be given later than the date they are actually received.

10.8 Not Employment Contract. Executive acknowledges that this Agreement does not constitute a contract of employment, does not imply that the Company will continue his employment for any period of time and does not change the at-will nature of his employment.

10.9 Survivorship. Upon the expiration or other termination of this Agreement, the respective rights and obligations of the parties hereto shall survive such expiration or other termination to the extent necessary to carry out the intentions of the parties under this Agreement.

10.10 Counterparts. This Agreement may be executed in separate facsimile or electronic counterparts, each of which is deemed to be an original and all of which taken together constitute one and the same agreement.

10.11 Representations. Executive hereby acknowledges that he understands this Agreement and enters into this Agreement voluntarily.

IN WITNESS THEREOF, Executive has hereunto set his hand, and the Company has caused this Agreement to be executed in its name and on its behalf, all as of the day and year first above written.

AILERON THERAPEUTICS, INC.	Allen Annis
/s/ Don Dougherty	/s/ Allen Annis
Name: Don Dougherty	
Title: Chief Financial Officer	

Exhibit 10.23

February 15, 2019

Kathryn Gregory

Dear Kathryn**:**

It is my great pleasure to extend to you this offer of employment with Aileron Therapeutics, Inc. (the "Company"). The purpose of this letter is to summarize the terms of your employment with the Company, should you accept our offer:

1. **Employment.** You will be employed to serve on a full-time basis as Senior Vice President, Chief Business Officer, reporting to the Company's chief executive officer, commencing February 25, 2019 (the "Effective Date"). You agree to devote your best efforts, skill, knowledge, attention and energies to the advancement of the Company's business and interests and to the performance of your duties and responsibilities as an employee of the Company.

2. **Base Salary and Bonus.** Your base salary will be at the rate of $14,166.67 per semi-monthly pay period (equivalent to $340,000 annualized) less all applicable taxes and withholdings, to be paid in installments in accordance with the Company's regular payroll practices. Your base salary may be adjusted in the sole discretion of the Company from time to time in accordance with normal business practices. Following the end of each calendar year in which you are employed by the Company, you may be eligible for a discretionary performance bonus of up to 35% of your then current annualized base salary, as may be determined by the Company's Board of Directors ("Board") in its sole discretion. Any such bonus shall be based on the achievement of performance milestones for that calendar year as may be determined by the Board in its sole discretion. Any such discretionary bonus shall be paid to you in the subsequent calendar year in accordance with the Company's customary practices. You must be an active employee of the Company on the date the bonus is distributed in order to be eligible for and to earn any bonus award, as it also serves as an incentive to remain employed by the Company. You will be eligible for this annual bonus award beginning with 2019 calendar year performance. All compensation payable to you will be subject to applicable taxes and withholdings.
3. **Equity.** Subject to approval by the Board, you will receive options to purchase up to 100,000 shares of the Company's Common Stock under the Company's 2017 Stock Incentive Plan (the "Plan") for a price per share equal to the fair market value of one share of the Common Stock on the date of the option grant as determined by the Board and pursuant and subject to the terms of the Company's option agreement (which must be executed to receive the grant) and the Plan. The stock options will vest (become exercisable) as follows: 25% of the shares underlying the options shall vest upon the twelve (12) month anniversary of the Effective Date and 1/36th of the remainder of such shares will vest on a monthly basis in thirty-six (36) equal monthly installments with the first such installment vesting on the thirteenth month anniversary

of the Effective Date, subject to your continued employment with the Company through each vesting date. You may also be eligible for other grants of stock or stock options as determined by and in the sole discretion of the Board. Any such grant of stock or stock options will be subject to all of the terms and conditions of the relevant stock plan and stock or stock option agreement.

4. **Location and Relocation Expenses.**

(a) From the Effective Date until the earliest of (i) the first anniversary of the Effective Date, (ii) the nine-month anniversary of the Company's completion of a fundraising transaction which the Company believes will enable it to fund its operations into at least May 2020 and (iii) your relocation to Massachusetts (the "Initial Employment Period"), you will be required to work a minimum of four business days per week in the Company's headquarters. During the Initial Employment Period, upon presentation of appropriate documentation, you will be reimbursed up to a total of $36,000 for expenses to be applied to travel and living accommodations reasonably incurred by you in order for you while working at the Company's headquarters. Your schedule will be agreed upon between you and the chief executive officer. In addition to managing the Company's business development activities, it is expected that you will play a leadership role in the Company. As such, it is understood that working in the Company's headquarters for a minimum of four business days and interacting with employees is a necessary component of your employment. When you are working outside of the Company's headquarters, you will be available for calls and to participate in meetings telephonically during regular business hours and as required by business needs. It is further understood that the needs of the Company may from time-to-time require you to spend more than four business days in the Company's headquarters during the Initial Employment Period, and by accepting this offer of employment you hereby agree to do so as reasonably required in consultation with the chief executive officer and to travel as required by the Company's business needs.

(b) You will be required to relocate and work full time from the Company's headquarters prior to the date that is nine months following the end of the Initial Employment Period; provided, however, that during the period from the end of the Initial Employment Period until your relocation (if any) (the "Post-Initial Employment Period"), you shall continue to work in compliance with Section 4(a) as if such period were the Initial Employment Period. Upon presentation of appropriate documentation, you will be reimbursed up to a total of $50,000 for expenses reasonably incurred by you in connection with your relocation. Notwithstanding the foregoing, you agree that if, prior to the second anniversary of your relocation, you terminate your employment with the Company other than for Good Reason or the Company terminates your employment for Cause (as such terms are defined in the Severance Agreement (as defined below)), you shall pay to the Company within 15 days of such termination an amount determined by multiplying the amount actually reimbursed to you up to $50,000 by a fraction, the numerator of which equals the number of days in such two-year period that you are not an employee of the Company and the denominator of which equals the total number of days in such two-year period.

5. Benefit Programs. You may choose to participate in any and all benefit programs that the Company establishes and makes available to its employees from time to time, provided you are eligible under (and subject to all provisions of) the plan documents governing those programs. This presently includes (among other benefits) health and dental insurance, paid holidays, and a 401(k) savings program. Our benefits also include four (4) weeks of paid vacation per calendar year to be taken at such times as may be approved in advance by the Company, which approval will not be unreasonably withheld. The number of vacation days for which you are eligible shall accrue at the rate of 1.67 days per month that you are employed during such calendar year. You will also be entitled to sick leave and all Company holidays as determined by the Company, on the same terms as similarly situated senior executives. Where a particular benefit is subject to a formal plan, eligibility to participate in and receive any particular benefit is governed solely by the applicable plan document. Benefits are subject to change at any time in the Company's sole discretion.

6. **Business Expenses.** The Company will reimburse you for all documented, reasonable and necessary business expenses in accordance with the Company's expense reimbursement policy.

7. **Termination Benefits**. Concurrently with the execution of this Agreement, the Company and you shall sign the Severance Agreement attached hereto as Exhibit A (the "Severance Agreement").

8. **Indemnification and Insurance.** In connection with your employment with the Company, you will be entitled to indemnification to the fullest extent permitted by the Company's By-Laws and will be entitled to coverage under the Company's directors' and officers' liability insurance policy to the same extent as other senior executives of the Company.

9. **Confidentiality, Inventions and Non-Solicitation Agreement.** In order to protect the Company's substantial investment of time and money in the creation and maintaining of its Confidential Information and good-will, employees are required as a condition of employment, and continued employment, to execute the Proprietary Rights, Non-Disclosure, and Non-Solicitation Agreement (the "NSA") between you and the Company . The terms and conditions of the NSA will apply, regardless of any change in the nature of your duties, compensation or employment with any entity related to the Company.

   Just as the Company regards the protection of our confidential information as a matter of great importance, we also respect that you may have an obligation to your prior employers to safeguard the confidential information of those companies. The Company respects these obligations, and expects you to honor them as well. To that end, you hereby represent that you have disclosed and provided copies of any agreement that you have with a prior employer that relates to any obligations of the type and nature reflected in our NSA. We also expect that you have not taken any documents or other confidential information from your employer, and that you will make certain that you do not maintain any information that you may have received electronically. Further, we want to make it perfectly clear that you should not bring with you to the Company, or use in the performance of your responsibilities for the Company, any proprietary business or technical information, materials or documents of a former employer, or otherwise disclose or use any former employer's confidential information.

10. **Company Policies and Procedures.** As an employee of the Company, you will be required to comply with all Company policies and procedures, as in effect from time to time. Violations of the Company's policies may lead to immediate termination of your employment. Further, the Company's premises, including all workspaces, furniture, documents and other tangible materials, and all information technology resources of the Company (including computers, data and other electronic files, and all Internet and e-mail usage) are subject to oversight and inspection by the Company at any time. Company employees should have no expectation of privacy with regard to any Company premises, materials, resources or information, including any personal emails or other communications that are delivered into or out of a Company system.

11. **<u>Proof of Legal Right to Work.</u>** For purposes of federal immigration law, you will be required to provide the Company with documentary evidence of your identity and eligibility for employment in the United States. Such documentation must be provided to the Company within three (3) business days of your date of hire, or our employment relationship with you may be terminated. You may need to obtain a work visa in order to be eligible to work in the United States. If that is the case, your employment with the Company will be conditioned upon your obtaining a work visa in a timely manner as determined by the Company.

12. **<u>Nature of the Relationship</u>.** While we obviously are hopeful and confident that our relationship will be mutually rewarding, satisfactory and sustaining, this letter shall not be construed as an agreement, either express or implied, to employ you for any stated term, and shall in no way alter the Company's policy of employment at will, under which both you and the Company remain free to end the employment relationship. Similarly, nothing in this letter shall be construed as an agreement, either express or implied, to pay you any compensation of any kind, or grant you any benefit beyond the end of your employment with the Company. Also, this letter and the exhibits attached to this letter constitutes our entire offer regarding the terms and conditions of your employment by the Company, it supersedes any prior agreements, or other promises or statements (whether oral or written) regarding the offered terms of employment. Your employment with the Company shall be governed by and construed under the internal laws of the Commonwealth of Massachusetts, without giving effect to conflict of law principles.

[Remainder of Page Intentionally Left Blank]

This offer is contingent on your authorization and completion of reference checks, all being completed to the satisfaction of the Company. Such activities shall be completed prior to the Effective Date.

We are excited about the prospect of having you join the Company. We look forward to receiving your response acknowledging, by signing below, that you have accepted this offer of employment.

Very truly yours,

By: /s/ Manuel Aivado
Manuel Aivado, MD, PhD
President and Chief Executive Officer

Accepted and Agreed To:

/s/ Kathryn J. Gregory
Name: Kathryn Gregory

Date: 2/17/2019

EXHIBIT A

Severance Agreement

SEVERANCE AGREEMENT

This SEVERANCE AGREEMENT (this "Agreement") is made and entered into as of February 25, 2019 by and between Kathryn Gregory ("Executive") and Aileron Therapeutics, Inc. (the "Company").

WHEREAS, Executive is employed as a senior executive of the Company, and the Company desires to continue to retain the services of Executive; and

WHEREAS, the Company is entering into this Agreement in order to provide certain compensation and benefits to Executive in the event Executive's employment with the Company is terminated under certain circumstances.

NOW, THEREFORE, for good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the Company and Executive agree as follows:

1. Definitions.

1.1 "Affiliated Entity" means any corporation, partnership, trust or other entity of which the Company and/or any of its Affiliated Entities directly or indirectly owns a majority of the outstanding shares of any class of equity security thereof and any corporation, partnership, trust or other entity which directly or indirectly owns a majority of the outstanding shares of any class of any equity security of the Company or any of its Affiliated Entities.

1.2 "Cause" shall mean a finding by the Board that Executive: (i) materially breached Executive's Confidentiality, Inventions, Non-Competition and Non-Solicitation Agreement or any similar agreement between Executive and the Company (a "Confidentiality Agreement"); (ii) engaged in fraud, or embezzlement; (iii) engaged in willful misconduct or gross negligence with regard to the Company that the Board determines in good faith is, or is reasonably likely to be, materially injurious to the Company and its reputation; (iv) materially violated the Company's published policies, including those prohibiting unlawful harassment and discrimination, as in effect from time to time; or (v) was convicted of, or pleaded guilty or nolo contendere to any felony (other than traffic-related offenses).

1.3 "Change in Control Event" means

1.3.1 the acquisition by an individual, entity or group (within the meaning of Section 13(d)(3) or 14(d)(2) of the Securities Exchange Act of 1934, as amended) (a "Person") of beneficial ownership of any capital stock of the Company if, after such acquisition, such Person beneficially owns (within the meaning of Rule 13d-3 under the Securities Exchange Act of 1934, as amended) 50% or more of either (x) the then-outstanding shares of common stock of the

Company (the “Outstanding Company Common Stock”) or (y) the combined voting power of the then-outstanding securities of the Company entitled to vote generally in the election of directors (the “Outstanding Company Voting Securities”); provided, however, that for purposes of this Subsection 1.3.1, the following acquisitions shall not constitute a Change in Control Event: (A) any acquisition directly from the Company or (B) any acquisition by any corporation pursuant to a Business Combination (as defined below) which complies with clauses (x) and (y) of Subsection 1.3.2 of this definition;

1.3.2 the consummation of a merger, consolidation, reorganization, recapitalization or share exchange involving the Company or a sale or other disposition of all or substantially all of the assets of the Company (a “Business Combination”), unless, immediately following such Business Combination, each of the following two conditions is satisfied: (x) the Outstanding Company Common Stock and Outstanding Company Voting Securities immediately prior to such Business Combination represent more than 50% of the then-outstanding shares of common stock or other common equity and the combined voting power of the then-outstanding securities entitled to vote generally in the election of directors or other governing body, respectively, of the resulting or acquiring entity in such Business Combination (which shall include, without limitation, an entity which as a result of such transaction owns the Company or substantially all of the Company’s assets either directly or through one or more subsidiaries) (such resulting or acquiring corporation is referred to herein as the “Acquiring Entity”) and (y) no Person (excluding any employee benefit plan (or related trust) maintained or sponsored by the Company or by the Acquiring Entity) beneficially owns, directly or indirectly, 50% or more of the then-outstanding shares of common stock of the Acquiring Entity, or of the combined voting power of the then-outstanding securities of such entity entitled to vote generally in the election of directors or other governing body (except to the extent that such ownership existed prior to the Business Combination); or

1.3.3 the liquidation or dissolution of the Company;

provided that such Change in Control Event also satisfies Treasury Regulation Section 1.409A-3(i)(5) where required for compliance with Section 409A of the Internal Revenue Code and the guidance issued thereunder (“Section 409A”).

1.4 “Date of Termination” means: (i) if Executive’s employment ends other than for death, Executive’s last day of employment with the Company and, (ii) if Executive’s employment is terminated by reason of death, the date of Executive’s death.

1.5 “Disability” shall mean any long-term disability or incapacity due to physical or mental illness that renders Executive unable to substantially perform his duties for at least ninety (90) consecutive days or one hundred twenty (120) total days during any twelve (12) month period, provided that it may occur in a shorter period if, after its commencement, it is determined to be total and permanent by a physician selected by the Company and its insurers and such determination is acceptable to Executive or to Executive’s legal representative (with such agreement on acceptability not to be unreasonably withheld).

1.6 “Good Reason” means (i) a material diminution in the nature or scope of Executive’s duties, responsibilities, or authority; (ii) a material reduction in Executive’s base salary then in effect; (iii) a material reduction by the Company in the kind or level of employee benefits to which Executive is entitled immediately prior to such reduction with the result that the overall benefits package is materially reduced, other than a reduction comparable to reductions generally applicable to similarly situated employees of the Company; or (iv) the Company’s requiring Executive’s ongoing and regular services to be performed at a location more than fifty (50) miles from the geographic location at which Executive was providing services before such requirement. In order to terminate Executive’s employment for Good Reason, Executive must (w) give notice to the Company of Executive’s intention to resign for Good Reason within ninety (90) days after the occurrence of the event (or series of events) that Executive asserts entitles Executive to resign for Good Reason, (x) state in that notice the event that Executive considers to provide Executive with Good Reason to resign, (y) provide the Company with at least thirty (30) days after Executive’s notice to cure the event, and (z) if the event is not cured within such thirty-day cure period, resign for Good Reason within thirty (30) days after the end of the thirty-day cure period.

2. Obligations of the Company upon Termination.

2.1 Termination for Any Reason or No Reason. In the event of the termination of Executive’s employment for any reason or for no reason, the Company will pay to Executive (or to his estate) (i) the portion of his annualized base salary that has accrued prior to such termination and has not yet been paid and, to the extent consistent with general Company policy, accrued but unused paid time off through and including the Date of Termination, (ii) any bonus amount not yet paid that was earned by and approved for payment to Executive by the Board during or with respect to the calendar year preceding the Date of Termination; (iii) reimbursement for expenses properly incurred by Executive on behalf of the Company prior to such termination and properly documented in accordance with Company policy, and (iv) to the extent not theretofore paid or provided, any other amounts or benefits required to be paid or provided or which Executive is eligible to receive under any plan or agreement of or with the Company through the Date of Termination (all such amounts, collectively, the “Accrued Obligations”). The Accrued Obligations will be paid as required by law but in any event promptly after termination or as provided by any applicable policy, plan or agreement.

2.2 Termination by the Company Other Than for Cause or by Reason of Executive's Death or Disability; By Executive for Good Reason; and Other than Upon or within Twelve Months following a Change in Control Event. Subject to the satisfaction of the Severance Conditions (as defined below), if Executive's employment is terminated (i) by the Company other than (x) for Cause or (y) by reason of Executive's death or Disability, or (ii) by Executive for Good Reason, and, in each case, other than upon or within twelve (12) months following a Change in Control Event (the "CIC Period"), then in addition to the Accrued Obligations, the Company shall:

2.2.1 Pay to Executive a sum equal to nine (9) months of base salary at Executive's most recent base salary rate, such payment to be made in approximately equal installments according to the Company's then-current payroll practices.

2.2.2 Provided that Executive is eligible for and elects to continue receiving medical insurance pursuant to the federal "COBRA" law, 29 U.S.C. § 1161 et seq., continue to pay on Executive's behalf the share of the monthly premiums for such coverage that it pays for active and similarly situated employees receiving the same type of coverage for a period of up to nine (9) months following the Date of Termination. The remaining balance of the premium costs and all premium costs after such nine (9) month period shall be paid by Executive on a monthly basis for as long as, and to the extent that, he remains eligible for and elects to continue receiving continued coverage under COBRA; provided, however, that notwithstanding the foregoing, in the event Executive becomes eligible during the nine (9) month period for the same or substantially similar group health insurance coverage through another employer, Executive shall immediately notify the Company in writing of the date of eligibility for such coverage (the "Eligibility Date"), and the Company's obligation to make monthly premium payments pursuant to this Subsection 2.2.2 shall end on the Eligibility Date. Notwithstanding the foregoing, payments by the Company under this Subsection 2.2.2 (but not eligibility for COBRA) shall end early if the Company determines that the continued payments are reasonably likely to result in penalties on the Company, taxation of any other employee, or taxation of Executive on income other than the payment of the premiums; provided, however, that if the Company is able to reasonably conclude that making a taxable lump sum payment to Executive in the amount of and in lieu of any remaining COBRA premiums that would otherwise be paid by the Company on Executive's behalf under this Subsection 2.2.2 would not result in any such penalties or taxation, the Company will make such lump sum payment no later than the last day of the nine (9) month period following the Date of Termination.

2.3 Termination By the Company for Cause; By Reason of Executive's Death or Disability; Or By Executive Other than for Good Reason. If Executive's employment is terminated by the Company for Cause, or by reason of Executive's death or Disability, or by Executive for any reason other than for Good Reason, this Agreement shall terminate without further obligations to Executive or Executive's legal representatives under this Agreement, other than for payment of the Accrued Obligations.

2.4 Effect of Termination on Other Positions. If, on the Date of Termination, Executive is a member of the Company's Board of Directors (the "Board") or the board of directors of any Affiliated Entity, or holds any other office or position with the Company or any Affiliated Entity, Executive shall, unless otherwise requested by the Company, be deemed to have resigned from all such offices and positions as of the Date of Termination. Executive agrees to execute such documents and take such other actions as the Company may request to reflect such resignation.

2.5 Conditions to Payment of Post-Separation Benefits. As a condition of Executive's receipt of the post-separation benefits in Section 2.2 and Section 3.1, Executive must execute and return to the Company a severance and release of claims agreement provided by and satisfactory to the Company (the "Release Agreement"), and such Release Agreement must become binding, enforceable and irrevocable within sixty (60) calendar days after Executive's termination of employment (the "Severance Conditions"). Payments will begin in the first pay period beginning after the Severance Conditions have been satisfied or as promptly as practicable thereafter, provided that if the foregoing sixty (60) day period would end in a calendar year subsequent to the year in which Executive's employment ends, payments will not be made before the first payroll period of the subsequent year (the "Payment Date"). Notwithstanding the foregoing, the acceleration of vesting of the Equity Awards contemplated by Subsection 3.1.4 below shall take immediate effect upon the Date of Termination; provided, however, that Executive agrees that the portion of such Equity Awards that shall have been accelerated pursuant to Subsection 3.1.4 (the "Accelerated Portion") shall not be exercised prior to the date on which the Severance Conditions have been satisfied, that any shares to be issued or retained under other Equity Awards will not be issued or retained prior to the date on which the Severance Conditions have been satisfied and that if the Severance Conditions have not been satisfied within the prescribed time period, than, as of such date, the Accelerated Portion shall be cancelled and cease to be exercisable, forfeited, or not issued, as applicable on the basis of the type of Equity Award.

3. <u>Change in Control</u>.

3.1 Subject to the satisfaction of the Severance Conditions, if, during the CIC Period, Executive's employment is terminated by the Company without Cause and not for death or Disability, or if Executive resigns his employment for Good Reason, then, in addition to the Accrued Obligations, the Company shall:

3.1.1 Pay to Executive a sum equal to twelve (12) months of base salary at Executive's most recent base salary rate, such payment to be made in approximately equal installments according to the Company's then-current payroll practices.

3.1.2 Provided that Executive is eligible for and elects to continue receiving medical insurance under COBRA, continue to pay on Executive's behalf the share of the monthly premiums for such coverage that it pays for active and similarly situated employees receiving the same type of coverage for a period of up to twelve (12) months following the Date of Termination. The remaining balance of the premium costs and all premium costs after such twelve (12) month period shall be paid by Executive on a monthly basis for as long as, and to the extent that, he remains eligible for and elects to continue receiving continued coverage under COBRA; provided, however, that notwithstanding the foregoing, in the event Executive becomes eligible during the twelve (12) month period for the same or substantially similar group health insurance coverage through another employer, Executive shall immediately notify the Company in writing of the Eligibility Date, and the Company's obligation to make monthly premium payments pursuant to this Subsection 3.1.2 shall end on the Eligibility Date. Notwithstanding the foregoing, payments by the Company under this Subsection 3.1.2 (but not eligibility for COBRA) shall end early if the Company determines that the continued payments are reasonably likely to result in penalties on the Company, taxation of any other employee, or taxation of Executive on income other than the payment of the premiums; provided, however that if the Company is able to reasonably conclude that making a taxable lump sum payment to Executive in the amount of and in lieu of any remaining COBRA premiums that would otherwise be paid by the Company on Executive's behalf under this Subsection 3.1.2 would not result in any such penalties or taxation, the Company will make such lump sum payment no later than the last day of the twelve (12) month period following the Date of Termination.

3.1.3 Pay to Executive, on the Payment Date, a lump sum equal to one times (1 x) Executive's target bonus award for the year in which the Date of Termination occurs without regard to whether the performance goals applicable to such target bonus had been established or satisfied at the Date of Termination.

3.1.4 Notwithstanding the terms of any stock option agreement, restricted stock agreement or other stock award ("Equity Award"), other than terms more favorable to Executive, effective as of the Termination Date, accelerate the vesting of all Equity Awards held by Executive at the Termination Date (other than Equity Awards that vest on the basis of performance and do not provide solely for time-based vesting), such that such Equity Awards shall become 100% vested.

3.2 280G. Notwithstanding any other provision of this Agreement to the contrary, if payments made hereunder or otherwise are considered "excess parachute payments" under Section 280G of the Internal Revenue Code of 1986, as amended (the "Code"), then such excess parachute payments plus any other payments made by the Company and its affiliates that Executive is entitled to receive that are considered excess parachute payments shall be limited to the greatest amount that may be paid to Executive under Section 280G of the Code without causing any loss of deduction to the Company under such Code Section, but only if, by reason of such reduction, the "Net After Tax Benefit" (as defined below) to Executive exceeds the net after tax benefit if such reduction was not made. "Net After Tax Benefit" for purposes of this Agreement shall mean the sum of (i) the total amounts payable to Executive that would constitute an "excess parachute payment" within the meaning of Section 280G of the Code, less (ii) the amount of federal, state and other income taxes payable with respect to the foregoing calculated at the maximum marginal tax rate for each year in which the foregoing shall be paid to Executive (based upon the rate in effect for such year as set forth in the Code at the time of termination of Executive's employment or the change in control), less (iii) the amount of excise taxes imposed with respect to the payments and benefits described above by Section 4999 of the Code. The determination of whether payments would be considered excess parachute payments and the calculation of all the amounts referred to in this section shall be made reasonably and in good faith by the parties, *provided*, that if the parties cannot agree, then such determination (and supporting calculations) shall be made by attorneys, accountants, or an executive compensation consulting firm each as selected by the Company at the expense of the Company (the "280G Service Providers"). Any determination by the 280G Service Providers made in good faith shall be binding upon the Company and Executive.

4. No Mitigation. In no event, except as set forth expressly in this or another agreement signed by Executive, shall Executive be obligated to seek other employment or take any other action by way of mitigation of the amounts payable to Executive under any of the provisions of this Agreement and, subject to the aforesaid exception, such amounts shall not be reduced whether or not Executive obtains other employment.

5. Restrictive Covenants. As a condition of the effectiveness of this Agreement, Executive shall have previously, or contemporaneously with the execution of this Agreement, executed and delivered to the Company a Confidentiality Agreement in form and substance reasonably acceptable to the Company and Executive.

6. Payments Subject to Section 409A. Subject to the provisions in this Section 6, any severance payments or benefits under this Agreement shall begin only upon the date of Executive's "separation from service" (determined as set forth below) which occurs on or after the date of termination of employment. The following rules shall apply with respect to distribution of the payments and benefits, if any, to be provided to Executive under this Agreement:

6.1 It is intended that each installment of the severance payments and benefits provided under this Agreement shall be treated as a separate "payment" for purposes of Section 409A. Neither Executive nor the Company shall have the right to accelerate or defer the delivery of any such payments or benefits except to the extent specifically permitted or required by Section 409A.

6.2 If, as of the date of Executive's "separation from service" from the Company, Executive is not a "specified employee" (within the meaning of Section 409A), then each installment of the severance payments and benefits shall be made on the dates and terms set forth in this Agreement

6.3 If, as of the date of Executive's "separation from service" from the Company, Executive is a "specified employee" (within the meaning of Section 409A), then:

6.3.1 Each installment of the severance payments and benefits due under this Agreement that, in accordance with the dates and terms set forth herein, will in all circumstances, regardless of when the separation from service occurs, be paid within the short-term deferral period (as defined under Section 409A) shall be treated as a short-term deferral within the meaning of Treasury Regulation Section 1.409A-1(b)(4) to the maximum extent permissible under Section 409A and shall be paid at the time and in the matter set forth in this Agreement; and

6.3.2 Each installment of the severance payments and benefits due under this Agreement that is not described in Subsection 6.3.1 above and that would, absent this subsection, be paid within the six-month period following Executive's "separation from service" from the Company shall not be paid until the date that is six months and one day after such separation from service (or, if earlier, Executive's death), with any such installments that are required to be delayed being accumulated during the six-month period and paid in a lump sum on the date that is six months and one day following Executive's separation from service and any subsequent installments, if any, being paid in accordance with the dates and terms set forth herein; provided, however, that the preceding provisions of this sentence shall not apply to any installment of severance payments and benefits if and to the maximum extent that such installment is deemed to be paid under a separation pay plan that does not provide for a deferral of compensation by reason of the application of Treasury Regulation 1.409A-1(b)(9)(iii) (relating to separation pay upon an involuntary separation from service). Any installments that qualify for the exception under Treasury Regulation Section 1.409A-1(b)(9)(iii) must be paid no later than the last day of Executive's second taxable year following the taxable year in which the separation from service occurs.

6.4 The determination of whether and when Executive's separation from service from the Company has occurred shall be made in a manner consistent with, and based on the presumptions set forth in, Treasury Regulation Section 1.409A-1(h). Solely for purposes of this Section 6.4, "Company" shall include all persons with whom the Company would be considered a single employer as determined under Treasury Regulation Section 1.409A-(h)(3).

6.5 All reimbursements and in-kind benefits provided under this Agreement shall be made or provided in accordance with the requirements of Section 409A to the extent that such reimbursements or in-kind benefits are subject to Section 409A, including, where applicable, the requirement that (i) any reimbursement is for expenses incurred during Executive's lifetime (or during a shorter period of time specified in this Agreement), (ii) the amount of expenses eligible for reimbursement during a calendar year may not affect the expenses eligible for reimbursement in any other calendar year, (iii) the reimbursement of an eligible expense will be made on or before the last day of the calendar year following the year in which the expense is incurred, and (iv) the right to reimbursement is not subject to set off or liquidation or exchange for any other benefit.

7. Return of Company Property. Upon termination of employment for any reason, Executive shall promptly return to the Company any keys, credit cards, passes, confidential documents or material, computer equipment, or other property belonging to the Company, and Executive shall also return all writings, files, records, correspondence, notebooks, notes and other documents and things (including any copies thereof) containing confidential information or relating to the business or proposed business of the Company or the Affiliated Entities or containing any trade secrets relating to the Company or the Affiliated Entities. For purposes of the preceding sentence, the term "trade secrets" shall have the meaning ascribed to it under the Uniform Trade Secrets Act. Executive agrees to represent in writing to the Company upon termination of employment that he has complied with the foregoing provisions of this Section.

8. Assistance with Claims. Executive agrees that, consistent with Executive's business and personal affairs, during and after his employment by the Company he will assist the Company and the Affiliated Entities in the defense of any claims, or potential claims that may be made or are threatened to be made against any of them in any action, suit or proceeding, whether civil, criminal, administrative or investigative (a "Proceeding"), and will assist the Company and the Affiliated Entities in the prosecution of any claims that may be made by the Company or the Affiliated Entities in any Proceeding, to the extent that such claims may relate to Executive's employment or the period of Executive's employment by the Company. The Company agrees to (i) reimburse Executive for all of Executive's reasonable out-of-pocket expenses associated with such assistance, including travel expenses and (ii) with respect to assistance provided after Executive's employment, compensate Executive on an hourly basis, based on a rate commensurate with Executive's base salary (assuming a forty (40) hour work week) in effect on the Date of Termination, for time Executive spends in excess of ten (10) hours in any calendar quarter providing such assistance to the Company, provided that such time shall not include any time spent testifying in any arbitration, trial, administrative hearing or other proceeding. Any amounts to be paid to Executive pursuant to this Section 8 shall be paid by the Company no later than thirty (30) days of the date on which Executive provides documentation to the Company that such expenses were incurred.

9. Successors. This Agreement is personal to Executive and shall not be assignable by Executive without the prior written consent of the Company. This Agreement and any rights and benefits hereunder shall inure to the benefit of and be enforceable by Executive's legal representatives, heirs or legatees. This Agreement and any rights and benefits hereunder shall inure to the benefit of and be binding upon the Company and its successors and assigns, including any corporation with which or into which the Company may be merged or which may succeed to its assets or business.

10. Miscellaneous.

10.1 Entire Agreement/Modification/Choice of Law/Enforceability/Jury Waiver. Both Executive and the Company acknowledge that this Agreement is the entire agreement of the parties, and supersedes any prior or contemporaneous discussions, understandings, or agreements, with respect to the subject matter hereof. For the avoidance of doubt and without limiting the foregoing, (a) Executive shall not be eligible to receive severance or similar post-employment payments or benefits under any severance plan, program or policy now or hereafter maintained by the Company, and (b) any employment offer letter or employment agreement between Executive and the Company (such offer letter or employment agreement, the "Employment Agreement") shall survive the execution and delivery of this Agreement and remain in full force and effect in accordance with its original terms; provided, however, that any provisions of the Employment Agreement relating to severance and post-employment payments and benefits shall be superseded hereby in their entirety and shall hereafter cease to be of any force or effect. This Agreement may be amended only in a written agreement duly executed by the parties hereto. This Agreement shall be deemed to have been made in the Commonwealth of Massachusetts and shall be governed by and construed in accordance with the laws of such Commonwealth, without giving effect to conflict of law principles. Both parties agree that any action, demand, claim or counterclaim relating to the terms and provisions of this Agreement, or to its formation or breach, or to Executive's employment or the termination thereof, shall be commenced only in Massachusetts in a court of competent jurisdiction, and further acknowledge that venue for such actions shall lie exclusively in Massachusetts. Both parties hereby waive and renounce in advance any right to a trial by jury in connection with such legal action.

10.2 Withholding. The Company may withhold from any amounts payable under this Agreement such Federal, state, local or foreign taxes as shall be required to be withheld pursuant to any applicable law or regulation.

10.3 No Guarantee of any Tax Consequences. The Company makes no guarantee of any tax consequences with respect to any payment hereunder including, without limitation, under Section 409A.

10.4 Severability. The invalidity or unenforceability of any provision of this Agreement will not affect the validity or enforceability of any other provision of this Agreement, and this Agreement will be construed as if such invalid or unenforceable provision were omitted (but only to the extent that such provision cannot be appropriately reformed or modified).

10.5 Waiver of Breach. No waiver by any party hereto of a breach of any provision of this Agreement by any other party, or of compliance with any condition or provision of this Agreement to be performed by such other party, will operate or be construed as a waiver of any subsequent breach by such other party of any similar or dissimilar provisions and conditions at the same or any prior or subsequent time.

10.6 Notices. Notices and all other communications provided for in this Agreement shall be in writing and shall be delivered personally or sent by registered or certified mail, return receipt requested, postage prepaid, or prepaid overnight courier to the parties at the addresses set forth below (or such other addresses as shall be specified by the parties by like notice):

to the Company:

Aileron Therapeutics, Inc.
490 Arsenal Way
Watertown, MA 02472
Attention: Chief Executive Officer

with a copy to:

Wilmer Cutler Pickering Hale and Dorr, LP
60 State Street
Boston, MA 02109
Attention: Stuart Falber

or to Executive:

At the most recent address maintained
by the Company in its personnel records

10.7 Each party, by written notice furnished to the other party, may modify the applicable delivery address, except that notice of change of address shall be effective only upon receipt. Such notices, demands, claims and other communications shall be deemed given in the case of delivery by overnight service with guaranteed next day delivery, the next day or the day designated for delivery; or in the case of certified or registered U.S. mail, five days after deposit in the U.S. mail; provided, however, that in no event shall any such communications be deemed to be given later than the date they are actually received.

10.8 Not Employment Contract. Executive acknowledges that this Agreement does not constitute a contract of employment, does not imply that the Company will continue his employment for any period of time and does not change the at-will nature of his employment.

10.9 Survivorship. Upon the expiration or other termination of this Agreement, the respective rights and obligations of the parties hereto shall survive such expiration or other termination to the extent necessary to carry out the intentions of the parties under this Agreement.

10.10 Counterparts. This Agreement may be executed in separate facsimile or electronic counterparts, each of which is deemed to be an original and all of which taken together constitute one and the same agreement.

10.11 Representations. Executive hereby acknowledges that he understands this Agreement and enters into this Agreement voluntarily.

IN WITNESS THEREOF, Executive has hereunto set his hand, and the Company has caused this Agreement to be executed in its name and on its behalf, all as of the day and year first above written.

AILERON THERAPEUTICS, INC.	NAME
/s/ Manuel Aivado	/s/ Kathryn J. Gregory
Name: Manuel Aivado	
Title: President and CEO	

Exhibit 10.25

AILERON THERAPEUTICS

CONSULTING AGREEMENT

This Consulting Agreement (the "**Agreement**"), made this 30th day of September, 2018, is entered into by Aileron Therapeutics, Inc., a Delaware corporation (the "**Company**"), and John P. Longenecker, an individual residing at 1436 Tres Hermanas Way, Encinitas, CA, 92024 (the "**Consultant**").

WHEREAS, the Company and the Consultant desire to establish the terms and conditions under which the Consultant will provide services to the Company following the termination of the Consultant's employment relationship with the Company on the date hereof.

NOW, THEREFORE, in consideration of the mutual covenants and promises contained herein and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged by the parties hereto, the parties agree as follows:

1. Services. The Consultant agrees to perform such consulting, advisory and related services to and for the Company as may be reasonably requested from time to time [by the Company][by the Chief Executive Officer of the Company], including advising the Company's Chief Executive Officer on business matters, including but not limited to, corporate governance, business strategies, financing strategies, intellectual property, business development and investor relations. The Consultant shall not be obligated to perform services hereunder for more than four days in any calendar month unless otherwise agreed by the Company and the Consultant.

2. Term. This Agreement shall commence upon the termination of the Consultant's employment with the Company, which shall terminate on the date hereof, and shall continue until December 31, 2018 (such period, as it may be extended or sooner terminated in accordance with the provisions of Section 4, being referred to as the "**Consultation Period**").

3. Compensation.

3.1 Consulting Fees. The Company shall pay to the Consultant a consulting fee of $12,000 per month payable in arrears on the last day of each calendar month (it being understood that the consulting fee for the period from September 30, 2018 to October 31, 2018 shall be $12,000). Payment for any partial month shall be prorated.

3.2 Expenses. The Company shall reimburse the Consultant for all reasonable and necessary documented out of pocket expenses incurred or paid by the Consultant in connection with, or related to, the performance of Consultant's services under this Agreement. The Consultant shall submit to the Company itemized monthly statements, in a form satisfactory to the Company, of the expenses incurred on behalf of the Company pursuant to this Agreement in the previous month. The Company shall pay to the Consultant amounts shown on each such statement within thirty (30) days after receipt thereof. Notwithstanding the foregoing, the Consultant shall not incur total expenses in excess of $500.00 per month without the prior written approval of the Company.

3.3 Benefits. The Consultant shall not be entitled to any benefits, coverages or privileges, including, without limitation, health insurance, social security, unemployment, medical or pension payments, made available to employees of the Company.

4. Termination. This Agreement may be terminated at any time in the following manner: (a) by either the Company or the Consultant upon not less than fifteen (15) days prior written notice to the other party; (b) by the non-breaching party, upon twenty-four (24) hours prior written notice to the breaching party if one party has materially breached this Agreement; or (c) at any time upon the mutual written consent of the parties hereto. In the event of termination, the Consultant shall be entitled to payment for services performed prior to the effective date of termination that have not been previously paid. Such payment shall constitute full settlement of any and all claims of the Consultant of every description against the Company. Notwithstanding the foregoing, the Company may terminate this Agreement effective immediately by giving written notice to the Consultant if the Consultant breaches or threatens to breach any provision of Section 7 of this Agreement or the Confidentiality, Inventions, and Restrictive Covenant Agreement previously executed by the Consultant for the benefit of the Company (the "**Confidentiality, Inventions, and Restrictive Covenant Agreement**").

5. Cooperation. The Consultant shall use Consultant's best efforts in the performance of Consultant's obligations under this Agreement. The Company shall provide such access to its information and property as may be reasonably required in order to permit the Consultant to perform Consultant's obligations hereunder. The Consultant shall cooperate with the Company's personnel, shall not interfere with the conduct of the Company's business and shall observe all rules, regulations and security requirements of the Company concerning the safety of persons and property.

6. Invention, Non-Disclosure, Non-Competition and Non-Solicitation Obligations. The Consultant acknowledges and reaffirms his obligations under the Confidentiality, Inventions, and Restrictive Covenant Agreement, which obligations shall remain in full force and effect during the Consultation Period as if the Consultant were an employee of the Company during such period, other than those obligations set forth under the captains "Employment Period Non-Compete" and "Non-Solicitation and Non-Interference", which obligations shall terminate as of the date hereof.

7. Non-Solicitation. During the Consultation Period and ending on September 30, 2020, the Consultant shall not, either alone or in association with others, (i) solicit, or permit any organization directly or indirectly controlled by the Consultant to solicit, any employee of the Company to leave the employ of the Company; and/or (ii) solicit or permit any organization directly or indirectly controlled by the Consultant to solicit any person who is employed or engaged by the Company.

8. Other Agreements; Warranty.

8.1 The Consultant hereby represents that, except as the Consultant has disclosed in writing to the Company, the Consultant is not bound by the terms of any agreement with any third party to refrain from using or disclosing any trade secret or confidential or proprietary information in the course of Consultant's consultancy with the Company, to refrain from competing, directly or indirectly, with the business of such third party or to refrain from soliciting employees, customers or suppliers of such third party. The Consultant further represents that Consultant's performance of all the terms of this Agreement and the performance of the services as a consultant of the Company do not and will not breach any agreement with any third party to which the Consultant is a party (including, without limitation, any nondisclosure or non-competition agreement), and that the Consultant will not disclose to the Company or induce the Company to use any confidential or proprietary information or material belonging to any current or previous employer or others.

8.2 The Consultant hereby represents, warrants and covenants that Consultant has the skills and experience necessary to perform the services, that Consultant will perform said services in a professional, competent and timely manner, that Consultant has the power to enter into this Agreement and that Consultant's performance hereunder will not infringe upon or violate the rights of any third party or violate any federal, state or municipal laws.

9. Independent Contractor Status.

9.1 The Consultant shall perform all services under this Agreement as an "independent contractor" and not as an employee or agent of the Company. The Consultant is not authorized to assume or create any obligation or responsibility, express or implied, on behalf of, or in the name of, the Company or to bind the Company in any manner.

9.2 The Consultant shall have the right to control and determine the time, place, methods, manner and means of performing the services. In performing the services, the amount of time devoted by the Consultant on any given day will be entirely within the Consultant's control, and the Company will rely on the Consultant to put in the amount of time necessary to fulfill the requirements of this Agreement. The Consultant will provide all equipment and supplies required to perform the services. The Consultant is not required to attend regular meetings at the Company. However, upon reasonable notice, the Consultant shall meet with representatives of the Company at a location to be designated by the parties to this Agreement.

9.3 In the performance of the services, the Consultant has the authority to control and direct the performance of the details of the services, the Company being interested only in the results obtained. However, the services contemplated by the Agreement must meet the Company's standards and approval and shall be subject to the Company's general right of inspection and supervision to secure their satisfactory completion.

9.4 The Consultant shall not use the Company's trade names, trademarks, service names or service marks without the prior approval of the Company.

9.5 The Consultant shall be solely responsible for all state and federal income taxes, unemployment insurance and social security Ftaxes in connection with this Agreement and for maintaining adequate workers' compensation insurance coverage.

10. Non-Exclusivity. The Consultant retains the right to contract with other companies or entities for Consultant's consulting services without restriction [provided, that during the Consultation Period, the Consultant will not, without the Company's prior written consent, directly or indirectly become employed or other engaged in any capacity (including without limitation as a principal, employee, consultant, partner or stockholder) with any business or enterprise that is competitive with the Company's business, including, but not limited to, any business or enterprise that develops, manufactures, designs, licenses, produces, markets, sells or renders any product or service competitive with any product or service developed, manufactured, designed, licensed, produced, marketed, sold or rendered by the Company or planned to be developed, manufactured, designed, licensed, produced, marketed, sold or rendered by the Company].

11. Remedies. The Consultant acknowledges that any breach of the provisions of Sections 6, 7 or 10 of this Agreement or the provisions of the Confidentiality, Inventions, and Restrictive Covenant Agreement may result in serious and irreparable injury to the Company for which the Company cannot be adequately compensated by monetary damages alone. The Consultant agrees, therefore, that, in addition to any other remedy the Company may have, the Company shall be entitled to enforce the specific performance of this Agreement and Confidentiality, Inventions, and Restrictive Covenant Agreement by the Consultant and to seek both temporary and permanent injunctive relief (to the extent permitted by law) without the necessity of proving actual damages or posting a bond.

12. Indemnification. The Consultant shall be solely liable for, and shall indemnify, defend and hold harmless the Company and its successors and assigns from any claims, suits, judgments or causes of action initiated by any third party against the Company where such actions result from or arise out of the services performed by the Consultant under this Agreement. The Consultant shall further be solely liable for, and shall indemnify, defend and hold harmless the Company and its successors and assigns from and against any claim or liability of any kind (including penalties, fees or charges) resulting from the Consultant's failure to pay the taxes, penalties, and payments referenced in Section 9.5 of this Agreement. The Consultant shall further indemnify, defend and hold harmless the Company and its successors and assigns from and against any and all loss or damage resulting from any misrepresentation, or any non-fulfillment of any representation, responsibility, covenant or agreement on Consultant's part, as well as any and all acts, suits, proceedings, demands, assessments, penalties, judgments of or against the Company relating to or arising out of the activities of the Consultant and the Consultant shall pay reasonable attorneys' fees, costs and expenses incident thereto.

13. Notices. All notices required or permitted under this Agreement shall be in writing and shall be deemed effective upon personal delivery or upon deposit in the United States Post Office, by registered or certified mail, postage prepaid, addressed to the other party at the address shown above, or at such other address or addresses as either party shall designate to the other in accordance with this Section 13.

14. Pronouns. Whenever the context may require, any pronouns used in this Agreement shall include the corresponding masculine, feminine or neuter forms, and the singular forms of nouns and pronouns shall include the plural, and vice versa.

15. Entire Agreement. Except as provided herein, this Agreement constitutes the entire agreement between the parties and supersedes all prior agreements and understandings, whether written or oral, relating to the subject matter of this Agreement. The parties agree that the Consultant's employment relationship with the Company be and hereby is terminated effective on the date hereof.

16. Amendment. This Agreement may be amended or modified only by a written instrument executed by both the Company and the Consultant.

17. Non-Assignability of Contract. This Agreement is personal to the Consultant and the Consultant shall not have the right to assign any of Consultant's rights or delegate any of Consultant's duties without the express written consent of the Company. Any non-consented-to assignment or delegation, whether express or implied or by operation of law, shall be void and shall constitute a breach and a default by the Consultant.

18. Governing Law. This Agreement shall be governed by and construed in accordance with the laws of the Commonwealth of Massachusetts without giving effect to any choice or conflict of law provision or rule that would cause the application of laws of any other jurisdiction.

19. Successors and Assigns. This Agreement shall be binding upon, and inure to the benefit of, both parties and their respective successors and assigns, including any corporation with which, or into which, the Company may be merged or which may succeed to its assets or business, provided, however, that the obligations of the Consultant are personal and shall not be assigned by Consultant.

20. Interpretation. If any restriction set forth in this Agreement is found by any court of competent jurisdiction to be unenforceable because it extends for too long a period of time or over too great a range of activities or in too broad a geographic area, it shall be interpreted to extend only over the maximum period of time, range of activities or geographic area as to which it may be enforceable.

21. Survival. Sections 4 through 22 shall survive the expiration or termination of this Agreement.

22. Miscellaneous.

22.1 No delay or omission by the Company in exercising any right under this Agreement shall operate as a waiver of that or any other right. A waiver or consent given by the Company on any one occasion shall be effective only in that instance and shall not be construed as a bar or waiver of any right on any other occasion.

22.2 The captions of the sections of this Agreement are for convenience of reference only and in no way define, limit or affect the scope or substance of any section of this Agreement.

22.3 In the event that any provision of this Agreement shall be invalid, illegal or otherwise unenforceable, the validity, legality and enforceability of the remaining provisions shall in no way be affected or impaired thereby.

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREOF, the parties hereto have executed this Consulting Agreement as of the date and year first above written.

COMPANY:

AILERON THERAPEUTICS, INC.

By: /s/ Manuel Aivado
Name: Manuel Aivado
Title: President & CEO

CONSULTANT:

/s/ John Longenecker
Name: John Longenecker

AILERON THERAPEUTICS

December 17, 2018

John P. Longenecker, Ph.D.
1436 Tres Hermanas Way
Encinitas, CA 92024

Dear John,

Reference is made to that certain Consulting Agreement between Aileron Therapeutics, Inc. (the "Company") and you, dated September 30, 2018 (the "Consulting Agreement"). This letter will confirm our agreement that the Consulting Period (as defined in the Consulting Agreement) shall be extended to June 30, 2019, subject to further extension or earlier termination in accordance with the Consulting Agreement.

All other terms and conditions of the Consulting Agreement will remain in full force and effect.

Please acknowledge your agreement with this letter by signing below and returning a copy to me by fax or PDF.

Sincerely,

Aileron Therapeutics, Inc.

/s/ Manuel Aivado, M.D., Ph.D.
Manuel Aivado, M.D., Ph.D.
President and Chief Executive Officer

Agreed and acknowledged:

/s/ John P. Longenecker
John P. Longenecker

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statement on Form S-8 (No. 333-219158) of Aileron Therapeutics, Inc. of our report dated March 28, 2019 relating to the financial statements, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts
March 29, 2019

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(s) 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 29, 2019

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

Exhibit 31.2

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

I, Donald V. Dougherty, certify that:

1. I have reviewed this Annual Report on Form 10-K of Aileron Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) 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 29, 2019

/s/ Donald V. Dougherty
Donald V. Dougherty
Principal Financial Officer and Chief Financial Officer

Exhibit 32.1

**CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with the Annual Report on Form 10-K of Aileron Therapeutics, Inc. (the “Company”) for the year ended December 31, 2018, 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, to my knowledge on the date hereof:

(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 results of operations of the Company.

Date: March 29, 2019

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

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

**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 year ended December 31, 2018, 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, to my knowledge on the date hereof:

(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 results of operations of the Company.

Date: March 29, 2019

/s/ Donald V. Dougherty

Donald V. Dougherty
Principal Financial Officer and Chief Financial Officer