Confidentially submitted to the Securities and Exchange Commission on May 26, 2017 as Amendment No. 4 to the Confidential Submission File No. 377-01150

Registration No. 333-

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

FORM S-1
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

Aileron Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**2834**	**13-4196017**
(State or other jurisdiction of incorporation or organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification No.)

281 Albany Street
Cambridge, MA 02139
(617) 995-0900
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Joseph A. Yanchik III
President and Chief Executive Officer
Aileron Therapeutics, Inc.
281 Albany Street
Cambridge, MA 02139
(617) 995-0900
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Stuart M. Falber, Esq.
Joshua D. Fox, Esq.
Wilmer Cutler Pickering Hale and Dorr LLP
60 State Street
Boston, MA 02109
Telephone: (617) 526-6000
Fax: (617) 526-5000

Peter N. Handrinos, Esq.
Latham & Watkins LLP
John Hancock Tower
200 Clarendon Street
Boston, MA 02116
Telephone: (617) 948-6000

Approximate date of commencement of proposed sale to the public:
As soon as practicable after this Registration Statement is declared effective.

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933 check the following box. ☐

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

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 ☒ (Do not check if a smaller reporting company)	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 7(a)(2)(B) of the Securities Act. ☒

CALCULATION OF REGISTRATION FEE

Class of Securities To Be Registered	**Proposed Maximum Aggregate Offering Price(1)**	**Amount of Registration Fee(2)**
Common Stock, $0.001 par value per share	$	$

(1) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(o) under the Securities Act of 1933, as amended.

(2) Calculated pursuant to Rule 457(o) based on an estimate of the proposed maximum aggregate offering price.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

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The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

Subject to Completion
Preliminary Prospectus dated , 2017

PROSPECTUS

Shares

Common Stock

This is Aileron Therapeutics, Inc.'s initial public offering. We are selling shares of our common stock.

We expect the public offering price to be between $ and $ per share. Currently, no public market exists for the shares. After pricing of the offering, we expect that the shares will trade on The NASDAQ Global Market under the symbol "ALRN".

We are an "emerging growth company" under federal securities laws and are subject to reduced public company disclosure standards. See "Summary—Implications of Being an Emerging Growth Company."

Investing in the common stock involves risks that are described in the "Risk Factors" section beginning on page 11 of this prospectus.

	Per Share	Total
Public offering price	$	$
Underwriting discount(1)	$	$
Proceeds, before expenses, to us	$	$

(1) We refer you to "Underwriting" beginning on page 174 of this prospectus for additional information regarding underwriting compensation.

The underwriters may also exercise their option to purchase up to an additional shares from us, at the public offering price, less the underwriting discount, for 30 days after the date of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The shares will be ready for delivery on or about , 2017.

Joint Book-Running Managers

BofA Merrill Lynch **Jefferies**

William Blair **Canaccord Genuity**

The date of this prospectus is , 2017.

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Neither we nor the underwriters have authorized anyone to provide you with any information or to make any representations other than those contained in this prospectus, any amendment or supplement to this prospectus or in any free writing prospectus we may authorize to be delivered or made available to you. Neither we nor the underwriters take responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date on the front cover of this prospectus, regardless of the time of delivery of this prospectus or any sale of shares of our common stock. Our business, financial condition, results of operations and prospects may have changed since that date.

For investors outside the United States: We have not, and the underwriters have not, done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus outside the United States.

SUMMARY

This summary highlights, and is qualified in its entirety by, the more detailed information and financial statements included elsewhere in this prospectus. This summary does not contain all of the information that may be important to you. You should read and carefully consider the entire prospectus, especially our financial statements and the notes thereto appearing at the end of this prospectus and the "Risk Factors" section of this prospectus, before deciding to invest in our common stock. Except as otherwise indicated herein or as the context otherwise requires, references in this prospectus to "Aileron," "the company," "we," "us" and "our" refer to Aileron Therapeutics, Inc.

Overview

We are a clinical-stage biopharmaceutical company that is focused on developing and commercializing a novel class of therapeutics called stapled peptides. Our lead product candidate, ALRN-6924, targets the tumor suppressor p53 for the treatment of a wide variety of cancers. ALRN-6924, which is currently being tested in multiple clinical trials, reactivates p53-mediated tumor suppression by targeting the two primary p53 suppressor proteins, MDMX and MDM2. Our ongoing clinical trials of ALRN-6924 consist of a Phase 1 trial for the treatment of advanced solid tumors or lymphomas, a Phase 2a trial for the treatment of peripheral T-cell lymphoma, or PTCL, a Phase 1 trial for the treatment of acute myeloid leukemia, or AML, and advanced myelodysplastic syndrome, or MDS, as a monotherapy and a Phase 1b trial for the treatment of AML/MDS in combination with cytosine arabinoside, or Ara-C.

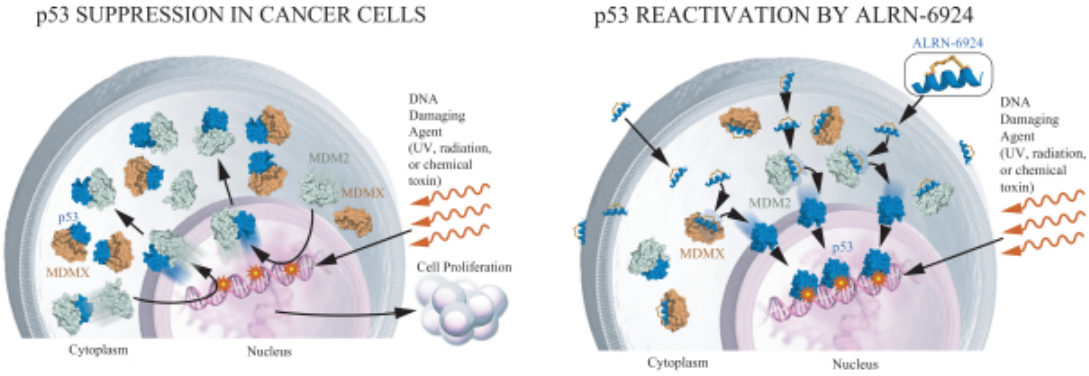
As of December 28, 2016, we had administered ALRN-6924 to over 75 cancer patients in our clinical trials, and we believe it has been generally well tolerated in these patients. Of the 55 evaluable patients in our Phase 1 trial for the treatment of advanced solid tumors or lymphomas, as of December 28, 2016, 25 patients (or 45%) demonstrated disease control, consisting of two patients who achieved complete responses, two patients who achieved partial responses and 21 patients who achieved stable disease, with 33% of stable disease patients experiencing shrinkage of the tumor. Nine patients remained on treatment in the trial as of December 28, 2016, including the four patients who achieved complete or partial responses. In addition, as of December 28, 2016, in a subset of 35 patients whose cells did not contain mutant p53 and who received doses of at least 0.8 mg/kg per administration, which we believe to be the minimal clinically relevant dose in this trial, 20 patients (or 57%) demonstrated disease control, consisting of two patients who achieved complete responses, two patients who achieved partial responses and 16 patients who achieved stable disease, with 44% of the patients with stable disease experiencing shrinkage of the tumor. In the 20 patients who demonstrated disease control, as of December 28, 2016, the median time on drug was 109 days, with an average of 172 days and a maximum for one patient of 555 days. We believe that, based on preclinical data and preliminary evidence of safety and anti-tumor activity in our ongoing clinical trials, there may be a significant opportunity to develop ALRN-6924 as a monotherapy or combination therapy for a wide variety of solid and liquid tumors.

We believe that by using our proprietary stapled peptide drug platform, we can develop first-in-class molecules, like ALRN-6924, that contain a novel set of properties. As such, our stapled peptide drugs may be able to address historically undruggable targets and complex mechanisms, such as intracellular protein-protein interactions like p53, that underlie many diseases with high unmet medical need. We believe that stapled 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.

P53 – "The Guardian of the Genome"

P53 has been a focus of researchers and the pharmaceutical industry due to its central role in preventing the initiation and progression of most solid and liquid tumors, and has long been referred to as "the guardian of

the genome" because it is the body's first line of cellular defense 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 and replicate. P53 function is primarily regulated by the suppressor proteins MDMX and MDM2, which bind to p53 to either reduce its levels through degradation or to control its activity, including the suppression of its 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, but that is functionally suppressed through the activation or overexpression of regulatory proteins, including, primarily, MDMX and MDM2. ALRN-6924 reactivates non-mutant or wild type, or WT, p53 by disrupting the interactions between p53 and these two suppressor proteins, thereby freeing p53 to transit to its DNA target 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 the p53 pathway and its function has been approved. Moreover, we believe that the only product candidates in clinical development targeted at p53 activation 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 equally important. We believe that ALRN-6924 is the first and only product candidate in clinical development that can bind to and disrupt the interaction of MDMX and MDM2 with p53 with equivalent effectiveness, or equipotently. As such, we believe that ALRN-6924's ability to bind to both MDMX and MDM2 may enable it to have an effect in a broader range of tumors, to have an improved safety profile and to be less prone to resistance as a result of different levels of MDMX and MDM2 in tumor cells. The figures below show the suppression of p53 in cancer cells by MDMX and MDM2 and ALRN-6924 inhibiting both MDMX and MDM2 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 MDMX and MDM2, thereby causing the release of the bound p53.



Our Lead Product Candidate – ALRN-6924

We are currently conducting multiple clinical trials of ALRN-6924 in various cancer indications. Most of the patients in these trials have undergone multiple procedures and received a number of approved and experimental treatments. In our clinical trials we have observed preliminary evidence of anti-tumor activity across a broad spectrum of cancer patients, durable effect by trial responders and, to date, a favorable safety profile. We are conducting a Phase 1 trial of ALRN-6924 in adult patients with advanced solid tumors or lymphomas expressing WT p53 that are refractory to or intolerant of standard therapy, or for which no standard therapy exists. We refer to this trial as our Phase 1 All-comers trial. We designed our Phase 1 All-comers trial to evaluate safety, to determine a recommended Phase 2 dose and dosing schedule and to evaluate the preliminary anti-tumor activity of ALRN-6924. We completed enrollment of this trial in January 2017 with a total of 71 patients enrolled. We treated patients with 24 different tumor types in this trial.

In addition to the Phase 1 All-comers trial, we are conducting clinical trials of ALRN-6924 in PTCL and AML/MDS. We are conducting our Phase 2a trial in relapsed and/or refractory PTCL patients whose cells contain WT p53 and who have failed at least one prior line of therapy. Based on the anticipated timing of our Phase 2a PTCL trial, and subject to the data from the trial, we may seek discussions with the U.S. Food and Drug Administration, or FDA, regarding the possibility of an expedited clinical development and registration pathway for ALRN-6924 in PTCL patients and the design of a single agent pivotal Phase 2/3 clinical trial as early as the first half of 2018. We expect to report interim data from the Phase 2a PTCL trial in the first half of 2018. We are also conducting a Phase 1 trial of ALRN-6924 as a monotherapy and a Phase 1b trial of ALRN-6924 in combination with Ara-C, each in AML or MDS patients whose cells contain WT p53. We expect to complete enrollment in our AML/MDS clinical trials in the fourth quarter of 2017. In April 2017, the FDA granted orphan drug designation to ALRN-6924 for use in the treatment of AML.

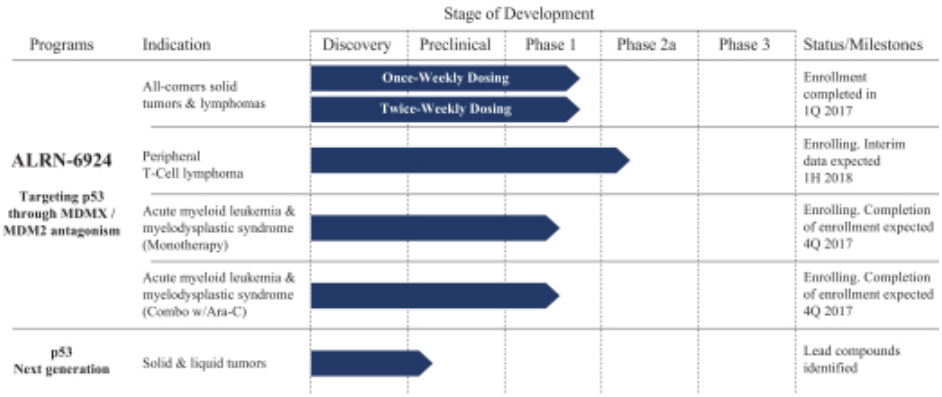
We plan to conduct, alone or in collaboration with third parties, additional clinical trials of ALRN-6924, as warranted by the clinical data. The goal of these clinical trials will be to broaden the application of ALRN-6924 by studying safety and potential anti-tumor activity in additional distinct subgroups of patients with specific solid tumors or hematological malignancies that commonly present with WT p53, such as certain leukemias, breast cancers and melanomas. As many approved drugs and drug candidates for cancer require a functioning p53 pathway, we may also conduct additional clinical trials of ALRN-6924 in combination with other anti-cancer agents. We believe the mechanism of action and safety profile of ALRN-6924 may provide the potential for its combination with conventional and novel therapies, such as targeted therapies, chemotherapy, radiotherapy and immuno-therapy.

Our Platform – Stapled Peptides

Our integrated understanding of peptide chemistry and molecular biology as it relates to the physiological functions of stabilized and cell-penetrating peptides forms the basis of our ability to generate novel product candidates. We seek to rationally design sequences of amino acids and “staple” them with hydrocarbon bonds that maintain their natural alpha-helical shape, the most common protein structure at the interface of protein-protein interactions. 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. While the conventional approaches to modulate these significant targets have been based on small molecules, we believe that our ability to target and activate or inhibit key intrinsic cellular proteins and their functions, including p53 and apoptosis, using our proprietary stapled peptides, 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 virulent cancers.

Our Development Pipeline

The following table summarizes key information about our programs:



Since our inception, we have created over 10,000 stapled 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, it is our intention to make selective investments into some of these 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.

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 April 30, 2017, we owned or had an exclusive license to over 175 patents and over 200 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 stapled peptide technology. Key elements of our strategy to achieve this goal include the following:

- Pursue a broad development strategy for our lead product candidate, ALRN-6924, as a monotherapy or combination therapy across multiple oncology indications.
- Rapidly advance ALRN-6924 through clinical development and regulatory approval.
- Maximize the global commercial value of ALRN-6924 and other product candidates.
- Leverage our proprietary stapled peptide technology to develop additional product candidates across oncology and other diseases with unmet medical need.

- Maintain our leading position in stapled peptides by continuing to develop our proprietary platform.

Risks Associated with Our Business

Our business is subject to a number of risks of which you should be aware before making an investment decision. These risks are discussed more fully in the "Risk Factors" section of this prospectus immediately following this prospectus summary. These risks include the following:

- We have incurred significant losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability. As of March 31, 2017, we had an accumulated deficit of $118.9 million.

- Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability. Our lead product candidate, ALRN-6924, is currently in multiple clinical trials and all of our other product candidates are in preclinical research.

- We believe that the net proceeds from this offering, together with our existing cash, cash equivalents and investments, will enable us to fund our operating expenses and capital expenditure requirements through at least . We expect that the net proceeds from this offering and our existing cash, cash equivalents and investments will be sufficient to enable us to complete each of our ongoing clinical trials. We do not expect that the net proceeds from this offering and our existing cash, cash equivalents and investments will be sufficient, however, to enable us to conduct through completion any additional clinical trials of ALRN-6924 or to otherwise complete the development of ALRN-6924. Accordingly, we will need substantial additional funding. 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 or commercialization efforts.

- We are dependent on the success of ALRN-6924 and cannot be certain that we will receive marketing approval for ALRN-6924 or will successfully commercialize ALRN-6924 even if we receive such marketing approval.

- 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 stapled peptide technology. Neither we nor any other company has received marketing approval to market therapeutics utilizing stapled peptides. Moreover, we believe that we are the first to clinically test a molecule that binds directly to both MDMX and MDM2. As such, the effect of binding to and simultaneously disrupting the interactions of MDMX and MDM2 with WT p53 in cancer patients has not been established in clinical trials.

- If we experience delays or difficulties in the enrollment of patients in clinical trials, we may not be able to initiate or complete clinical trials for our product candidates on a timely basis.

- The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results.

- 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.

- We rely on third parties to conduct our clinical trials, some aspects of our research and preclinical studies and the manufacturing of our product candidates. If these third parties do not perform satisfactorily, including by failing to meet deadlines for the completion of such trials, research and studies, we could be delayed in our clinical development activities or in our efforts to obtain marketing approval of our product candidates.

- 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, including ALRN-6924, their respective components, formulations, methods used to manufacture them and methods of treatment, as well as successfully defending these patents against third-party challenges. We may not be able to ensure their protection.

Our Corporate Information

We were incorporated under the laws of the State of Delaware on August 6, 2001 under the name Renegade Therapeutics, Inc. We commenced principal operations in 2006 and we subsequently changed our name to Aileron Therapeutics, Inc. in February 2007. Our executive offices are located at 281 Albany Street, Cambridge, MA 02139, and our telephone number is (617) 995-0900. Our website address is www.aileronrx.com. The information contained on, or that can be accessed through, our website is not a part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

In this prospectus, unless otherwise stated or the context otherwise requires, references to “Aileron,” “the company,” “we,” “us,” “our” and similar references refer to Aileron Therapeutics, Inc. Aileron and other trademarks or service marks of Aileron appearing in this prospectus are the property of Aileron. The other trademarks, trade names and service marks appearing in this prospectus are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus are referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

Implications of Being an Emerging Growth Company

As a company with less than $1.07 billion of revenue during our last fiscal year, we qualify as 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 for up to five years, 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 and other requirements that are applicable to other public companies that are not emerging growth companies. In particular, in this prospectus, we have provided only two years of audited financial statements, along with unaudited interim financial statements, with correspondingly reduced “Management’s Discussion and Analysis of Financial Condition and Results of Operations” disclosure, and we have not included all of the executive compensation-related information that would be required if we were not an emerging growth company. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold stock.

THE OFFERING

Common stock offered by us	shares
Common stock to be outstanding immediately following this offering	shares
Option to purchase additional shares	The underwriters have the option to purchase an additional shares of common stock. The underwriters may exercise this option at any time within 30 days from the date of this prospectus.
Use of proceeds	We estimate that the net proceeds to us from this offering, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, will be approximately $ million, or approximately $ million if the underwriters exercise their option to purchase additional shares from us in full, assuming an initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus. We intend to use the net proceeds from this offering, together with our existing cash, cash equivalents and investments, to fund our ongoing clinical trials of ALRN-6924, to fund additional research and clinical development activity related to ALRN-6924 and other programs, and for working capital and other general corporate purposes. See the "Use of Proceeds" section in this prospectus for a more complete description of the intended use of proceeds from this offering.
Risk factors	You should read the "Risk Factors" section of this prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.
Proposed NASDAQ Global Market symbol	"ALRN"

The number of shares of our common stock to be outstanding after this offering is based on 4,476,277 shares of our common stock outstanding as of April 30, 2017 and 104,435,674 additional shares of our common stock issuable upon the automatic conversion of all outstanding shares of our preferred stock upon the closing of this offering.

The number of shares of our common stock to be outstanding after this offering excludes:

- 12,942,900 shares of our common stock issuable upon the exercise of stock options outstanding as of April 30, 2017, at a weighted average exercise price of $0.48 per share;
- 4,219,259 shares of our common stock available for future issuance as of April 30, 2017 under our 2016 stock incentive plan; and

- additional shares of our common stock that will become available for future issuance upon the closing of this offering under our 2017 stock incentive plan and our 2017 employee stock purchase plan.

Unless otherwise indicated, all information in this prospectus assumes:

- no exercise of the outstanding options described above;
- no exercise by the underwriters of their option to purchase up to additional shares of our common stock;
- the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 104,435,674 shares of our common stock upon the closing of this offering; and
- the restatement of our certificate of incorporation and the amendment and restatement of our bylaws upon the closing of this offering.

SUMMARY FINANCIAL DATA

You should read the following summary financial data together with our financial statements and the related notes appearing at the end of this prospectus and the "Selected Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" sections of this prospectus. We have derived the statement of operations data for the years ended December 31, 2015 and 2016 and the balance sheet data as of December 31, 2016 from our audited financial statements appearing at the end of this prospectus. The statement of operations data for the three months ended March 31, 2016 and 2017 and the balance sheet data as of March 31, 2017 have been derived from our unaudited financial statements appearing at the end of this prospectus and have been prepared on the same basis as the audited financial statements. In the opinion of management, the unaudited data reflect all adjustments, consisting only of normal recurring adjustments, necessary for a fair statement of the financial information in those statements. Our historical results are not necessarily indicative of results that should be expected in any future period, and our results for any interim period are not necessarily indicative of results that should be expected for any full year.

	Year Ended December 31,		Three Months Ended March 31,	
	2015	2016	2016	2017
	(in thousands, except per share data)			
Statement of Operations Data:				
Revenue	$ —	$ —	$ —	$ —
Operating expenses:				
Research and development	7,832	10,276	2,493	2,942
General and administrative	5,059	7,893	1,446	1,647
Total operating expenses	12,891	18,169	3,939	4,589
Loss from operations	(12,891)	(18,169)	(3,939)	(4,589)
Interest and other income	13	46	14	32
Net loss	(12,878)	(18,123)	(3,925)	(4,557)
Accretion of redeemable convertible preferred stock to redemption value	(71)	(75)	(18)	(20)
Net loss attributable to common stockholders	$ (12,949)	$ (18,198)	$ (3,943)	$ (4,577)
Net loss per share attributable to common stockholders—basic and diluted(1)	$ (3.25)	$ (4.26)	$ (0.93)	$ (1.06)
Weighted average common shares outstanding—basic and diluted(1)	3,982	4,270	4,238	4,300
Pro forma net loss per share attributable to common stockholders—basic and diluted (unaudited)(2)		$ (0.19)		$ (0.04)
Pro forma weighted average common shares outstanding—basic and diluted (unaudited)(2)		94,393		108,457

(1) See Note 10 to our financial statements appearing at the end of this prospectus for details on the calculation of basic and diluted net loss per share attributable to common stockholders.

(2) See Note 11 to our financial statements appearing at the end of this prospectus for details on the calculation of basic and diluted pro forma net loss per share attributable to common stockholders.

The following table sets forth summary balance sheet data as of March 31, 2017:

- on an actual basis;
- on a pro forma basis to give effect to the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 104,435,674 shares of common stock upon the closing of this offering; and
- on a pro forma as adjusted basis to give further effect to our issuance and sale of shares of our common stock in this offering at an assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

	As of March 31, 2017		
	Actual	Pro Forma	Pro Forma As Adjusted(2)
		(in thousands)	
Balance Sheet Data:			
Cash, cash equivalents and investments	$ 15,294	$ 15,294	$
Working capital(1)	13,111	13,111	
Total assets	17,155	17,155	
Redeemable convertible preferred stock	130,391	—	
Total stockholders' equity (deficit)	(116,111)	14,280	

(1) We define working capital as current assets less current liabilities.

(2) A $1.00 increase or decrease in the assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase or decrease the pro forma as adjusted amount of each of cash, cash equivalents and investments, working capital, total assets and total stockholders' equity by $ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions. An increase or decrease of shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase or decrease the pro forma as adjusted amount of each of cash, cash equivalents and investments, working capital, total assets and total stockholders' equity by $ million, assuming no change in the assumed initial public offering price per share and after deducting estimated underwriting discounts and commissions. This pro forma as adjusted information is illustrative only and will depend on the actual initial public offering price and other terms of this offering determined at pricing.

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before you decide to invest in our common stock, you should consider carefully the risks described below, together with the other information contained in this prospectus, including our financial statements and the related notes appearing at the end of this prospectus. We believe the risks described below are the risks that are material to us as of the date of this prospectus. 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. In these circumstances, the market price of our common stock could decline, and you may lose all or part of your investment.

Risks Related to Our Financial Position and Need for Additional Capital

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 $18.1 million for the year ended December 31, 2016 and $4.6 million for the three months ended March 31, 2017. As of March 31, 2017, we had an accumulated deficit of $118.9 million. We have not generated any revenue to date from sales of any drugs and have financed our operations principally through private placements of our preferred stock and, to a lesser extent, 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 transition to 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 drugs 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 you to lose all or part of your investment.

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

We are an early-stage company. We were incorporated in 2001 and commenced principal operations in 2006. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, developing our stapled 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 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 you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, as a business with a limited operating history, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. 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.

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, you should not rely upon the results of any particular quarterly or annual periods as indications of future operating performance.

We will need substantial additional funding. 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 or future commercialization efforts.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. We expect our expenses to increase in connection with our ongoing activities, particularly as we conduct clinical trials of, and seek marketing approval for, ALRN-6924 and our other product candidates. In addition, if we obtain marketing approval for any of our product candidates, 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. Furthermore, commencing upon the closing of this offering, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on

attractive terms, we may be forced to delay, reduce and/or eliminate our research and drug development programs or future commercialization efforts.

We plan to use the net proceeds from this offering to fund our ongoing clinical trials of ALRN-6924 and additional research and clinical development activity related to ALRN-6924 and other programs and for working capital and other general corporate purposes, which may include additional research, hiring additional personnel, capital expenditures and the costs of operating as a public company. We will be required to expend significant funds in order to advance the development of ALRN-6924, as well as any other product candidates. 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. In any event, the net proceeds from this offering and our existing 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, debt financings, collaborations and licensing arrangements or other sources. We do not have any committed external source of funds. Adequate additional financing may not be available to us on acceptable terms, 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.

We believe that the net proceeds from this offering, together with our existing cash, cash equivalents and investments, will enable us to fund our operating expenses and capital expenditure requirements through at least . Our estimate as to how long we expect the net proceeds from this offering, together with our existing cash, cash equivalents and investments, to be able to continue to fund our operations is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Further, changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned. 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.

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 at all. If we are unable to obtain product approvals or generate significant commercial revenues, our business will be materially harmed.

Raising additional capital may cause dilution to our stockholders, including purchasers of common stock in this offering, restrict our operations or require us to relinquish rights to our product candidates.

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 drugs, 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, your ownership interest may be diluted, and the terms of these securities could include liquidation or other preferences and anti-dilution protections that could adversely affect your rights as a common stockholder. 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. In addition, securing financing could require a substantial amount of time and attention from our management and may 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.

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 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 would otherwise prefer to develop and market ourselves.

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 believe that it is the current view of the U.S. Food and Drug Administration, or FDA, that in the event that we decide to seek marketing approval of ALRN-6924 with a label limited to non-mutated or wild type, or WT, p53 cancer patients, we would be required to have a companion *in vitro* diagnostic approved for use with ALRN-6924. We would also expect that we would 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 status, or develop such a diagnostic ourselves, in each case requiring approval of the diagnostic by regulatory authorities. Companion diagnostics are subject to regulation as medical devices and must be separately approved or cleared for marketing by the FDA or certain other foreign regulatory agencies. We are not permitted to market or promote ALRN-6924, or any other product candidates, before we receive marketing approval from 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 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 stapled peptide technology, and our future success depends on the successful development of this technology and products based on stapled peptide technology. Neither we nor any other company has received marketing approval to market therapeutics utilizing stapled 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 stapled 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 stapled 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 stapled 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, our lead product candidate, ALRN-6924, reactivates p53 by disrupting the interactions between p53 and MDMX and MDM2, 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 MDMX and MDM2 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 MDMX and MDM2 in reactivating 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 MDMX and MDM2. As such, the effect of binding to and simultaneously disrupting the interactions of MDMX and MDM2 with WT p53 in cancer patients has not been established in clinical trials. In addition, the role of factors other than MDMX and MDM2 in circumventing the p53 mechanism, such as HPV, 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.

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 stapled 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 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 stapled 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 stapled 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. 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, 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.

Based on safety data in our ongoing Phase 1 clinical trial of ALRN-6924 in advanced solid tumors or lymphomas, which we refer to as our Phase 1 All-comers trial, we consider ALRN-6924 to be well tolerated by patients in that trial. In our Phase 1 All-comers trial, as of December 28, 2016, treatment-related adverse events were seen across all dose levels in 96% of patients, with 75% of those patients reporting maximum treatment-related adverse events of grade 1 or 2, with a limited number of patients reporting maximum treatment-related adverse events of grade 3 or 4. The most frequent treatment-related adverse events were gastrointestinal side effects, fatigue, anemia and headache. Dose limiting toxicities, or DLTs, were grade 3 fatigue at 3.1 mg/kg, and grade 3 hypotension, grade 3 alkaline phosphatase elevation, grade 3 anemia and grade 4 neutropenia at 4.4 mg/kg. Infusion-related reactions were seen in seven patients, with three treatment discontinuations. The most common non-hematologic adverse events were gastrointestinal side effects, fatigue, anemia and headache. From a hematologic perspective, patients have experienced treatment-related hematologic adverse events of anemia, thrombocytopenia, a condition in which a patient has a low blood platelet count, and neutropenia, a condition in which the patient has abnormally low levels of neutrophils, a type of white blood cell, in the blood. Three patients experienced grade 3 anemia, one patient experienced grade 3 neutropenia and two patients experienced grade 4 neutropenia.

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 candidate that may be the subject of the clinical trial. Even if the deaths are not related to our product candidate, the deaths could affect perceptions regarding the safety of our product candidate.

If any of our product candidates is associated with adverse events or undesirable side effects or has properties that are unexpected, 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, 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 cancer patients, we would be required to have a companion *in vitro* diagnostic approved for use with ALRN-6924. We would also expect that we would 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 status, or develop such a diagnostic ourselves, 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 clinical trials of ALRN-6924 to identify WT p53 status. We do not have experience or capabilities in developing or commercializing companion diagnostics.

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

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

Because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable drugs. 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 stapled peptide technology 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, Amgen Inc., Novartis AG and Daiichi Sankyo Co., Ltd. If ALRN-6924 were to be approved for the indications for which we currently have ongoing clinical trials, it will compete with currently-marketed drugs or drugs that may be approved for marketing by the FDA in the future and such competition will not be limited to drugs that act through the reactivation of p53.

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. We cannot assure you 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 stapled peptide product candidates, we may enter into strategic collaborations for the development, marketing and commercialization of ALRN-6924 and our other stapled 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 stapled 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. For example, in 2013, Roche terminated the research collaboration to which we were a party.

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, Materia, Inc., or Materia, 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 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 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, Materia 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 the patent families to third parties, but they would not have been able to license any of the other patent families licensed to us under the license agreement or any of our own patents or patent applications to third parties. 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, Harvard has not pursued its assertion of our material breach further. However, 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 country 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 referendum 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.

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 expect to seek orphan drug designation for ALRN-6924 for PTCL and MDS and may 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 Trump administration may impact our business and industry. Namely, the Trump 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, President Trump issued an Executive Order, applicable to all executive agencies, including the FDA, that 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 requires 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 OMB on February 2, 2017, the administration indicates 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, President Trump 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 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, and a change in existing government regulations and policies, 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.

In the United States and some foreign jurisdictions, there have been and continue to be 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 our future collaborators, to profitably sell any drugs for which we, or they, obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and additional downward pressure on the price that we, or our future collaborators, may receive for any approved drugs.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, changed the way Medicare covers and pays for pharmaceutical products and could decrease the coverage and price that we, or our future collaborators, may receive for any approved drugs. While the MMA only addresses 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 MMA may result in a similar reduction in payments from private payors.

In March 2010, then-President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the Affordable Care Act, or ACA, which substantially changes the way healthcare is financed by both governmental and private insurers. The provisions of the Affordable Care Act of potential importance to our product candidates 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 Medicaid rebates a manufacturer must pay under the Medicaid Drug Rebate Program and extension of the rebate program to individuals enrolled in Medicaid managed care organizations;
- expansion of healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers and enhanced penalties for 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 of applicable brand drugs and therapeutic biologics to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer’s outpatient drugs and therapeutic biologics to be covered under Medicare Part D;
- 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 certain others, including reporting "transfers of value" made or distributed to prescribers and other healthcare providers and reporting investment interests held by physicians and their immediate family members;

- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians;

- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and

- a new Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription drugs.

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 2025 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 bills designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products.

We expect that the ACA, 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.

Legislative changes to or regulatory changes under the ACA remain possible and appear likely in the 115th U.S. Congress and under the Trump administration. The nature and extent of any legislative or regulatory changes to the ACA are uncertain at this time, particularly given the introduction of the American Health Care Act of 2017, or AHCA, which would repeal and replace key portions of the ACA. The AHCA was passed by the U.S. House of Representatives but remains subject to passage by the U.S. Senate. It is possible that the AHCA or other repeal and replacement initiatives, if enacted into law, could ultimately result in fewer individuals having health insurance coverage or in individuals having insurance coverage with less generous benefits. The scope of potential future legislation to repeal and replace ACA provisions is highly uncertain in many respects.

Additional changes that may affect our business include the expansion of new programs such as Medicare payment for performance initiatives for physicians under the Medicare Access and CHIP Reauthorization Act of 2015, or MACRA, which will be fully implemented in 2019. At this time, it is unclear how the introduction of the Medicare quality payment program will impact overall physician reimbursement. The costs of prescription pharmaceuticals in the United States has also been the subject of considerable discussion in the United States, and members of Congress and the Administration have stated that they will address such costs through new legislative and administrative measures. This focus has resulted in several Congressional inquiries

and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products.

We expect that these and other healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved drug. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our drugs. 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 drug candidates or additional pricing pressures.

The cost of prescription pharmaceuticals in the United States has also been the subject of considerable discussion in the United States, and members of Congress and the Administration have stated that they will address such costs through new legislative and administrative measures. The pricing of prescription pharmaceuticals is also subject to governmental control outside the United States. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidates to that of other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our ability to generate revenues and become profitable could be impaired.

Legislative and regulatory proposals have also 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. In addition, increased scrutiny by the United States 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 drug labeling and post-marketing testing and other requirements.

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

We may seek a breakthrough therapy 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. For drugs and biologics that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. 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.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe that one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. Even if we receive breakthrough therapy designation, the receipt of such designation for a product candidate 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. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that the product candidates no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

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

If a drug is intended for the treatment of a serious condition and nonclinical or clinical data demonstrate the potential to address unmet medical need for this condition, a drug sponsor may apply for FDA fast track designation. If we seek fast track designation for a product candidate, we may not receive it from the FDA. However, even if we receive fast track designation, fast track designation does not ensure that we will receive marketing approval or that approval will be granted within any particular timeframe. We may not experience a faster development or regulatory review or approval process with fast track designation compared to conventional FDA procedures. In addition, the FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program. Fast track designation alone does not guarantee qualification for the FDA's priority review procedures.

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

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. A priority review designation means that the goal for the FDA to review an application is six months, rather than the standard review period of ten months. We may request priority review for our product candidates. The FDA has broad discretion with respect to whether or not to grant priority review status to a product candidate, so even if we believe a particular product candidate is eligible for such designation or status, the FDA may decide not to grant it. Moreover, a priority review designation does not necessarily mean a faster development or regulatory review or approval process or necessarily confer any advantage with respect to approval compared to conventional FDA procedures. Receiving priority review from the FDA does not guarantee approval within the six-month review cycle or at all.

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 healthcare anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing 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 or service, for which payment may be made under federal and state healthcare programs, such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- *False Claims Act*—the federal False Claims Act imposes criminal and civil penalties, including through civil whistleblower or *qui tam* actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment by
a federal healthcare program or making a false statement or record material to payment of a false

claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties, currently set at $5,500 to $11,000 per false claim;

- *HIPAA*—the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and its implementing regulations, also imposes obligations on certain covered entity healthcare providers, health plans, and healthcare clearinghouse as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information, including mandatory contractual terms and technical safeguards, with respect to safeguarding the privacy, security and transmission of individually identifiable health information, and require notification to affected individuals and regulatory authorities of certain breaches of security of individually identifiable health information;

- *HIPAA Privacy Provisions*—as amended by HITECH and its implementing regulations, also imposes obligations on certain covered entity healthcare providers, health plans, and healthcare clearinghouse as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information, including mandatory contractual terms and technical safeguards, with respect to safeguarding the privacy, security and transmission of individually identifiable health information, and require notification to affected individuals and regulatory authorities of certain breaches of security of individually identifiable health information;

- *Transparency Requirements*—the federal legislation commonly referred to as the Physician Payments Sunshine Act, enacted as part of the Affordable Care Act, and its implementing regulations, which requires certain manufacturers of drugs, devices, therapeutic biologics and medical supplies reimbursable under Medicare, Medicaid, and Children's Health Insurance Programs to report annually to the Department of Health and Human Services information related to certain payments and other transfers of value, including consulting fees, travel reimbursements, research grants, and other payments or gifts with values over $10 made to physicians, other healthcare providers and teaching hospitals, as well as ownership and investment interests held by physicians and other healthcare providers and their immediate family members;

- *FDCA*—the FDCA, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices; and

- *Analogous State and Foreign Laws*—analogous state and foreign fraud and abuse laws and regulations, such as state anti-kickback and false claims laws that may apply to sales or marketing arrangements and claims involving healthcare items or services 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.

Numerous statements made by President Trump and members of the U.S. Congress indicate that it is likely that legislation that repeals the ACA, in whole or in part, and/or introduces a new form of healthcare reform will be approved by Congress and signed into law by President Trump. However, it is unclear at this point whether such legislation will be approved and, if approved, when it will become effective. Because of the uncertainty surrounding this replacement healthcare reform legislation, we cannot predict with any certainty the likely impact of the ACA's repeal or the adoption of any other healthcare reform legislation on our financial condition or operating results. Whether or not there is alternative healthcare legislation enacted in the United States, there is likely to be significant disruption to the healthcare market in the coming months and years.

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 President and Chief Executive Officer, our Senior Vice President, Chief Medical Officer, and other key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on Joseph A. Yanchik III, our President and Chief Executive Officer, and Manuel Aivado, M.D., Ph.D., our Senior Vice President, Chief Medical Officer, as well as the other principal members of our management and scientific teams. Our agreements with Mr. Yanchik and Dr. Aivado do not prevent them from terminating their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our 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 experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, clinical operations, regulatory affairs and, potentially, sales and marketing. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The 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.

Risks Related to Our Common Stock and this Offering

After this offering, our executive officers, directors and principal stockholders will maintain the ability to control all matters submitted to stockholders for approval.

Upon the closing of this offering, our executive officers, directors and stockholders who each owned more than 5% of our outstanding common stock before this offering will, in the aggregate, beneficially own shares representing approximately % of our common stock. As a result, if these stockholders were to choose to act together, they would be able to control 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, would control 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 that will become effective upon the closing of this offering may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. 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.

If you purchase shares of common stock in this offering, you will suffer immediate dilution of your investment.

The initial public offering price of our common stock is substantially higher than the pro forma as adjusted net tangible book value per share of our common stock. Therefore, if you purchase shares of our

common stock in this offering, you will pay a price per share that substantially exceeds our pro forma as adjusted net tangible book value per share after this offering. To the extent shares are issued under outstanding options, you will incur further dilution. Based on the initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover of this prospectus, you will experience immediate dilution of $ per share, representing the difference between our pro forma as adjusted net tangible book value per share after giving effect to this offering and the assumed initial public offering price per share. In addition, purchasers of common stock in this offering will have contributed approximately % of the aggregate price paid by all purchasers of our stock but will own only approximately % of our common stock outstanding after this offering.

An active trading market for our common stock may not develop.

Prior to this offering, there has been no public market for our common stock. The initial public offering price for our common stock will be determined through negotiations with the underwriters. Although we have applied to list our common stock on The NASDAQ Global Market, an active trading market for our shares may never develop or be sustained following this offering. If an active market for our common stock does not develop or is not sustained, it may be difficult for you to sell shares you purchase in this offering without depressing the market price for the shares, or at all.

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 will rely in part on the research and reports that industry or financial analysts publish about us or our business. We do not currently have and may never obtain research coverage by industry or financial analysts. If no or few analysts commence coverage of us, the trading price of our stock would likely decrease. Even if we do obtain analyst coverage, 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 may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock in this offering.

Our stock price is likely to be volatile. 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, you may not be able to sell your common stock at or above the initial public offering price. 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 have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

We are an “emerging growth company,” and the reduced disclosure requirements applicable to emerging growth 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 for up to five years, 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, being permitted to present only two years of audited financial statements and a correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure in this prospectus, reduced disclosure obligations regarding executive compensation and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. In this prospectus, we have not included all of the executive compensation related information that would be required if we were not an emerging growth company. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

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

As a public company, 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. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance.

Pursuant to Section 404, we will be required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps 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.

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 your sole source of gain.

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

A significant portion of our total outstanding shares are restricted from immediate resale but may be sold into the market in the near future, 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. After this offering, we will have outstanding shares of common stock based on the number of shares outstanding as of , 2017. This includes the shares that we are selling in this offering, which may be resold in the public market immediately without restriction, unless purchased by our affiliates. Of the remaining shares, 108,911,951 shares are currently restricted as a result of securities laws or lock-up agreements but will be able to be sold after the offering as described in the "Shares Eligible for Future Sale" section of this prospectus. Moreover, after this offering, holders of an aggregate of 104,576,635 shares of our common stock will have rights, subject to certain 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. We also intend to register all shares of common stock that we may issue under our equity compensation plans. Once we register these shares, they can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and the lock-up agreements described in the "Underwriting" section of this prospectus.

Our certificate of incorporation that will become effective upon the closing of this offering 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 that will become effective upon the closing of this offering 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.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This prospectus contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this prospectus, 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;
- 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;
- the potential benefits of any future collaboration;
- our expectations related to the use of proceeds from this offering;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- 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 included in this prospectus, 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 prospectus and the documents that we have filed as exhibits to the registration statement of which this prospectus is a part 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 prospectus 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.

USE OF PROCEEDS

We estimate that the net proceeds from our issuance and sale of shares of our common stock in this offering will be approximately $ million, assuming an initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise in full their option to purchase additional shares, we estimate that the net proceeds from this offering will be approximately $ million.

A $1.00 increase or decrease in the assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase or decrease our net proceeds from this offering by approximately $ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions. An increase or decrease of shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase or decrease our net proceeds from this offering by approximately $ million, assuming no change in the assumed initial public offering price per share and after deducting estimated underwriting discounts and commissions.

As of March 31, 2017, we had cash, cash equivalents and investments of $15.3 million. We currently estimate that we will use the net proceeds from this offering, together with our existing cash, cash equivalents and investments, as follows:

- approximately $ million to fund our ongoing clinical trials of ALRN-6924, including approximately $ million to fund our Phase 1 All-comers trial, approximately $ million to fund our Phase 2a PTCL trial and approximately $ million to fund our Phase 1/1b AML/MDS trials;
- approximately $ million to fund additional research and clinical development activity related to ALRN-6924 and other programs; and
- the remainder for working capital and other general corporate purposes, which may include funding for additional research, hiring additional personnel, capital expenditures and the costs of operating as a public company.

This expected use of the net proceeds from this offering and our existing cash, cash equivalents and investments represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development and commercialization efforts, the status of and results from clinical trials, any collaborations that we may enter into with third parties for our product candidates and any unforeseen cash needs. Moreover, our estimates of the costs to fund our trials are based on the current designs of the trials. If we were to modify the design of any of these trials, for instance, to increase the number of patients in the trials, our costs to fund the trials could increase. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering.

Based on our current plans, we believe that our existing cash, cash equivalents and investments, together with the net proceeds from this offering, will be sufficient to enable us to fund our operating expenses and capital expenditure requirements at least through . We have based this estimate on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. We expect that the net proceeds from this offering and our existing cash, cash equivalents and investments will be sufficient to enable us to complete each of our ongoing clinical trials. We do not expect that the net proceeds from this offering and our existing cash, cash equivalents and investments will be sufficient, however, to enable us to conduct through completion any additional clinical trials of ALRN-6924 or to otherwise complete the development of ALRN-6924.

Pending our use of the net proceeds from this offering, we intend to invest the net proceeds in a variety of capital preservation investments, including short-term, investment-grade, interest-bearing instruments and U.S. government securities.

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.

CAPITALIZATION

The following table sets forth our cash, cash equivalents and investments and our capitalization as of March 31, 2017:

- on an actual basis;
- on a pro forma basis to give effect to the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 104,435,674 shares of common stock upon the closing of this offering and the filing and effectiveness of our restated certificate of incorporation; and
- on a pro forma as adjusted basis to give further effect to our issuance and sale of shares of our common stock in this offering at an assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

Our capitalization following the closing of this offering will depend on the actual initial public offering price and other terms of this offering determined at pricing. You should read this table together with our financial statements and the related notes appearing at the end of this prospectus and the sections of this prospectus titled “Selected Financial Data” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations.”

	As of March 31, 2017		
	Actual	Pro Forma	Pro Forma As Adjusted
	(in thousands, except share and per share data)		
Cash, cash equivalents and investments	$ 15,294	$ 15,294	$
Redeemable convertible preferred stock (Series A, A-1, B, C-1, C-2, D, D-1, E, E-1, E-2, E-3 and F), $0.01 par value; 151,557,293 shares authorized, 106,114,520 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	$ 130,391	$ —	$
Stockholders’ equity (deficit):			
Preferred stock, $0.001 par value; no shares authorized, issued or outstanding, actual; shares authorized and no shares issued or outstanding, pro forma and pro forma as adjusted	—	—	
Common stock, $0.001 par value; 143,500,000 shares authorized, 4,446,277 shares issued and outstanding, actual; shares authorized, 108,881,951 shares issued and outstanding, pro forma; shares authorized, shares issued and outstanding, pro forma as adjusted	4	109	
Additional paid-in capital	2,784	133,070	
Accumulated deficit	(118,899)	(118,899)	
Total stockholders’ equity (deficit)	(116,111)	14,280	
Total capitalization	$ 14,280	$ 14,280	$

A $1.00 increase or decrease in the assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase or decrease the pro forma as adjusted amount of each of cash, cash equivalents and investments, additional paid-in capital, total

stockholders' equity and total capitalization by $ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions. An increase or decrease of shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase or decrease the pro forma as adjusted amount of each of cash, cash equivalents and investments, additional paid-in capital, total stockholders' equity and total capitalization by $ million, assuming no change in the assumed initial public offering price per share and after deducting estimated underwriting discounts and commissions.

The table above does not include:

- 13,385,405 shares of our common stock issuable upon the exercise of stock options outstanding as of March 31, 2017, at a weighted average exercise price of $0.48 per share;
- 3,806,754 shares of our common stock available for future issuance as of March 31, 2017 under our 2016 stock incentive plan; and
- additional shares of our common stock that will become available for future issuance upon the closing of this offering under our 2017 stock incentive plan and our 2017 employee stock purchase plan.

DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted immediately to the extent of the difference between the public offering price per share of our common stock and the pro forma as adjusted net tangible book value per share of our common stock after this offering.

Our historical net tangible book value (deficit) as of March 31, 2017 was $(116.3) million, or $(26.16) per share of our common stock. Our historical net tangible book value (deficit) is the amount of our total tangible assets less our total liabilities and preferred stock, which is not included within stockholders' equity (deficit). Historical net tangible book value (deficit) per share represents our historical net tangible book value (deficit) divided by the 4,446,277 shares of our common stock outstanding as of March 31, 2017.

Our pro forma net tangible book value as of March 31, 2017 was $14.1 million, or $0.13 per share of our common stock. Pro forma net tangible book value represents the amount of our total tangible assets less our total liabilities, after giving effect to the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 104,435,674 shares of our common stock upon the closing of this offering. Pro forma net tangible book value per share represents pro forma net tangible book value divided by the total number of shares outstanding as of March 31, 2017, after giving effect to the automatic conversion of all outstanding shares of our preferred stock into common stock upon the closing of this offering.

After giving further effect to our issuance and sale of shares of our common stock in this offering at an assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of March 31, 2017 would have been $ million, or $ per share. This represents an immediate increase in pro forma as adjusted net tangible book value per share of $ to existing stockholders and immediate dilution of $ in pro forma as adjusted net tangible book value per share to new investors purchasing common stock in this offering. Dilution per share to new investors is determined by subtracting pro forma as adjusted net tangible book value per share after this offering from the assumed initial public offering price per share paid by new investors. The following table illustrates this dilution on a per share basis:

Assumed initial public offering price per share		$
Historical net tangible book value (deficit) per share as of March 31, 2017	$(26.16)	
Increase per share attributable to the automatic conversion of preferred stock upon the closing of this offering	26.29	
Pro forma net tangible book value per share as of March 31, 2017	0.13	
Increase in pro forma as adjusted net tangible book value per share attributable to new investors purchasing shares in this offering		
Pro forma as adjusted net tangible book value per share after this offering		
Dilution per share to new investors purchasing shares in this offering		$

A $1.00 increase or decrease in the assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase or decrease our pro forma as adjusted net tangible book value by $ million, our pro forma as adjusted net tangible book value per share after this offering by $ and dilution per share to new investors purchasing shares in this offering by $, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions. An increase of shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase the pro forma as adjusted net tangible book value per share after this offering by $ and decrease the dilution per share to new investors participating in this offering by $, assuming no change in the assumed initial public

offering price and after deducting estimated underwriting discounts and commissions. A decrease of shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would decrease the pro forma as adjusted net tangible book value per share after this offering by $ and increase the dilution per share to new investors participating in this offering by $, assuming no change in the assumed initial public offering price and after deducting estimated underwriting discounts and commissions.

If the underwriters exercise their option to purchase additional shares in full, our pro forma as adjusted net tangible book value per share after this offering would be $ per share, representing an immediate increase in pro forma as adjusted net tangible book value per share of $ to existing stockholders and immediate dilution in pro forma as adjusted net tangible book value per share of $ to new investors purchasing common stock in this offering, assuming an initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. If any shares are issued upon exercise of outstanding options, you will experience further dilution.

The following table summarizes, on the pro forma as adjusted basis described above, the differences between the number of shares of common stock purchased from us, the total consideration paid to us and the average price per share paid by existing stockholders and by new investors purchasing shares of common stock in this offering. The calculation below is based on an assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, before deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us:

	Shares Purchased		Total Consideration		Average Price Per Share
	Number	Percent	Amount	Percent	
Existing stockholders		%	$	%	$
New investors					$
Total		100.0%	$	100.0%	

A $1.00 increase or decrease in the assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase or decrease the total consideration paid by new investors by $ million and, in the case of an increase, would increase the percentage of total consideration paid by new investors by percentage points and, in the case of a decrease, would decrease the percentage of total consideration paid by new investors by percentage points, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same. An increase or decrease of shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase or decrease the total consideration paid by new investors by $ million and, in the case of an increase, would increase the percentage of total consideration paid by new investors by percentage points and, in the case of a decrease, would decrease the percentage of total consideration paid by new investors by percentage points, assuming no change in the assumed initial public offering price.

The table above assumes no exercise of the underwriters' option to purchase additional shares in this offering. If the underwriters' option to purchase additional shares is exercised in full, the number of shares of our common stock held by existing stockholders would be reduced to % of the total number of shares of our common stock outstanding after this offering, and the number of shares of common stock held by new investors participating in the offering would be increased to % of the total number of shares of our common stock outstanding after this offering.

The number of shares purchased from us by existing stockholders is based on 108,881,951 shares of our common stock outstanding as of March 31, 2017, after giving effect to the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 104,435,674 shares of common stock upon the closing of this offering, and excludes:

- 13,385,405 shares of our common stock issuable upon the exercise of stock options outstanding as of March 31, 2017, at a weighted average exercise price of $0.48 per share;
- 3,806,754 additional shares of our common stock available for future issuance as of March 31, 2017 under our 2016 stock incentive plan; and
- additional shares of our common stock that will become available for future issuance upon the closing of this offering under our 2017 stock incentive plan and our 2017 employee stock purchase plan.

SELECTED FINANCIAL DATA

You should read the following selected financial data together with our financial statements and the related notes appearing at the end of this prospectus and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this prospectus. We have derived the statement of operations data for the years ended December 31, 2015 and 2016 and the balance sheet data as of December 31, 2015 and 2016 from our audited financial statements appearing at the end of this prospectus. The statement of operations data for the three months ended March 31, 2016 and 2017 and the balance sheet data as of March 31, 2017 have been derived from our unaudited financial statements appearing at the end of this prospectus and have been prepared on the same basis as the audited financial statements. In the opinion of management, the unaudited data reflect all adjustments, consisting only of normal recurring adjustments, necessary for a fair statement of the financial information in those statements. Our historical results are not necessarily indicative of results that should be expected in any future period, and our results for any interim period are not necessarily indicative of results that should be expected for any full year.

	Year Ended December 31,		Three Months Ended March 31,	
	2015	2016	2016	2017
	(in thousands, except per share data)			
Statement of Operations Data:				
Revenue	$ —	$ —	$ —	$ —
Operating expenses:				
Research and development	7,832	10,276	2,493	2,942
General and administrative	5,059	7,893	1,446	1,647
Total operating expenses	12,891	18,169	3,939	4,589
Loss from operations	(12,891)	(18,169)	(3,939)	(4,589)
Interest and other income	13	46	14	32
Net loss	(12,878)	(18,123)	(3,925)	(4,557)
Accretion of redeemable convertible preferred stock to redemption value	(71)	(75)	(18)	(20)
Net loss attributable to common stockholders	$ (12,949)	$ (18,198)	$(3,943)	$ (4,577)
Net loss per share attributable to common stockholders—basic and diluted(1)	$ (3.25)	$ (4.26)	$ (0.93)	$ (1.06)
Weighted average common shares outstanding—basic and diluted(1)	3,982	4,270	4,238	4,300
Pro forma net loss per share attributable to common stockholders—basic and diluted (unaudited)(2)		$ (0.19)		$ (0.04)
Pro forma weighted average common shares outstanding—basic and diluted (unaudited)(2)		94,393		108,457

(1) See Note 10 to our financial statements appearing at the end of this prospectus for details on the calculation of basic and diluted net loss per share attributable to common stockholders.

(2) See Note 11 to our financial statements appearing at the end of this prospectus for details on the calculation of basic and diluted pro forma net loss per share attributable to common stockholders.

	As of December 31, 2015	As of December 31, 2016	As of March 31, 2017
		(in thousands)	
Balance Sheet Data:			
Cash, cash equivalents and investments	$ 3,768	$ 20,715	$ 15,294
Working capital(1)	1,477	17,002	13,111
Total assets	5,940	22,021	17,155
Redeemable convertible preferred stock	97,681	129,745	130,391
Total stockholders' deficit	(94,319)	(111,806)	(116,111)

(1) We define working capital as current assets less current liabilities.

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 the "Selected Financial Data" section of this prospectus and our financial statements and the related notes included at the end of this prospectus. This discussion and other parts of this prospectus contain forward-looking statements that involve risks and uncertainties, such as statements of our plans, objectives, expectations and intentions. As a result of many factors, including those factors set forth in the "Risk Factors" section of this prospectus, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a clinical-stage biopharmaceutical company that is focused on developing and commercializing a novel class of therapeutics called stapled peptides. Our lead product candidate, ALRN-6924, targets the tumor suppressor p53 for the treatment of a wide variety of cancers. ALRN-6924, which is currently being tested in multiple clinical trials, reactivates p53-mediated tumor suppression by targeting the two primary p53 suppressor proteins, MDMX and MDM2. Our ongoing clinical trials of ALRN-6924 consist of a Phase 1 trial for the treatment of advanced solid tumors or lymphomas, which we refer to as our Phase 1 All-comers trial, a Phase 2a trial for the treatment of peripheral T-cell lymphoma, or PTCL, a Phase 1 trial for the treatment of acute myeloid leukemia, or AML, and advanced myelodysplastic syndrome, or MDS, as a monotherapy and a Phase 1b trial for the treatment of AML/MDS in combination with cytosine arabinoside, or Ara-C. We believe that, based on preclinical data and preliminary evidence of safety and anti-tumor activity in our ongoing clinical trials, there may be significant opportunity to develop ALRN-6924 as a monotherapy or combination therapy for a wide variety of solid and liquid tumors. We believe that by using our proprietary stapled peptide drug platform, we can develop first-in-class molecules, like ALRN-6924, that contain a novel set of properties. As such, our stapled peptide drugs may be able to address historically undruggable targets and complex mechanisms, such as intracellular protein-protein interactions like p53, that underlie many diseases with high unmet medical need. We believe that stapled 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 were incorporated in 2001 and commenced principal operations in 2006. We have devoted substantially all of our resources to developing our product candidates, including ALRN-6924, developing our stapled peptide platform, building our intellectual property portfolio, business planning, raising capital and providing general and administrative support for these operations. To date, we have financed our operations through private placements of preferred stock and, to a lesser extent, from payments received under a collaboration agreement. Through March 31, 2017, we had received gross proceeds of $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 ability to generate product revenue sufficient to achieve profitability will depend on the successful development and eventual commercialization of one or more of our product candidates. Our net losses were $12.9 million and $18.1 million for the years ended December 31, 2015 and 2016, respectively, and were $3.9 million and $4.6 million for the three months ended March 31, 2016 and 2017, respectively. As of March 31, 2017, we had an accumulated deficit of $118.9 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 increasing operating losses for at least the next several years.

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; and
- add operational, financial and management information systems and personnel, including personnel to support our drug development, any future commercialization efforts and our transition to a public company.

In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. Furthermore, commencing upon the closing of this offering, we expect to incur additional costs associated with operating as a public company.

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 a combination of public or private equity or debt financings or other sources, which may include collaborations with third parties. We may be unable to raise additional funds or enter into other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as and when needed, we may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our product candidates.

Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. 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 March 31, 2017, we had cash, cash equivalents and investments of $15.3 million. We believe that the anticipated net proceeds from this offering, together with our existing cash, cash equivalents and investments, will enable us to fund our operating expenses and capital expenditure requirements through at least . We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. See “—Liquidity and Capital Resources.”

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;
- 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 unallocated research and development expenses in the table below.

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

	Year Ended December 31,		Three Months Ended March 31,	
	2015	2016	2016	2017
	(in thousands)			
ALRN-6924	$4,082	$ 6,392	$ 1,461	$ 1,736
Other early-stage development programs	211	266	44	72
Unallocated research and development expenses	3,539	3,618	988	1,134
Total research and development expenses	$7,832	$10,276	$ 2,493	$ 2,942

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 that our research and development expenses will continue to increase for the foreseeable future as we 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.

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 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 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 our Phase 1 All-comers trial, our Phase 2a PTCL trial and our Phase 1/1b AML/MDS trials. At this time, we cannot reasonably estimate the cost for initiating and completing 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 also include legal fees relating to patent and corporate matters; professional fees for accounting, auditing, tax and consulting services; insurance costs; travel expenses; and facility-related expenses, which include direct depreciation costs and allocated expenses for rent and maintenance of facilities and other operating costs.

We expect that our general and administrative expenses will 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 being a public company, including costs of accounting, audit, legal, regulatory and tax-related services associated with maintaining compliance with exchange listing and Securities and Exchange Commission, or SEC, requirements; director and officer insurance costs; and investor and public relations costs.

Interest and Other Income

Interest and other income consists of interest income earned on our cash, cash equivalents and investments. Our interest income has not been significant due to low investment balances and low interest earned on those balances. We anticipate that our interest income will increase in the future as we expect our investment balances to be higher due to anticipated cash proceeds from this offering.

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, 2016, we had federal and state net operating loss carryforwards of $107.3 million and $103.8 million, respectively, which begin to expire in 2029 and 2030, respectively. As of December 31, 2016, we also had federal and state research and development tax credit carryforwards of $1.6 million and $1.2 million, respectively, which begin to expire in 2025 and 2024, respectively.

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 prospectus, 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.

For stock-based awards granted to non-employees, compensation expense is recognized over the period during which services are rendered by such non-employees until completed. At the end of each financial reporting period prior to the completion of the service, the fair value of these awards is remeasured using the then-current fair value of our common stock and updated assumption inputs in the Black-Scholes option-pricing model.

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

As there has been no public market for our common stock to date, the estimated fair value of our common stock has been 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*. Our 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. These third-party valuations were performed at various dates, which resulted in valuations of our common stock of $0.47 per share as of March 1, 2016 and $0.58 per share as of December 31, 2016.

In addition to considering the results of these third-party valuations, our board of directors considered various objective and subjective factors to determine the fair value of our common stock as of each grant date, including:

- the prices at which we sold shares of preferred stock and the superior rights and preferences of the preferred stock relative to our common stock at the time of each grant;
- the progress of our research and development programs, including the status and results of preclinical studies and clinical trials for our product candidates;
- our stage of development and commercialization and our business strategy;
- external market conditions affecting the biopharmaceutical industry and trends within the biopharmaceutical industry;
- our financial position, including cash on hand, and our historical and forecasted performance and operating results;
- the lack of an active public market for our common stock and our preferred stock;
- the likelihood of achieving a liquidity event, such as an initial public offering, or IPO, or sale of our company in light of prevailing market conditions; and
- the analysis of IPOs and the market performance of similar companies in the biopharmaceutical industry.

The assumptions underlying these valuations represented management's best estimate, which involved inherent uncertainties and the application of management's judgment. As a result, if we had used significantly different assumptions or estimates, the fair value of our common stock and our stock-based compensation expense could have been materially different.

Once a public trading market for our common stock has been established in connection with the closing of this offering, it will no longer be necessary for our board of directors to estimate the fair value of our common stock in connection with our accounting for granted stock options and other such awards we may grant, as the fair value of our common stock will be determined based on the quoted market price of our common stock.

Options Granted

The following table summarizes by grant date the number of shares subject to options granted between January 1, 2016 and April 30, 2017, the per share exercise price of the options, the fair value of common stock underlying the options on each grant date, and the per share estimated fair value of the options:

Grant Date	Number of Shares Subject to Options Granted	Per Share Exercise Price of Options	Fair Value of Common Stock per Share on Date of Option Grant	Per Share Estimated Fair Value of Options
June 16, 2016	293,000	$ 0.47	$ 0.47	$ 0.33
March 2, 2017	3,600,000	$ 0.58	$ 0.65(1)	$ 0.45
March 21, 2017	785,000	$ 0.58	$ 0.65(1)	$ 0.45

(1) At the time of the option grants on March 2, 2017 and March 21, 2017, our board of directors determined that the fair value of our common stock of $0.58 per share calculated in the third-party valuation as of December 31, 2016 reasonably reflected the per share fair value of common stock as of the grant dates. However, as described below, the fair value of common stock at the dates of these grants was adjusted to $0.65 per share in connection with a retrospective fair value assessment for accounting purposes.

In the course of preparing for this offering, in May 2017, we performed a retrospective fair value assessment and concluded that the fair value of our common stock underlying stock options we granted on March 2, 2017 and March 21, 2017 was $0.65 per share for accounting purposes. This reassessed value, which we applied to determine the fair values of the March 2, 2017 and March 21, 2017 option grants to calculate stock-based compensation expense for accounting purposes, was based in part upon a third-party valuation of our common stock as of March 2, 2017, performed on a retrospective basis. The March 2, 2017 valuation was prepared using the hybrid method, which used a market approach to estimate our enterprise value.

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 Three Months Ended March 31, 2016 and 2017

The following table summarizes our results of operations for the three months ended March 31, 2016 and 2017:

	Three Months Ended March 31,		Increase (Decrease)
	2016	2017	
	(in thousands)		
Revenue	$ —	$ —	$ —
Operating expenses:			
Research and development	2,493	2,942	449
General and administrative	1,446	1,647	201
Total operating expenses	3,939	4,589	650
Loss from operations	(3,939)	(4,589)	(650)
Interest and other income	14	32	18
Net loss	$(3,925)	$(4,557)	$ (632)

Research and Development Expenses

	Three Months Ended March 31,		Increase (Decrease)
	2016	2017	
	(in thousands)		
ALRN-6924	$ 1,461	$ 1,736	$ 275
Other early-stage development programs	44	72	28
Unallocated research and development expenses	988	1,134	146
Total research and development expenses	$ 2,493	$ 2,942	$ 449

Research and development expenses for the three months ended March 31, 2016 were $2.5 million, compared to $2.9 million for the three months ended March 31, 2017. The increase of $0.4 million was due primarily to an increase of $0.3 million in research expenses associated with our lead product candidate, ALRN-6924. The increase in ALRN-6924 expenses was due primarily to an increase in clinical trial costs in the three months ended March 31, 2017 associated with our ongoing Phase 2a PTCL trial and our Phase 1/1b AML/MDS trials, each of which commenced in the second half of 2016.

General and Administrative Expenses

General and administrative expenses were $1.4 million for the three months ended March 31, 2016, compared to $1.6 million for the three months ended March 31, 2017. The increase of $0.2 million was primarily due to an increase of $0.3 million in professional fees, partially offset by a decrease of $0.1 million in personnel-related expenses. The increase in professional fees was due to an increase in legal fees and in the use of outside professionals.

Interest and Other Income

Interest and other income for the three months ended March 31, 2016 was comparable to interest and other income for the three months ended March 31, 2017. Our interest income has not been significant due to low investment balances and low interest earned on those balances.

Comparison of the Years Ended December 31, 2015 and 2016

The following table summarizes our results of operations for the years ended December 31, 2015 and 2016:

	Year Ended December 31,		Increase (Decrease)
	2015	2016	
	(in thousands)		
Revenue	$ —	$ —	$ —
Operating expenses:			
Research and development	7,832	10,276	2,444
General and administrative	5,059	7,893	2,834
Total operating expenses	12,891	18,169	5,278
Loss from operations	(12,891)	(18,169)	(5,278)
Interest and other income	13	46	33
Net loss	$(12,878)	$(18,123)	$ (5,245)

Research and Development Expenses

	Year Ended December 31,		Increase (Decrease)
	2015	2016	
	(in thousands)		
ALRN-6924	$4,082	$ 6,392	$ 2,310
Other early-stage development programs	211	266	55
Unallocated research and development expenses	3,539	3,618	79
Total research and development expenses	$7,832	$10,276	$ 2,444

Research and development expenses for the year ended December 31, 2015 were $7.8 million, compared to $10.3 million for the year ended December 31, 2016. The increase of $2.4 million was due primarily to an increase of $2.3 million in research expenses associated with our lead product candidate, ALRN-6924. The increase in ALRN-6924 expenses was due primarily to an increase in clinical trial costs in 2016 associated with our ongoing Phase 1 All-comers trial as well as with our Phase 2a PTCL trial and our Phase 1/1b AML/MDS trials, each of which commenced in 2016.

General and Administrative Expenses

General and administrative expenses were $5.1 million for the year ended December 31, 2015, compared to $7.9 million for year ended December 31, 2016. The increase of $2.8 million was due to an increase of $1.2 million in professional fees, an increase of $0.1 million in facility-related costs, which include direct depreciation costs and allocated expenses for rent and maintenance of facilities and other operating costs, and a charge of $1.5 million recognized in June 2016 related to the write-off of offering costs previously capitalized in connection with a postponed initial public offering. The increase in professional fees was due to increases in legal fees and in the use of outside professionals.

Interest and Other Income

Interest and other income for the year ended December 31, 2015 was comparable to interest and other income for the year ended December 31, 2016. Our interest income has not been significant due to low investment balances and low interest earned on those balances.

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. To date, we have financed our operations through private placements of our preferred stock and, to a lesser extent, through payments received under a collaboration agreement. Through March 31, 2017, we had received gross proceeds of $131.2 million from our sales of preferred stock and $34.9 million from the collaboration agreement. As of March 31, 2017, we had cash, cash equivalents and investments of $15.3 million.

Cash Flows

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

	Year Ended December 31,		Three Months Ended March 31,	
	2015	2016	2016	2017
	(in thousands)			
Cash used in operating activities	$(11,710)	$(15,014)	$ (3,748)	$ (5,952)
Cash provided by (used in) investing activities	10,629	(25)	(10,392)	(7,303)
Cash provided by (used in) financing activities	(1,359)	31,986	13,083	569
Net increase (decrease) in cash and cash equivalents	$ (2,440)	$ 16,947	$ (1,057)	$(12,686)

Operating Activities. During the three months ended March 31, 2017, operating activities used $6.0 million of cash, primarily resulting from our net loss of $4.6 million and cash used by changes in our operating assets and liabilities of $1.6 million, partially offset by non-cash charges of $0.2 million. Net cash used by changes in our operating assets and liabilities during the three months ended March 31, 2017 consisted primarily of a decrease of $0.8 million in accounts payable, a decrease of $0.4 million in accrued expenses and other current liabilities and an increase of $0.3 million in prepaid expenses and other current assets. The decrease in accounts payable was largely due to the timing of vendor invoicing and payments.

During the three months ended March 31, 2016, operating activities used $3.7 million of cash, primarily resulting from our net loss of $3.9 million, partially offset by non-cash charges of $0.2 million. Net cash used by changes in our operating assets and liabilities during the three months ended March 31, 2016 consisted primarily of a $0.2 million decrease in accrued expenses and other current liabilities, partially offset by an increase of $0.1 million in accounts payable and a decrease of $0.1 million in prepaid expenses and other current assets. The decrease in accrued expenses and other current liabilities was largely due to the payment of amounts previously accrued for payroll and payroll-related costs, partially offset by an increase of clinical trial-related accruals as we increased enrollment in our ongoing Phase 1 All-comers trial.

During the year ended December 31, 2016, operating activities used $15.0 million of cash, primarily resulting from our net loss of $18.1 million, partially offset by non-cash charges of $2.4 million and cash provided by changes in our operating assets and liabilities of $0.7 million. Net cash provided by changes in our operating assets and liabilities during the year ended December 31, 2016 consisted of an increase of $1.2 million in accounts payable and an increase of $0.3 million in accrued expenses and other current liabilities, partially offset by a $0.8 million increase in other assets and a $0.1 million increase in prepaid expenses and other current assets. The increases in accounts payable and accrued expenses and other current liabilities were largely due to an increase of clinical trial-related expenses as we increased enrollment in our Phase 1 All-comers trial and we commenced our Phase 2a PTCL trial and our Phase 1/1b AML/MDS trials. The increase in other assets was due to deposits paid to our CROs for our ongoing clinical trials.

During the year ended December 31, 2015, operating activities used $11.7 million of cash, primarily resulting from our net loss of $12.9 million, partially offset by non-cash charges of $0.9 million and cash provided by changes in our operating assets and liabilities of $0.2 million. Net cash provided by changes in our operating assets and liabilities during the year ended December 31, 2015 consisted of a $0.6 million increase in accrued expenses and other current liabilities, partially offset by a $0.2 million decrease in accounts payable and a $0.1 million increase in prepaid expenses and other current assets. The increase in accrued expenses and other current liabilities was largely due to the increase of clinical trial-related accruals as we increased enrollment in our ongoing Phase 1 All-comers trial of ALRN-6924.

Investing Activities. During the three months ended March 31, 2017, investing activities used $7.3 million of cash, consisting primarily of net purchases of investments.

During the three months ended March 31, 2016, investing activities used $10.4 million of cash, consisting primarily of net purchases of investments.

During the year ended December 31, 2016, we used an insignificant amount of cash in investing activities, consisting of net purchases of investments and an increase in restricted cash.

During the year ended December 31, 2015, investing activities provided $10.6 million of cash, consisting of net proceeds from sales of investments of $10.0 million and a decrease in restricted cash of $0.7 million, both of which were partially offset by purchases of property and equipment of $0.1 million.

We expect that purchases of property and equipment will increase over the next several years resulting from our expected move into a new office and laboratory facility in 2018.

Financing Activities. During the three months ended March 31, 2017, net cash provided by financing activities was $0.6 million, primarily due to the net proceeds from our sale of Series F preferred stock of $0.5 million.

During the three months ended March 31, 2016, net cash provided by financing activities was $13.1 million, primarily due to the net proceeds from our sales of Series E-1 preferred stock of $13.2 million, partially offset by the payment of initial public offering costs of $0.1 million.

During the year ended December 31, 2016, net cash provided by financing activities was $32.0 million, primarily due to the net proceeds from our sales of Series E-1 preferred stock and Series F preferred stock of $32.1 million, partially offset by the payment of initial public offering costs of $0.2 million.

During the year ended December 31, 2015, we used $1.4 million of net cash in financing activities, due to the payment of initial public offering costs of $1.3 million and the payment of issuance costs of $0.1 million related to our issuance of Series E-1 preferred stock, both partially offset by proceeds from the exercise of stock options.

Funding Requirements

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, commencing upon the closing of this offering, 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 transition to a public company.

As of March 31, 2017, we had cash, cash equivalents and investments of $15.3 million. We believe that the anticipated net proceeds from this offering, together with our existing cash, cash equivalents and investments, will enable us to fund our operating expenses and capital expenditure requirements through at least . We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect.

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 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, your ownership interest may be diluted, and the terms of these securities may include liquidation or other preferences and anti-dilution protections that could adversely affect your rights as a common stockholder. 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, and may require the issuance of warrants, which could potentially dilute your ownership interest.

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

The following table summarizes our contractual obligations at March 31, 2017:

	Payments Due by Period				
	Total	Less Than 1 Year	1 - 3 Years	4 - 5 Years	More Than 5 Years
	(in thousands)				
Operating lease commitments(1)	$ 602	$ 534	$ 68	$—	$ —
License agreement obligations(2)	1,470	245	490	490	245
Total	$2,072	$ 779	$558	$490	$ 245

(1) Represents minimum payments due for our lease of office and laboratory space in Cambridge, Massachusetts under an operating lease agreement that, as amended, expires in May 2018.

(2) Represents the aggregate minimum annual license maintenance fees payable under our existing licensing agreements with third parties. Amounts in the table reflect such fees payable through 2022, but we will be obligated to make such annual payments until the license agreements are terminated.

Under various licensing and related agreements to which we are a party, we may be required to make milestone payments and pay royalties and other amounts to third parties. We have not included any such contingent payment obligations in the table above as the amount, timing and likelihood of such payments are not known.

Under an amended and restated license agreement with President and Fellows of Harvard College, or Harvard, and Dana-Farber Cancer Institute, or DFCI, through March 31, 2017, we have paid aggregate milestone payments of $0.3 million related to achieving specified milestones for ALRN-6924 and another compound that we are not currently developing, and we have agreed to make additional milestone payments of up to $7.5 million and $7.65 million for each such product candidate, respectively, upon achieving additional specified clinical, regulatory and sales milestones. We have agreed to make milestone payments of up to $7.7 million per any additional licensed therapeutic product and up to $0.7 million per any additional licensed diagnostic product upon achieving specified clinical, regulatory and sales milestones with respect to each such product. In addition, we have agreed to pay royalties of low single-digit percentages on annual net sales of licensed products sold by us, our affiliates or our sublicensees. If we grant any sublicense rights under the license agreement, we have agreed to pay a percentage, up to the mid-twenties, of fees received by us in connection with our sublicense of the licensed products. In accordance with the terms of the agreement, our sublicense payment obligations may be subject to specified reductions, which have been and may potentially be substantial.

Under a license agreement with Materia, through March 31, 2017, we have paid aggregate milestone payments of $0.2 million related to achieving specified milestones for ALRN-6924 and another compound that we are not currently developing, and we have agreed to make additional milestone payments of up to $6.25 million and $6.35 million for each such product candidate, respectively, upon achieving additional specified clinical, regulatory and sales milestones. We have agreed to make milestone payments of up to $6.4 million upon achieving specified clinical, regulatory and sales milestones with respect to any other licensed product. In addition, we have also agreed to pay tiered royalties ranging in the low single-digit percentages on annual net sales of licensed products sold by us or our sublicensees.

In addition, under two other license agreements with third parties, we have agreed to make future milestone payments in a range of up to $0.4 million to $1.9 million per licensed product upon achieving specified clinical, regulatory and sales milestones. We have also agreed to pay royalties under each agreement ranging in the low single-digit percentages on annual net sales of each developed product. We do not currently utilize the technologies licensed under these two agreements in our clinical program.

We enter into contracts in the normal course of business with CROs and CMOs for clinical trials, preclinical research studies and testing, manufacturing and other services and products for operating purposes. These contracts do not contain any minimum purchase commitments and are cancelable by us upon prior notice of 30 days and, as a result, are not included in the table of contractual obligations above. Payments due upon cancelation consist only of payments for services provided and expenses incurred up to the date of cancelation.

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 prospectus, such standards will not have a material impact on our financial statements or do not otherwise apply to our operations.

Quantitative and Qualitative Disclosures about Market Risk

We are exposed to market risk related changes in interest rates. As of March 31, 2017, our cash equivalents consisted of money market accounts and investments in corporate notes and commercial paper that have contractual maturities of less than 90 days. As of March 31, 2017, our investments consisted of investments in corporate notes and commercial paper that have contractual maturities of less than one year. Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. However, because of the short-term nature of the investments in our portfolio, an immediate 10% change in market interest rates would not have a material impact on the fair market value of our investment portfolio or on our financial position or results of operations.

BUSINESS

Overview

We are a clinical-stage biopharmaceutical company that is focused on developing and commercializing a novel class of therapeutics called stapled peptides. Our lead product candidate, ALRN-6924, targets the tumor suppressor p53 for the treatment of a wide variety of cancers. ALRN-6924, which is currently being tested in multiple clinical trials, reactivates p53-mediated tumor suppression by targeting the two primary p53 suppressor proteins, MDMX and MDM2. Our ongoing clinical trials of ALRN-6924 consist of a Phase 1 trial for the treatment of advanced solid tumors or lymphomas, a Phase 2a trial for the treatment of peripheral T-cell lymphoma, or PTCL, a Phase 1 trial for the treatment of acute myeloid leukemia, or AML, and advanced myelodysplastic syndrome, or MDS, as a monotherapy and a Phase 1b trial for the treatment of AML/MDS in combination with cytosine arabinoside, or Ara-C.

As of December 28, 2016, we had administered ALRN-6924 to over 75 cancer patients in our clinical trials, and we believe it has been generally well tolerated in these patients. Of the 55 evaluable patients in our Phase 1 trial for the treatment of advanced solid tumors or lymphomas, as of December 28, 2016, 25 patients (or 45%) demonstrated disease control, consisting of two patients who achieved complete responses, two patients who achieved partial responses and 21 patients who achieved stable disease, with 33% of stable disease patients experiencing shrinkage of the tumor. Nine patients remained on treatment in the trial as of December 28, 2016, including the four patients who achieved complete or partial responses. In addition, as of December 28, 2016, in a subset of 35 patients whose cells did not contain mutant p53 and who received doses of at least 0.8 mg/kg per administration, which we believe to be the minimal clinically relevant dose in this trial, 20 patients (or 57%) demonstrated disease control, consisting of two patients who achieved complete responses, two patients who achieved partial responses and 16 patients who achieved stable disease, with 44% of the patients with stable disease experiencing shrinkage of the tumor. In the 20 patients who demonstrated disease control, as of December 28, 2016, the median time on drug was 109 days, with an average of 172 days and a maximum for one patient of 555 days. We believe that, based on preclinical data and preliminary evidence of safety and anti-tumor activity in our ongoing clinical trials, there may be a significant opportunity to develop ALRN-6924 as a monotherapy or combination therapy for a wide variety of solid and liquid tumors.

We believe that by using our proprietary stapled peptide drug platform, we can develop first-in-class molecules, like ALRN-6924, that contain a novel set of properties. As such, our stapled peptide drugs may be able to address historically undruggable targets and complex mechanisms, such as intracellular protein-protein interactions like p53, that underlie many diseases with high unmet medical need. We believe that stapled 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.

P53 has been a focus of researchers and the pharmaceutical industry due to its central role in preventing the initiation and progression of most solid and liquid tumors, and has long been referred to as “the guardian of the genome” because it is the body’s first line of cellular defense 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 and replicate. P53 function is primarily regulated by the suppressor proteins MDMX and MDM2, which bind to p53 to either reduce its levels through degradation or to control its activity, including the suppression of its 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, but that is functionally suppressed through the activation or overexpression of regulatory proteins, including, primarily, MDMX and MDM2. ALRN-6924 reactivates non-mutant or wild type, or WT, p53 by disrupting the interactions between p53 and these two suppressor proteins, thereby freeing p53 to

transit to its DNA target 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 the p53 pathway and its function has been approved. Moreover, we believe that the only product candidates in clinical development targeted at p53 activation 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 equally important. We believe that ALRN-6924 is the first and only product candidate in clinical development that can bind to and disrupt the interaction of MDMX and MDM2 with p53 with equivalent effectiveness, or equipotently. As such, we believe that ALRN-6924's ability to bind to both MDMX and MDM2 may enable it to have an effect in a broader range of tumors, to have an improved safety profile and to be less prone to resistance as a result of different levels of MDMX and MDM2 in tumor cells.

We are currently conducting multiple clinical trials of ALRN-6924 in various cancer indications. Most of the patients in these trials have undergone multiple procedures and received a number of approved and experimental treatments. In our clinical trials we have observed preliminary evidence of anti-tumor activity across a broad spectrum of cancer patients, durable effect by trial responders and, to date, a favorable safety profile. We are conducting a Phase 1 trial of ALRN-6924 in adult patients with advanced solid tumors or lymphomas expressing WT p53 that are refractory to or intolerant of standard therapy, or for which no standard therapy exists. We refer to this trial as our Phase 1 All-comers trial. We designed our Phase 1 All-comers trial to evaluate safety, to determine a recommended Phase 2 dose and dosing schedule and to evaluate the preliminary anti-tumor activity of ALRN-6924. We completed enrollment of this trial in January 2017 with a total of 71 patients enrolled. We treated patients with 24 different tumor types in this trial.

In addition to the Phase 1 All-comers trial, we are conducting clinical trials of ALRN-6924 in PTCL and AML/MDS. We are conducting our Phase 2a trial in relapsed and/or refractory PTCL patients whose cells contain WT p53 and who have failed at least one prior line of therapy. Based on the anticipated timing of our Phase 2a PTCL trial, and subject to the data from the trial, we may seek discussions with the U.S. Food and Drug Administration, or FDA, regarding the possibility of an expedited clinical development and registration pathway for ALRN-6924 in PTCL patients and the design of a single agent pivotal Phase 2/3 clinical trial as early as the first half of 2018. We expect to report interim data from the Phase 2a PTCL trial in the first half of 2018. We are also conducting a Phase 1 trial of ALRN-6924 as a monotherapy and a Phase 1b trial of ALRN-6924 in combination with Ara-C, each in AML or MDS patients whose cells contain WT p53. We expect to complete enrollment in our AML/MDS clinical trials in the fourth quarter of 2017. In April 2017, the FDA granted orphan drug designation to ALRN-6924 for use in the treatment of AML.

We plan to conduct, alone or 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 solid tumors or hematological malignancies that commonly present with WT p53, such as certain leukemias, breast cancers and melanomas. As many approved drugs and drug candidates for cancer require a functioning p53 pathway, we may also conduct additional clinical trials of ALRN-6924 in combination with other anti-cancer agents. We believe the mechanism of action and safety profile of ALRN-6924 may provide the potential for its combination with conventional and novel therapies, such as targeted therapies, chemotherapy, radiotherapy and immuno-therapy.

We believe that our ability to target and activate or inhibit key intrinsic cellular functions, such as p53 and apoptosis, using our proprietary stapled peptide platform and our scientific expertise in the design, application and development of stabilized alpha-helical peptides 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 resistance. As such, we believe the ability to directly impact these key intrinsic cellular functions, as we are striving to achieve with ALRN-6924 and p53, 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 virulent cancers.

Our integrated understanding of peptide chemistry and molecular biology as it relates to the physiological functions of stabilized and cell-penetrating peptides forms the basis of our ability to generate novel product candidates. We seek to rationally design sequences of amino acids and "staple" 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 stapled 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. While the conventional approaches to modulate these significant targets have been based on small molecules, we believe that our ability to target and activate or inhibit key intrinsic cellular proteins and their functions, including p53 and apoptosis, using our proprietary stapled peptides represents an important opportunity for developing novel drugs and addressing unmet medical need.

Since our inception, we have created over 10,000 stapled 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, it is our intention to make selective investments into some of these 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.

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 April 30, 2017, we owned or had an exclusive license to over 175 patents and over 200 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 stapled peptide technology. Key elements of our strategy to achieve this goal include the following:

Pursue a broad development strategy for our lead product candidate, ALRN-6924, as a monotherapy or combination therapy across multiple oncology indications. We plan to advance our lead product candidate, ALRN-6924, in a broad range of solid and liquid tumors, focusing on areas in which we believe ALRN-6924 may have anti-tumor activity and in which there are significant unmet medical needs. We are initially focusing our development efforts on solid and liquid tumors 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 is found in a broad range of solid and liquid tumors. We have observed preliminary evidence of anti-tumor activity in our Phase 1 All-comers trial in which we have treated patients with 24 different tumor types. We are also currently studying ALRN-6924 in PTCL and AML/MDS patients. We plan to conduct, alone or 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 solid tumors or hematological malignancies that commonly present with WT p53, such as certain leukemias, breast cancers and melanomas. As many approved drugs and drug candidates for cancer require a functioning p53 pathway, we may also conduct additional clinical trials of ALRN-6924 in combination with other anti-cancer agents. We believe the mechanism of action and safety profile of ALRN-6924 may provide the potential for its combination with conventional and novel therapies, such as targeted therapies, chemotherapy, radiotherapy or immuno-therapy.

Rapidly advance ALRN-6924 through clinical development and regulatory approval. We are currently conducting a Phase 2a trial of ALRN-6924 in relapsed and/or refractory PTCL patients whose PTCL cells contain WT p53 and who have failed at least one prior line of therapy. We are initially conducting the trial in up to 20 PTCL patients to provide preliminary insight into the responsiveness of this patient population. Based on the anticipated timing of our Phase 2a PTCL trial, and subject to the data from the trial, we may seek discussions with the FDA regarding the possibility of an expedited clinical development and registration pathway for ALRN-6924 in PTCL patients and the design of a single agent pivotal Phase 2/3 clinical trial as early as the first half of 2018. We expect to report interim data from the Phase 2a PTCL trial in the first half of 2018. Similarly, if we see sufficient evidence of a therapeutic effect in any of our future Phase 2 trials of ALRN-6924, we would also plan to meet with regulatory authorities to discuss the possibility of an expedited clinical development and regulatory pathway for ALRN-6924 in any such indications, including the scope and timing of a single agent pivotal trial.

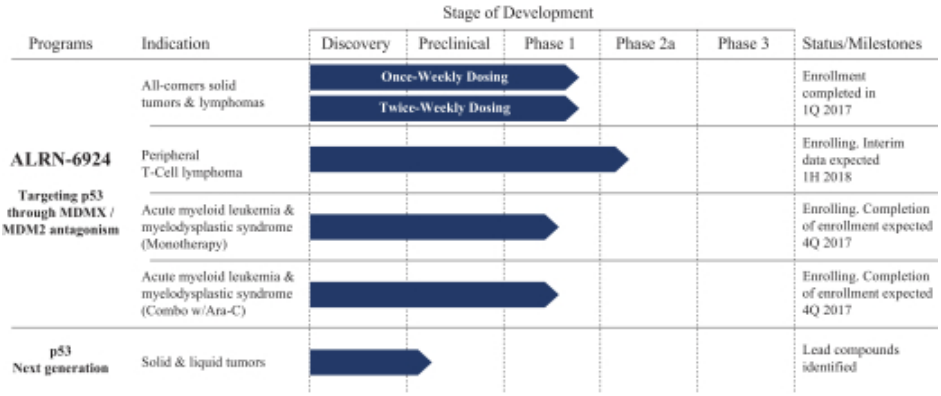
Maximize the global commercial value of ALRN-6924 and other product candidates. We have retained all commercial rights to ALRN-6924 and plan to retain all commercial rights to any other product candidates we develop. As we further develop ALRN-6924, we may build a commercial infrastructure with the capability to directly market in a variety of indications and geographies. Although we currently plan to retain all commercial rights to ALRN-6924 and any other product candidates we develop, we may seek to enter into strategic collaborations for the development, marketing and commercialization of ALRN-6924 and these other product candidates, particularly those directed towards complex oncology indications with large 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 stapled 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 stapled peptides, as well as the growing body of third-party publications that support the utility of stapled peptides against a wide variety of targets, we believe that our stapled 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 stapled peptide may confer advantages over small molecule or biologic therapeutics in delivering therapeutic benefits. We may also seek to develop additional stapled peptides to target p53 as changes in the chemical structures of our stapled peptides may engender these stapled peptides with varying affinities to MDMX and MDM2. 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.

Maintain our leading position in stapled peptides by continuing to develop our proprietary platform. We are developing novel computational chemistry, screening technology, purification and manufacturing processes to continually improve our technology platform as we advance our stapled peptide drug development program. We also support our scientific efforts with a strong patent estate that may provide a competitive advantage and position us as scientific leaders in the emerging field of stapled peptides. We intend to continue to strengthen our platform by developing and filing for patents on various aspects of our technology and product candidates and, when applicable, through in-licensing activities with research institutions and other biopharmaceutical companies.

Our Development Pipeline

The following table summarizes key information about our programs:



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 U.S. National Cancer Institute still estimates that over 1.6 million new cancer cases were diagnosed in the United States and approximately 595,690 people died from cancer in 2016. 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, which are currently the most common methods used in treating patients with cancer, whether individually or in combination, can be effective in specific situations. Surgery and radiation are particularly effective for patients in whom the disease is localized, but are unable to 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 kill cancer cells or to damage cellular components required for the proliferation of cancer cells. Drug therapy often is administered with 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 selectively kill only cancer cells. While heightened vigilance, new diagnostic tests, combination regimens and targeted therapies have resulted in improvements in overall survival for some cancer patients, we believe that 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 the disease. 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 stapled 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 resistance. As such, the ability to directly impact these key intrinsic cellular functions, as we are striving to achieve 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 virulent cancers.

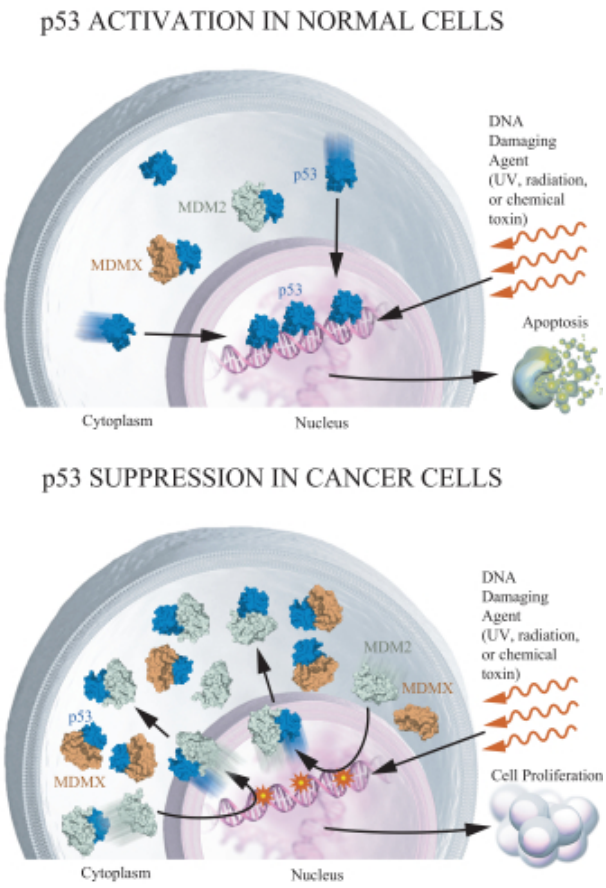
P53 and its Interaction with MDMX and MDM2

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 solid and liquid tumors. 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, and 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. We believe, however, that clinical progress against this target has been slowed due in part to the complex biology and limitations of traditional drug technologies, such as small molecules. We believe that a stapled peptide, such as ALRN-6924, is better suited to address this mechanism due to the inherent molecular properties of the stapled peptide.

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, primarily, MDMX and MDM2, 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.

As depicted in the figures below, p53 is regulated by MDMX and MDM2, which are two proteins known to bind to p53 and play non-redundant roles in modulating p53 protein activity. In normal cells, MDMX generally acts to sequester p53, whereas MDM2 primarily acts to shuttle p53 out of the nucleus and target it for degradation. By playing these roles, MDMX and MDM2 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 MDMX and MDM2 are found in a significant number of solid and liquid tumors 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.



Despite the structural similarity between MDMX and MDM2, there is important diversity in the p53 binding sites of these proteins that make the development of therapeutic antagonists that can bind to both MDMX and MDM2 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 for the treatment of solid tumors and lymphomas, 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.

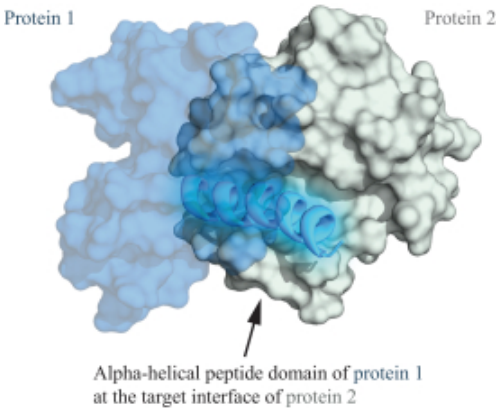
As tumor cells can have different levels of, and differential reliance on, MDMX and MDM2, the current data suggests that there is a limited set of tumors that are highly sensitive to MDM2 inhibition, while a broader set of tumors may be sensitive to both MDMX and MDM2 inhibition. We believe that ALRN-6924 is the first and only product candidate in clinical development that can equipotently bind to and disrupt the interaction of MDMX and MDM2 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 MDMX and MDM2 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 – Stapled Peptides

Our goal is to create a broad range of first-in-class therapeutics through our proprietary stapled 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 stapled 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.



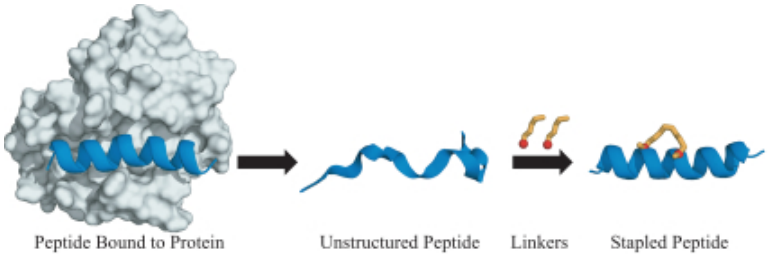
There are presently more than 60 approved peptide drugs, including insulin, liraglutide (Victoza), exenatide (Byetta), teriparatide (Forteo) and Linaclotide (Linzess), that have benefitted patients and improved their quality of life. Attractive attributes of peptide drugs include high specificity and 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 MDMX and MDM2, 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.

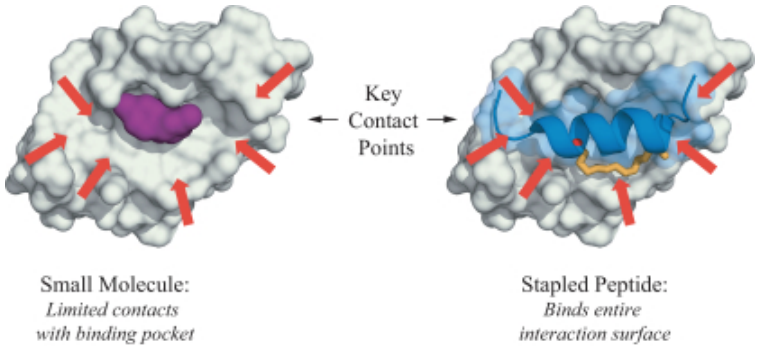
Our Solution

We believe our platform addresses and solves many of the inherent limitations of peptides and can potentially enable us to uniquely 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.

We stabilize peptides by “stapling” them with hydrocarbon bonds into their natural alpha-helical conformation. We achieve this by inserting two or more non-natural amino acids that, when catalyzed by a chemical reaction, form a bridge that often provides comparable stability to the endogenous protein structure and maintains the biological activity of the peptide. We believe that this chemical strategy may allow us to improve on many of the intrinsic limitations of peptides and to develop molecules that interact with high value targets that may not be amenable to small molecules or monoclonal antibodies.

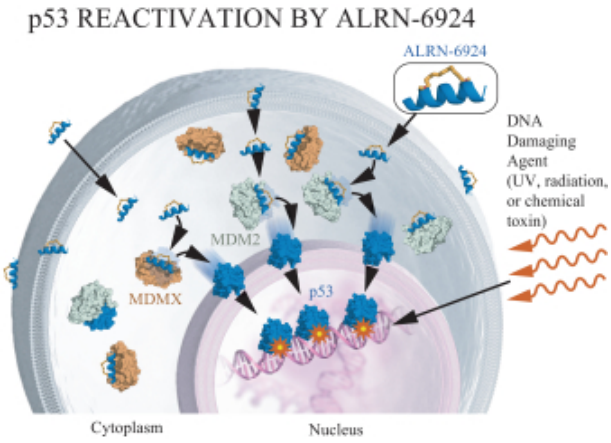


Unlike large proteins, such as monoclonal antibodies or other naturally occurring proteins, that do not penetrate cell membranes due to their size and biophysical properties, stabilized alpha-helical peptides can in many circumstances penetrate cells and still maintain high affinity to their large protein surface targets. Our stapled 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 stapled 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 is a stapled peptide designed to reactivate WT p53 by inhibiting both MDMX and MDM2. We believe that ALRN-6924, by inhibiting both MDMX and MDM2, 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 MDMX and MDM2 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 MDMX and MDM2, thereby causing the release of the bound p53.



We believe that, based on preclinical data and preliminary evidence of safety and anti-tumor activity in our ongoing clinical trials, there is significant opportunity to develop ALRN-6924 as a monotherapy or a combination therapy for a wide variety of solid and liquid tumors. We are focusing our development efforts on solid and liquid tumors that commonly present with WT p53. Approximately half of all cancer patients at initial

diagnosis are characterized as WT p53. Cancer indications in which WT p53 is believed to be prevalent include certain leukemias, breast cancers, melanomas, sarcomas, non-Hodgkin lymphomas, renal cell cancers, hepatocellular carcinoma, epithelial ovarian cancers and thymomas.

We are pursuing a broad registration-oriented clinical development program for ALRN-6924 in multiple solid tumor and hematological cancer indications that commonly present with WT p53. Based on preliminary evidence of safety, tolerability and anti-tumor activity that we observed in our Phase 1 All-comers trial, we commenced tumor-specific trials in PTCL and in AML/MDS. In determining to evaluate ALRN-6924 in PTCL, we considered our preclinical data, data from our Phase 1 All-comers trial, and published literature regarding the role of p53 in T-cell related malignancies. In determining to evaluate ALRN-6924 in AML/MDS, we considered our preclinical data, published literature regarding the role of p53 and MDMX and MDM2 in AML and MDS, that AML has recently been reported to respond to single agent therapy with MDM2 inhibitors in clinical trials conducted by third parties, and data from our compassionate use patient.

We plan to conduct, alone or 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 solid tumors or hematological malignancies that commonly present with WT p53, such as certain leukemias, breast cancers and melanomas. In addition, as many approved drugs and drug candidates for cancer require a functioning p53 pathway, we may also conduct additional clinical trials of ALRN-6924 in combination with other anti-cancer agents. We believe the mechanism of action and safety profile of ALRN-6924 may provide the potential for its combination with conventional and novel therapies, such as targeted therapies, chemotherapy, radiotherapy and immuno-therapy. We expect that we will determine which additional clinical trials we will conduct, if any, and in which indications following our review of the data from our ongoing clinical trials, including, potentially, an investigator-initiated clinical trial of ALRN-6924 as a combination therapy for breast cancer.

In June 2014, we submitted an investigational new drug application, or IND, to the FDA for ALRN-6924 for the treatment of patients with advanced solid tumors or lymphoma expressing WT p53, and in the fourth quarter of 2014, we initiated our ongoing Phase 1 All-comers trial of ALRN-6924 in adult patients with advanced solid tumors or lymphomas expressing WT p53 that are refractory to or intolerant of standard therapy, or for which no standard therapy exists, as a part of a planned Phase 1/2a clinical trial program. In the third quarter of 2016, we initiated a Phase 2a trial of ALRN-6924 in patients with relapsed and/or refractory PTCL whose cells contain WT p53, who have failed at least one prior line of therapy, as an expansion trial under such program. In November 2015, we submitted an IND for ALRN-6924 for the treatment of AML or MDS patients whose cells contain WT p53, and we initiated our Phase 1 and Phase 1b trials in AML/MDS in the second half of 2016 as part of a planned Phase 1/1b clinical trial program. In addition, under a single-patient emergency IND submitted in May 2016, ALRN-6924 was administered in connection with a compassionate use request in one patient with Li-Fraumeni Syndrome who was suffering from MDS that was transforming into AML and who was concurrently suffering from breast cancer.

If we see sufficient evidence of a therapeutic effect in our Phase 2a PTCL trial or any future Phase 2 clinical trials of ALRN-6924, we plan to meet with regulatory authorities to discuss the possibility of an expedited clinical development and regulatory pathway for ALRN-6924, including the scope and timing of a single agent pivotal Phase 2/3 trial that may include between 80 and 120 patients. Based on the anticipated timing of our Phase 2a PTCL trial, and subject to the data from the trial, we may seek discussions with the FDA regarding the registration pathway for PTCL and the design of a single agent pivotal clinical trial as early as the first half of 2018.

Depending on the completion and results of our Phase 1 AML/MDS trial as a monotherapy and our Phase 1b AML/MDS trial as a combination therapy with Ara-C, we may determine to conduct a Phase 2a clinical trial of ALRN-6924 for AML/MDS as a monotherapy and of ALRN-6924 as a combination therapy with Ara-C, in each case, as early as the first half of 2018.

Clinical Development of ALRN-6924

We are currently conducting multiple clinical trials of ALRN-6924: our Phase 1 All-comers trial, our Phase 2a PTCL trial, our Phase 1 AML/MDS trial as a monotherapy and our Phase 1b AML/MDS trial as a combination therapy with Ara-C. Most of the patients in these trials have undergone multiple procedures and/or received a number of approved and experimental treatments.

In our Phase 1 All-comers trial and our Phase 2a PTCL trial, we are conducting preliminary assessments of anti-tumor activity or response to ALRN-6924 using appropriate standard tumor assessment methods, such as computed tomography, or CT, imaging, which was used in the vast majority of patients. We are measuring anti-tumor activity using Response Evaluation Criteria in Solid Tumors 1.1, or RECIST 1.1 criteria, for patients with solid tumors and International Working Group (Cheson 2014), or IWG, criteria for patients with lymphomas, as a means to objectively evaluate whether a tumor has progressed, stabilized or shrunk.

RECIST 1.1 criteria define disease progression and tumor response based on the sum of the longest diameters of a set of target tumor lesions identified when the patient enters the trial. Potential responses include complete responses, partial responses, stable disease or progressive disease. The IWG-issued guidelines (Cheson 2014) provide clinicians guidelines to cover the use of a non-invasive imaging technique to measure and image lesions for assessing all types of lymphoma. Potential responses include complete responses, partial responses, stable disease and progressive disease.

In our Phase 1/1b AML/MDS trials, we are conducting preliminary assessments of anti-leukemic activity or response to ALRN-6924 using standard bone marrow assessment methods. We are measuring anti-leukemic activity using Modified IWG response criteria for patients with AML (Dohner 2010) and IWG criteria for patients with MDS (Cheson 2006), as a means to objectively evaluate whether the disease has progressed, stabilized or improved.

Phase 1 Clinical Trial in Advanced Solid Tumors or Lymphomas

We are conducting a Phase 1 open-label, multi-center, two-arm trial of ALRN-6924 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 of the trial in January 2017 with a total of 71 patients enrolled. These patients have 24 different tumor types. Most of the patients have undergone multiple procedures and/or received a number of approved and experimental treatments. The trial was designed to determine the recommended Phase 2 dose, to evaluate the safety, tolerability and pharmacokinetics, or PK, of ALRN-6924 and provide a preliminary assessment of anti-tumor activity. Treatment of patients in the trial will continue until documentation of progressive disease, unacceptable toxicity or patient or physician decision to discontinue study medication. As of December 28, 2016, nine patients continued to receive treatment in the trial.

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 trial. As of December 28, 2016, 41 patients had received treatment in the first two dose levels and Arm A, and 28 patients had received treatment in Arm B.

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 human papilloma virus, or 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 identify WT p53 patients in this trial, we relied upon commercially available third-party assays and also employed a central laboratory to conduct next generation sequencing on archived tumor tissue samples or fresh biopsy samples from patients taken prior to enrollment. Even though we did not require confirmation of WT p53 in patients prior to enrollment for the initial three dose levels (dose groups 1, 2, 3a and 3b), we attempted to establish WT p53 status through testing after enrollment. Seven of the 13 patients enrolled in those three dose levels who completed at least one cycle were confirmed to have WT p53 status.

In the trial, we are seeking a preliminary assessment of anti-tumor activity or response to ALRN-6924 through the use of standard imaging assessments, such as CT and positron emission tomography, or PET, scans from patients, depending on the number of cycles administered. Imaging is performed at the end of the second cycle and every two cycles thereafter in Arm A, or approximately within 56 days following initial dosing. Patients in Arm B are measured at the end of the third cycle and every three cycles thereafter, or approximately within 63 days following initial dosing. We are measuring anti-tumor activity using RECIST 1.1 criteria for patients with solid tumors and the IWG criteria (Cheson 2014) for patients with lymphomas, as a means to objectively evaluate whether a tumor has progressed, stabilized or shrunk.

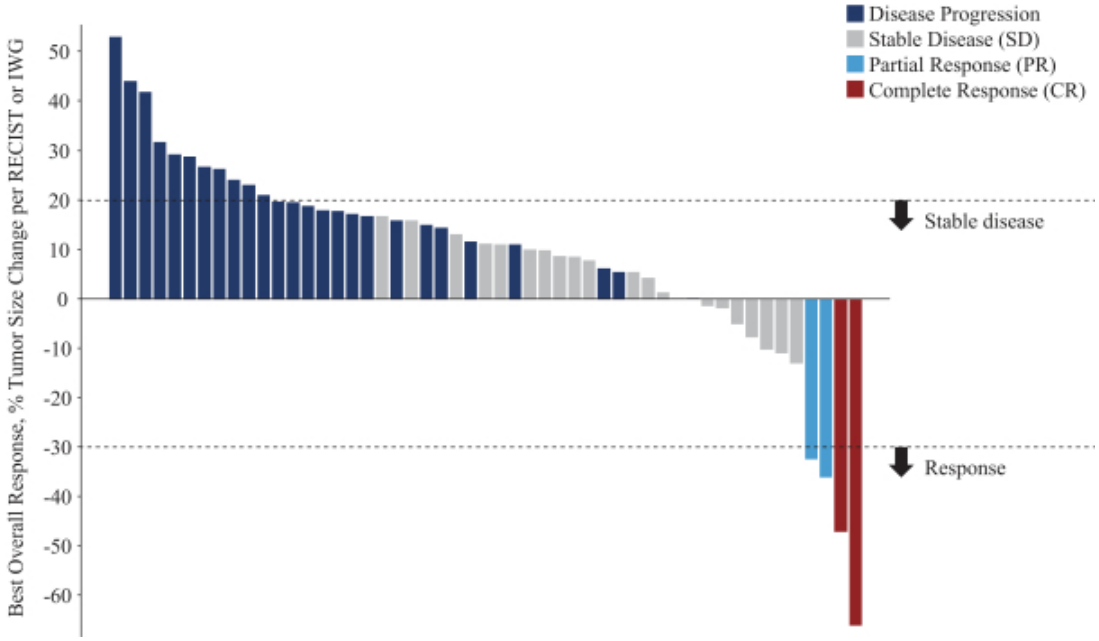
In the trial, we are also seeking a preliminary assessment of the effect of ALRN-6924 on biomarkers. Biomarkers provide us with information as to on-target activity, specific patient type response and early insight as to effect on tumor. We are assessing the effect of ALRN-6924 on potential biomarkers in different sources of biological samples, such as tumor biopsies, circulating tumor cells where detectable, mononuclear blood cells and blood samples. Dependent on the sample type, those biomarkers may include measures of MDMX, MDM2, p21, p53, apoptosis and macrophage inhibitory cytokine-1, or MIC-1. We believe that by evaluating these biomarkers, we may be able to develop a better understanding of the on-target effect, as well as support our understanding of potential future trial designs for ALRN-6924.

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.

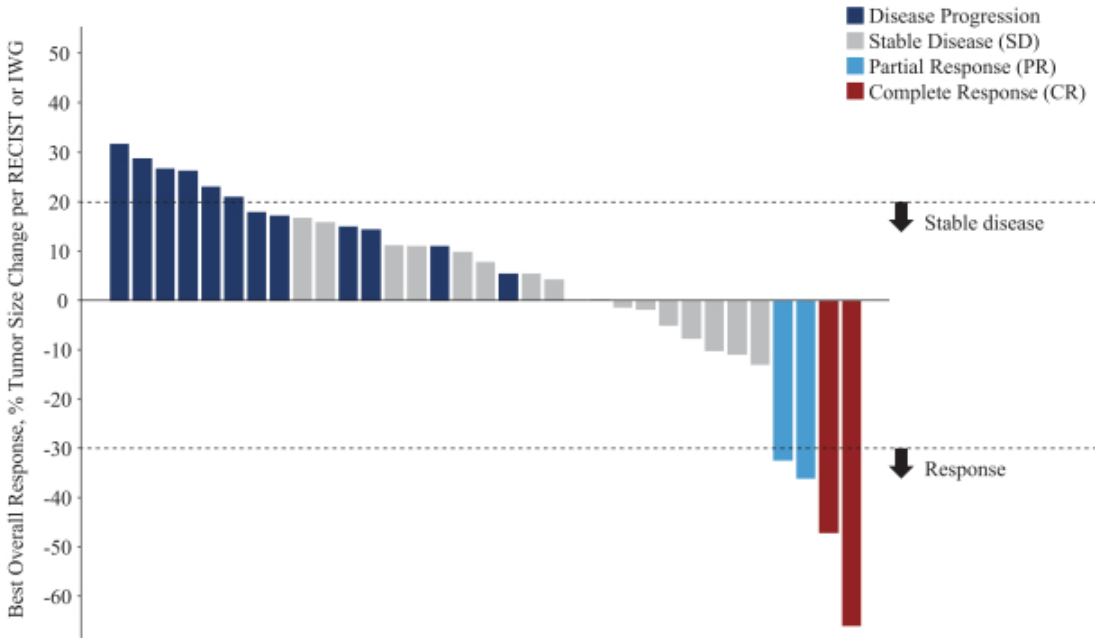
Clinical Activity

As of December 28, 2016, we had enrolled 69 patients in the trial, 55 of whom were evaluable. Of the 55 evaluable patients, 25 patients (or 45%) demonstrated disease control in at least one scan following the start of ALRN-6924 treatment, consisting of two patients who achieved complete responses, two patients who achieved partial responses and 21 patients who achieved stable disease, with 33% of the stable disease patients experiencing shrinkage of the tumor. For patients to be evaluable, they had to have received at least one dose of study medication and have undergone at least one tumor imaging with CT per protocol post-baseline or have experienced clinical progression as determined by the investigator without formal imaging. Of the 69 enrolled patients, 14 patients were not evaluable. Ten of those 14 patients were not evaluable because they had discontinued treatment without an efficacy assessment, including three patients who discontinued treatment due to adverse events, three patients who discontinued treatment due to noncompliance, and four patients who withdrew their informed consent. Four patients were not yet evaluable because they had not yet undergone one tumor imaging.

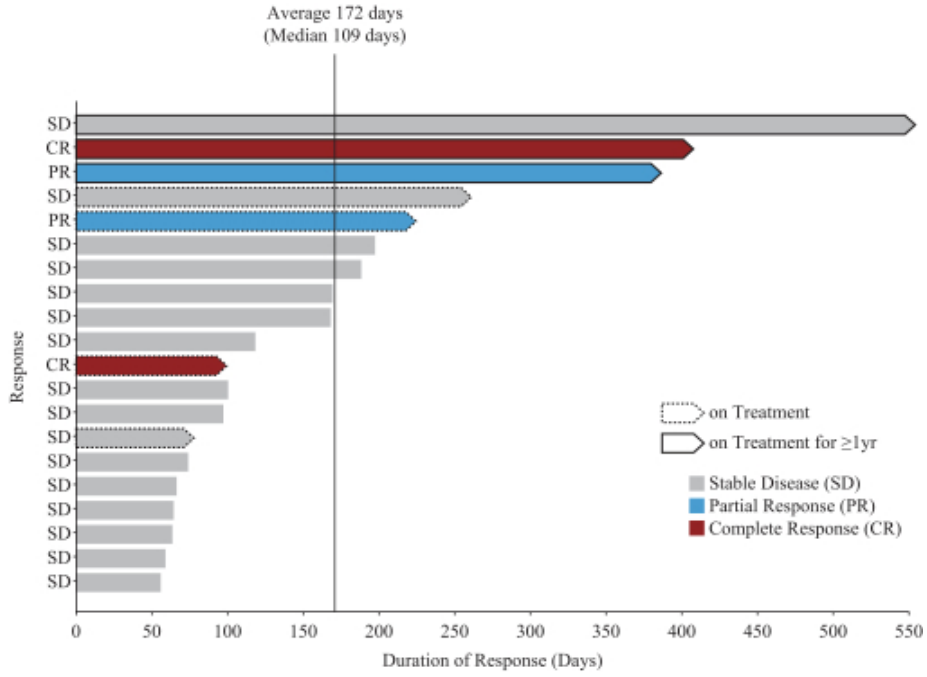
The anti-tumor activity for patients in our Phase 1 All-comers trial is shown in the “waterfall” plot below. In this figure, the percent change in tumor volume for each evaluable patient is plotted from highest to lowest value, or worst to best response, and each bar of the histogram colored by the best overall response measured for that patient per RECIST 1.1 or IWG criteria. The “waterfall” plot only shows the results for 51 of the 55 evaluable patients as of December 28, 2016. Four evaluable patients who left the trial due to clinical measures of disease progression without any scan are not shown.



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 per administration, which we believe to be the minimal clinically relevant dose in this trial. For this purpose, 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, as we do not believe that these doses are relevant to the future clinical development of ALRN-6924. In this subset of 35 evaluable patients as of December 28, 2016, 33 are represented in the "waterfall" plot below as two patients with clinical or objective evidence of disease progression did not receive a scan. Of these 35 evaluable patients, 20 (or 57%) 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 16 patients who achieved stable disease, with 44% of the patients with stable disease experiencing shrinkage of the tumor.



As of December 28, 2016, the median time on drug for all evaluable patients, including patients with mutant p53 status and patients dosed below the minimal clinically relevant level, was 64 days, with an average of 103 days, and a maximum for one patient of 555 days. In the figure below, the time-on-drug is shown for evaluable WT p53 patients in the clinically relevant subset who achieved a complete response, a partial response or stable disease as of December 28, 2016. In these 20 patients, as of December 28, 2016, the median time on drug was 109 days, with an average of 172 days, and a maximum for one patient of 555 days. As of December 28, 2016, three patients have been on drug for more than one year. All patients who have achieved a complete response or partial response since trial inception remain on ALRN-6924.



Safety Results

Based on safety data in our ongoing Phase 1 All-comers trial, we consider ALRN-6924 to be well tolerated by patients in that trial. Across all dose levels as of December 28, 2016, treatment-related adverse events were seen in 96% of patients. Of these patients, 75% reported maximum treatment-related adverse events of grade 1 or 2, 17% reported maximum treatment-related adverse events of grade 3 and 3% reported maximum treatment-related adverse events of grade 4. Fewer than 10% of patients experienced a treatment-related serious adverse event. The most frequent treatment-related adverse events were gastrointestinal side effects, fatigue, anemia and headache. Dose limiting toxicities, or DLTs, were grade 3 fatigue at 3.1 mg/kg, and grade 3 hypotension, grade 3 alkaline phosphatase elevation, grade 3 anemia and grade 4 neutropenia at 4.4 mg/kg, all in five patients in Arm A. All DLTs resolved following dose interruption, dose reduction or treatment discontinuation. Infusion-related reactions were seen in seven patients, with three treatment discontinuations.

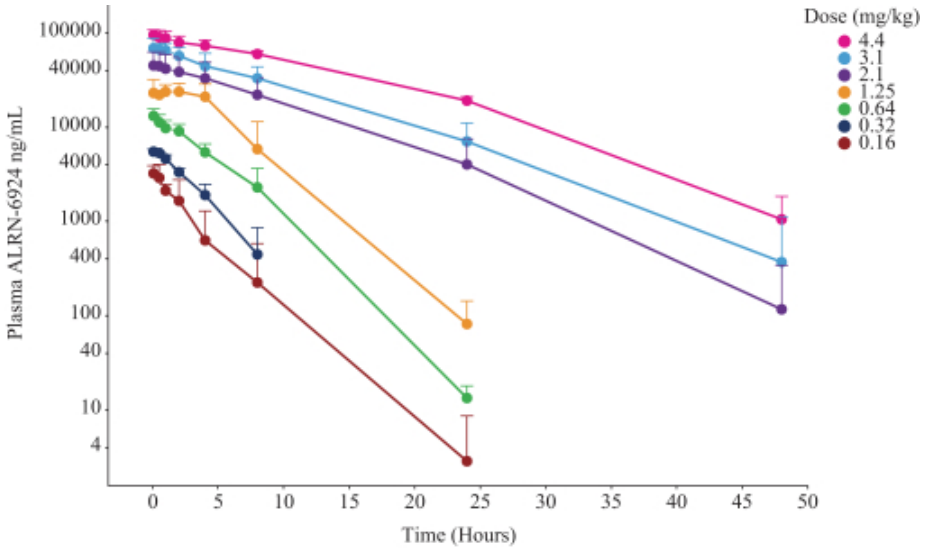
The table below shows the number of patients and percent of the 69 total patients across all dose levels of our Phase 1 All-comers trial experiencing a hematological abnormality as of December 28, 2016. Notably, only three patients (less than 5% in total) have experienced neutropenia of grade 3 or worse, and no patients have experienced thrombocytopenia of grade 3 or worse.

Anemia, Grade[†]				Neutropenia, Grade[†]				Thrombocytopenia, Grade[†]			
1	2	3	4	1	2	3	4	1	2	3	4
13 (19%)	21 (30%)	3 (4%)	0	3 (4%)	3 (4%)	1 (1%)	2 (3%)	14 (20%)	1 (1%)	0	0

[†]Number (%) of patients in our Phase 1 All-comers trial with hematological abnormalities

Pharmacokinetic Profile

We chose to deliver ALRN-6924 systemically in an intravenous administration given potential advantages of avoiding metabolic impact from hepatic and gastrointestinal enzymes as well as reproducible systemic bioavailability. In our Phase 1 All-comers trial, we measured drug concentrations in patient plasma as we increased the dose. As shown in the figure below (for the once-weekly arm), ALRN-6924 produced a dose-related increase in maximum drug plasma concentration in patients, as well as a longer corresponding half-life, up to 5.5 hours at the recommended Phase 2 dose of 3.1 mg/kg.



Clinical Development Plan

Based on the preliminary clinical data from the Phase 1 All-comers trial, we determined to pursue a broad registration-oriented clinical development program for ALRN-6924 in multiple solid tumor and hematological cancer indications that commonly present WT p53. We have chosen to initially evaluate ALRN-6924 as a monotherapy in relapsed and/or refractory PTCL patients whose cells contain WT p53 and in AML or MDS patients whose cells contain WT p53 both as a monotherapy and in combination with Ara-C. We plan to conduct, alone or 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 solid tumors or hematological malignancies that commonly present with WT p53. As many approved drugs and drug candidates for cancer require a functioning p53 pathway, we may also conduct additional clinical trials of ALRN-6924 in combination with other anti-cancer agents. We believe the mechanism of action and safety profile of ALRN-6924 may provide the potential for its combination with conventional and novel therapies, such as targeted therapies, chemotherapy, radiotherapy or immuno-therapy.

Peripheral T-Cell Lymphoma

We are conducting 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.

Lymphoma is the most common blood cancer and it primarily occurs when lymphocytes, a type of white blood cell, grow abnormally and accumulate in one or more lymph nodes. The body has two main types of lymphocytes that can develop into lymphomas: B-lymphocytes, or B-cells, and T-lymphocytes, or T-cells. PTCL comprises a group of rare and aggressive non-Hodgkin lymphomas, or NHL, that develop from mature T-cells. According to the Leukemia and Lymphoma Society, PTCL accounts for approximately 10% to 15% of all NHL cases in the United States, which suggests that 7,200 to 10,800 new cases of PTCL are diagnosed in the United States annually. In a study by the International T-cell Lymphoma Project, overall survival in the most common subtypes of PTCL, PTCL not otherwise specified (NOS) and angioimmunoblastic T-cell lymphoma, at five years was only 32%.

For most subtypes of PTCL, the front-line treatment is typically a combination chemotherapy regimen, such as CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone), EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin), or other multi-drug chemotherapeutic regimens. While over 50% of patients initially respond to these chemotherapeutic regimens, many patients with PTCL do not respond to these regimens or, after initially responding, later relapse. For second-line treatment, some oncologists recommend treating relapsed patients with a variety of intensive combination chemotherapy therapies, such as ICE (ifosfamide, carboplatin, etoposide), followed by an autologous stem cell transplant. Alternatively, patients with relapsed/refractory PTCL may be treated with the chemotherapeutic antifolate pralatrexate (Folotyn), the anti-CD30 antibody-drug conjugate brentuximab vedotin (Adcetris) or the histone deacetylase, or HDAC, inhibitors romidepsin (Istodax) and belinostat (Beleodaq) or a combination of a chemotherapy and one of the HDAC inhibitors. However, these treatments also have demonstrated limited efficacy and tolerability.

We enrolled the first patient in the Phase 2a PTCL trial in August 2016 and plan to initially enroll up to 20 patients in the trial. We are conducting the Phase 2a PTCL trial to provide preliminary insight into the responsiveness of this patient population to ALRN-6924. The primary endpoint of this trial is overall response rate as well as the safety and tolerability of ALRN-6924 in relapsed/refractory PTCL patients. Important secondary endpoints are the duration of response, progression-free and overall survival as well as time-to-response. ALRN-6924 will be administered at a dose of 3.1 mg/kg on days 1, 8 and 15 every 28 days with scans being performed after every two cycles. Treatment of patients will continue until documentation of disease progression, unacceptable toxicity or patient or physician decision to discontinue therapy.

Based on the anticipated timing of our Phase 2a PTCL trial, and subject to the data from the trial, we may seek discussions with the FDA regarding the possibility of an expedited clinical development and registration pathway for ALRN-6924 in PTCL patients and the design of a single agent pivotal Phase 2/3 clinical trial as early as the first half of 2018. We expect to report interim data from this trial in the first half of 2018.

AML/MDS

We are conducting a Phase 1 open label, multi-center clinical trial of ALRN-6924 as a monotherapy for the treatment of AML or MDS patients whose cells contain WT p53 and a Phase 1b open label, multi-center

clinical trial of ALRN-6924 in combination with Ara-C for the treatment of AML or MDS patients whose cells contain WT p53. In determining to evaluate ALRN-6924 in AML/MDS, we considered our preclinical results, published literature regarding the role of p53 in AML and MDS, that AML has recently been reported to respond to single agent therapy with MDM2 inhibitors in clinical trials conducted by third parties, and data from our compassionate use patient.

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. We believe that a total of approximately 41,000 new cases of AML are diagnosed each year in the United States, France, Germany, Italy, Spain, the United Kingdom and Japan. Survival is age-dependent and survival rates are extremely poor for the elderly. According to the U.S. National Cancer Institute, in the United States, while the five-year relative survival for AML patients age 20 to 49 years is 55%, it is only 6% for patients that are 65 years or older. 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 American Cancer Society, or ACS, estimates that there are 13,000 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 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.

The front-line treatment for patients with AML is typically a combination chemotherapy, such as intensive Ara-C-based induction chemotherapy followed by Ara-C-based consolidation therapy. Because Ara-C-based induction chemotherapies have significant toxicities, elderly patients with AML typically do not qualify for those therapies. We estimate that only approximately 57% of elderly patients receive front-line treatment for AML and that approximately 20% receive second-line treatment. Instead, elderly patients are treated with palliative measures encompassing best supportive care, low-dose Ara-C, or hypomethylating agents such as decitabine (Dacogen) or azacitidine (Vidaza), or they are referred to clinical trials with investigational agents. Once elderly patients experience disease progression following their initial treatment, they have a very poor expected survival rate and treatment represents a significant medical challenge. Many elderly patients go untreated after failure of these treatment options. Over the past two decades, many compounds have been evaluated in elderly patients with AML, but due to significant toxicities and/or lack of efficacy, only one new treatment with limited application has been specifically approved for AML.

We are conducting a Phase 1 open label, multi-center clinical trial of ALRN-6924 for the treatment of AML or MDS patients whose cells contain WT p53 as a monotherapy. We enrolled the first patient in the Phase 1 trial in the fourth quarter of 2016 and expect to enroll up to 15 patients in the trial. We expect to complete this enrollment in the fourth quarter of 2017. The trial is intended to establish the recommended Phase 2 dose of ALRN-6924 in patients with AML or MDS. The trial is also designed to evaluate the safety, tolerability and PK of ALRN-6924 in patients with AML or MDS and provide a preliminary assessment of anti-leukemic activity. The trial uses a 3+3 dose escalation design. Patients receive ALRN-6924 once a week for three consecutive weeks over a 28-day cycle. We are treating the first cohort of patients in the trial with an initial dose of 3.1 mg/kg. Subsequent cohorts will be treated at increasing dose levels.

We are also conducting a Phase 1b open label, multi-center clinical trial of ALRN-6924 in combination with Ara-C for the treatment of AML or MDS patients whose cells contain WT p53. We enrolled the first patient in the Phase 1b trial in the fourth quarter of 2016 and expect to enroll up to 15 patients in the trial. We expect to complete this enrollment in the fourth quarter of 2017. The trial is intended to establish the recommended Phase 2 dose of ALRN-6924 in combination with Ara-C in patients with AML or MDS. The trial is also designed to evaluate the safety, tolerability and PK of ALRN-6924 in combination with Ara-C in patients with AML or MDS and provide a preliminary assessment of anti-leukemic activity. The trial uses a 3+3 dose escalation design. Patients receive ALRN-6924 in combination with Ara-C once a week for three consecutive weeks over a 28-day cycle. We are treating the first cohort of patients in the trial with an initial dose of 3.1 mg/kg plus 100 mg/m^2 of Ara-C. Subsequent cohorts will be treated at increasing dose levels of ALRN-6924 and/or Ara-C.

Treatment of patients will continue until documentation of progressive disease, unacceptable toxicity or patient or physician decision to discontinue study medication. Bone marrow assessments for hematologic

response are performed at the end of every second cycle for AML patients, at the end of every third cycle for MDS patients, and at the end of study or at relapse for both AML and MDS patients. If peripheral blood counts change in a manner suggestive of change in the underlying disease, a bone marrow assessment may be conducted outside the scheduled visits at the discretion of the investigator.

Additional Combination Trials

A standard treatment practice in oncology is the use of multiple agents in combination regimens to improve patient outcomes. Since p53 is involved in mediating cell cycle arrest and apoptosis in response to various approved anti-cancer agents, we believe that there is an opportunity to potentially amplify the anti-tumor effects of other therapeutic anti-cancer agents by combining them with ALRN-6924.

Our preclinical data and recent published data indicate that there may be synergy between p53-reactivating therapy and different anti-cancer agents, such as targeted therapies and chemotherapy. In addition to our AML/MDS combination study, we may also conduct additional clinical trials of ALRN-6924 in combination with other anti-cancer agents. We believe the mechanism of action and safety profile of ALRN-6924 may provide the potential for its combination with conventional and novel therapies. Prior to commencing these trials, we would plan to conduct preclinical studies of ALRN-6924 in combination with these other anti-cancer agents in *in vitro* studies and, where appropriate, subsequent *in vivo* xenograft studies to evaluate activity and tolerability of individual combinations with ALRN-6924.

Some of our studies combining ALRN-6924 with other anti-cancer agents have shown the potential benefits of combination therapy. In *in vitro* testing, we have investigated the combination of more than 20 drugs with ALRN-6924, including drugs that target a variety of pathways mediated by p53, including MAPK, mTOR and CDK4/6 inhibitors, and traditional chemotherapeutic agents, including demethylating agents, such as rituximab (Rituxan®), obinutuzumab (Gazyva®), palbociclib (Ibrance®), erverolimus (Afinitor®), pembrolizumab (Keytruda®), nivolumab (Opdivo®), dabrafenib (Tafinlar®), vemurafenib (Zelboraf®), capecitabine (Xeloda®) and trifurdine/tipiracil (Lonsurf®). The results indicate that almost all of the selected drugs are additive or synergistic with ALRN-6924 *in vitro*, with the exception of dexamethasone, which was expected to have no effect on ALRN-6924 activity. To date, no antagonism of any tested drugs with ALRN-6924 was found.

Companion Diagnostic

If we decide to seek marketing approval of ALRN-6924 with a label limited to WT p53 cancer patients, we would be required to have a companion *in vitro* diagnostic approved for use with ALRN-6924. We would also expect that we would 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 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 status.

Preclinical Studies

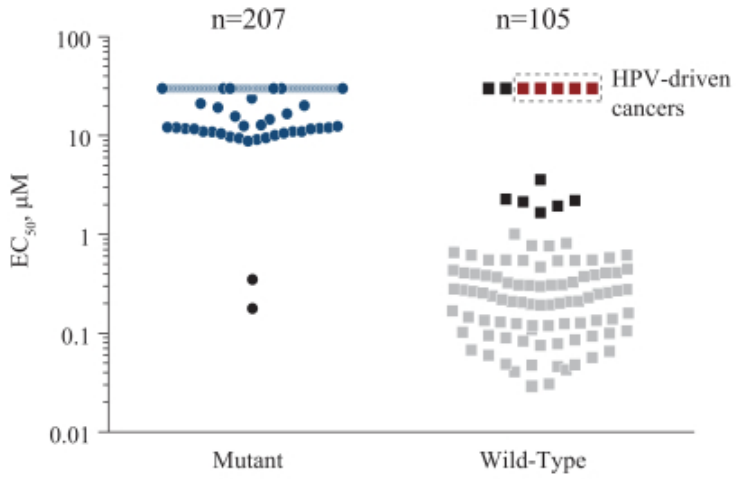
We conducted several *in vivo* and *in vitro* studies of ALRN-6924 that informed our approach to the design of our clinical trials and provided safety information needed to initiate patient selection and dosing in our trials. In these preclinical studies, ALRN-6924 bound to both MDMX and MDM2 with nanomolar 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, ALRN-6924 demonstrated tumor growth suppression, p53-dependent cell cycle arrest, apoptosis and anti-tumor activity in an MDMX/MDM2-overexpressing xenograft cancer model with clear correlation to on-target PK and pharmacodynamic activity.

ALRN-6924 has also been studied in a patient with Li-Fraumeni Syndrome who was suffering from MDS that was transforming into AML, and who was concurrently suffering from breast cancer, under a single-

patient emergency IND, or compassionate use. With respect to this patient, after harvesting leukemic cells as well as healthy control lymphocytes, the investigator measured intracellular protein levels of p53 and its downstream effector p21, in the patient's cells. Treatment with ALRN-6924 resulted in a 10-fold increase of intracellular levels of p53 and p21 within 12 hours in the leukemic stem cell compartment, whereas control healthy lymphocytes did not show any meaningful increase in p53 or p21 protein levels.

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 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.



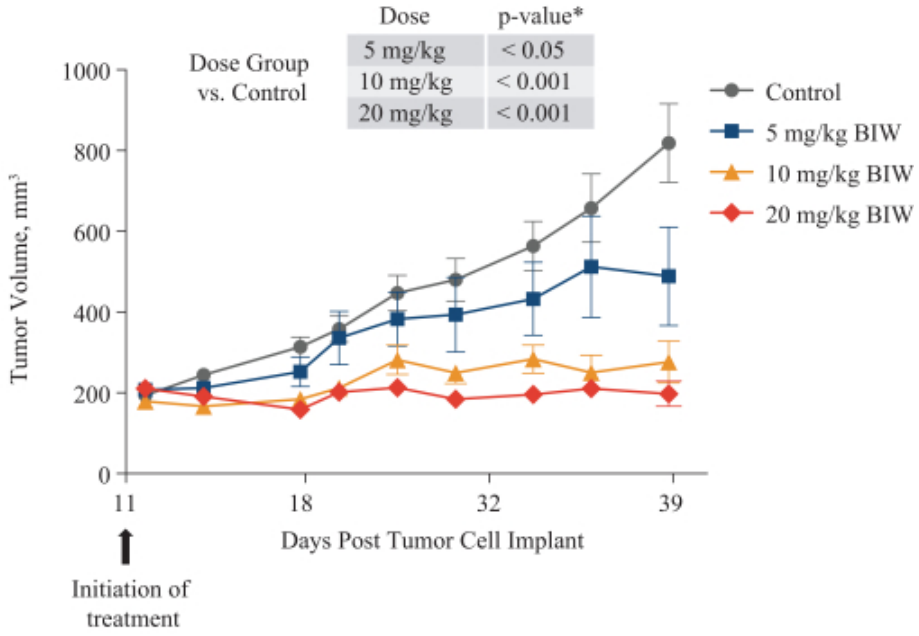
EC_{50} = Drug conc. at which 50% of tumor cells are killed
EC_{50} values ≥ 30 µM are shown as 30 µM

In another preclinical study, we measured the binding affinity of ALRN-6924 for MDMX and MDM2 relative to the binding affinity for MDMX and MDM2 of WT p53 and of a small molecule MDM2 inhibitor. The affinity of a drug to a receptor is the measure of how effectively that drug binds to its target and can provide insight on the potential for on-target effect and off-target toxicity. We have designed ALRN-6924 to bind to both MDMX and MDM2 with higher affinity than WT p53. As a result, ALRN-6924 is able to displace MDMX and MDM2, and thereby enable bound p53 to be released to reactivate p53 function. In this study, the MDM2 inhibitor displayed strong binding affinity to MDM2 and non-measurable binding affinity to MDMX. The table below shows ALRN-6924's ability to bind to MDMX and MDM2 relative to WT p53 and the small molecule MDM2 inhibitor. Lower nanomolar concentrations (nM) in the table reflect a stronger binding affinity (K_d) with MDMX or MDM2.

(measured in K_d, nM)	WT p53	ALRN-6924	MDM2 Inhibitor
MDM2	770	13.7	9.8
MDMX	480	8.9	> 3,000

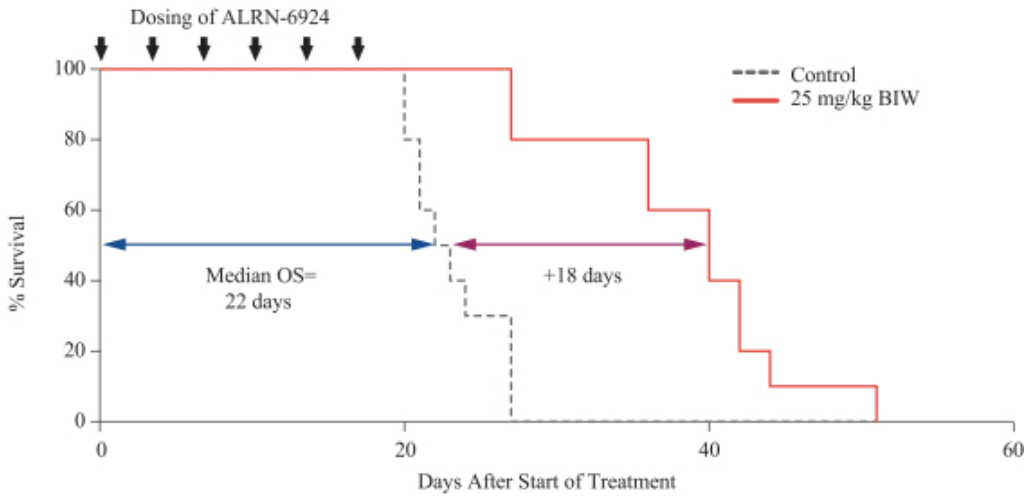
In Vivo

In our *in vivo* preclinical studies of ALRN-6924, we have studied the effects of ALRN-6924 in both solid and liquid tumors. In this study, 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 another 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, supported our belief that ALRN-6924 may potentially have an effect in liquid tumors with WT p53. The figure below shows the results of the preclinical study.



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 stapled peptides. We believe that specific changes in the chemical structures of our stapled peptides may engender our stapled peptides with varying affinities to MDMX and MDM2, enabling better targeting of cancers that are more dependent on one p53 suppressor protein or the other. 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 stapled peptides may be effective against a variety of cancer targets, as well as targets in other therapeutic areas, such as infectious disease, metabolic disease and immunology. 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 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, RORã, which is implicated in rheumatoid arthritis, RSV fusion protein, which is implicated in RSV, and HIF-1a, which is implicated in diabetes and metabolic disease.

Since our inception, we have created over 10,000 stapled 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, it is our intention to make selective investments into some of these 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 partnerships 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 a license agreement with Materia, pursuant to which 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. If Materia 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 Materia 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.

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 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, Amgen Inc., Novartis AG and Daiichi Sankyo Co., Ltd. Roche is currently conducting Phase 3 testing of its MDM2 agent in combination with high-dose Ara-C in AML patients between the ages of 18 and 60.

If ALRN-6924 was approved for the indications for which we currently have ongoing clinical trials, it will compete with currently-marketed drugs and will likely compete with other drugs that are currently in clinical development, each as discussed below.

PTCL

For most subtypes of PTCL, the front-line treatment is typically a combination chemotherapy regimen, such as CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone), EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin), or other multi-drug chemotherapeutic regimens. While over 50% of patients initially respond to these chemotherapeutic regimens, many patients with PTCL do not respond to these regimens or, after initially responding, later relapse. For second-line treatment, some oncologists recommend treating relapsed patients with a variety of intensive combination chemotherapy therapies, such as ICE (ifosfamide, carboplatin, etoposide), followed by an autologous stem cell transplant.

In addition, although treatment practices vary, there are currently four FDA-approved drugs specifically for the treatment of PTCL that are used for second-line treatment: pralatrexate (Folotyn), an antifolate chemotherapy marketed by Spectrum Pharmaceuticals, Inc. for the treatment of relapsed/refractory PTCL; belinostat (Beleodaq), an HDAC inhibitor marketed by Spectrum Pharmaceuticals, Inc. for the treatment of relapsed/refractory PTCL; romidepsin (Istodax), an HDAC inhibitor marketed by Celgene Corporation for the treatment of relapsed/refractory PTCL in patients who have received at least one prior therapy; and brentuximab vedotin (Adcetris), an anti-CD30 antibody-drug conjugate marketed by Seattle Genetics, Inc. for the treatment of a subtype of PTCL after failure of at least one prior multi-agent chemotherapy regimen. The approved drugs are being clinically tested in combination with a wide variety of agents. We are aware of multiple investigational agents in clinical development for PTCL, including product candidates from AstraZeneca PLC, Bristol-Myers Squibb Company, Celgene Corporation, Eisai Co., Ltd., Kura Oncology, Inc. and Merck & Co., Inc. If approved, these new product candidates may compete with currently-approved therapies.

AML/MDS

The front-line treatment for patients with AML is typically a combination chemotherapy, such as intensive Ara-C-based induction chemotherapy followed by Ara-C-based consolidation therapy. Because Ara-C-based induction chemotherapies have significant toxicities, elderly patients with AML typically do not qualify for those therapies. Instead, they are treated with palliative measures encompassing best supportive care, low-dose Ara-C, or hypomethylating agents such as decitabine (Dacogen) or azacitidine (Vidaza), or they are referred to clinical trials with investigational agents. Once elderly patients experience disease progression following their initial treatment, they have a very poor expected survival rate and treatment represents a significant medical challenge. Many elderly patients go untreated after failure of these treatment options. Over the past two decades, many compounds have been evaluated in elderly patients with AML, but due to significant toxicities and/or lack of efficacy, only one new treatment with limited application has been specifically approved for AML.

We are aware of numerous new therapies that are being developed for specific subsets of AML patients, including three product candidates for which NDAs have been submitted to the FDA: midostaurin (Novartis AG), a front-line treatment in combination with Ara-C standard induction chemotherapy for AML patients with FLT3 mutations, Vyxeos/CPX-351 (Jazz Pharmaceuticals plc) for adults with therapy-related AML or AML with myelodysplasia-related changes, and AG-221/CC-90007 (enasidenib) (Celgene Corporation), for patients with IDH2m+ hematologic malignancies. We are aware of a number of product candidates in late-stage clinical development being developed by Daiichi Sankyo Co., Ltd., Astex Pharmaceuticals, Inc., Agios Pharmaceuticals, Inc., AbbVie Inc., Seattle Genetics, Inc. and earlier-stage product candidates being developed by Astellas Pharma Inc., Boehringer Ingelheim GmbH, Janssen Research & Development, LLC, Karyopharm Therapeutics Inc. and Pfizer Inc.

AML and MDS are often treated similarly in clinical practice. The front-line treatment for patients with higher-risk MDS in the United States are combination chemotherapy or hypomethylating agents such as decitabine (Dacogen) or azacitidine (Vidaza). We are aware of several ongoing clinical trials aimed at expanding the use of approved chemotherapy and immunomodulatory agents in higher-risk MDS, as well as several new clinical programs testing novel technologies in this area, including product candidates from Astex Pharmaceuticals, Inc., Celgene Corporation, CTI BioPharma Corp., Cyclacel Pharmaceuticals, Inc., Eisai Co., Ltd., Karyopharm Therapeutics Inc., Onconova Therapeutics, Inc., and Takeda Pharmaceutical Company Limited.

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 April 30, 2017, we owned or had an exclusive license to at least 46 U.S. patents, at least 49 pending U.S. provisional or non-provisional patent applications, at least 134 foreign patents and at least 155 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 April 30, 2017, we owned or had an exclusive license to at least 20 U.S. patents, at least 19 pending U.S. provisional or non-provisional patent applications, at least 85 foreign patents and at least 75 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 April 30, 2017, at least 14 U.S. patents, at least four pending U.S. non-provisional patent applications, at least 97 foreign patents and at least 25 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, subject to certain rights with respect to products for indications for which we are not interested in pursuing development. 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. 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 March 31, 2017, we have paid non-refundable fees, consisting of license and maintenance fees, milestone payments and sublicense fees, of $4.4 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.

During the term of the agreement, we have agreed to purchase all of our olefin metathesis catalyst compositions from Materia at agreed prices, subject to potential cost-based increases over time. If Materia 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 Materia can meet our requirements and notifies us in writing.

As of March 31, 2017, we paid non-refundable fees, consisting of an up-front technology access fee and annual maintenance payments and milestone payments, to Materia of $800,000. We are obligated to pay Materia 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 Materia 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 Materia 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 Materia.

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, 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.

Review and Approval 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. Subsequently, through final guidance issued in April 2015, FDA indicated that a "chemically synthesized polypeptide" is any alpha amino acid polymer that (1) is made entirely by chemical synthesis; and (2) is less than 100 amino acids in size. 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 laboratory evaluation of product

chemistry, toxicity and formulation, as well as *in vitro* and 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 after the IND is submitted.

The IND and IRB Processes

An IND is an exemption from the FDCA that allows an unapproved drug to be shipped in interstate commerce for use in an investigational clinical trial and 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, the FDA may also place a clinical hold or partial clinical hold on that trial. 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 information provided by the sponsor correcting the deficiencies previously cited or otherwise 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 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. Other reasons for suspension or termination 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.

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 serious adverse events occur. In addition, IND safety reports must be submitted to the

FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. 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.

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 2017 is $2,038,100. The sponsor of an approved NDA is also subject to annual product and establishment user fees, which for fiscal year 2017 are $97,750 per product and $512,200 per establishment.

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.

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

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 and priority review 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.

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 irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. 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 addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

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. 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.

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 Studies and Exclusivity

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.

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.

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.

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. 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 would 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 an application fee, which exceeds $250,000 for most PMAs. 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, then-President Obama signed 21st Century Cures Act, or the Cures Act, 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 will become applicable by October 2018. 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.

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 European Union. In the European Union, new chemical entities 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 Regulation (EC) No 726/2004, as amended, and Directive 2001/83/EC, as amended. Data exclusivity prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic (abbreviated) 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 the innovator's data may be referenced, but no generic medicinal product can be marketed 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.

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 U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under 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, which may apply to healthcare items or services that 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.

Healthcare Reform

A primary trend in the United States healthcare industry and elsewhere is cost containment. 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 other medical products, government control and other changes to the healthcare system in the United States

In March 2010, the United States Congress enacted the Affordable Care Act, or ACA, which, among other things, includes changes to the coverage and payment for drug products under government healthcare programs. Among the provisions of the ACA of importance to our potential drug candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;

- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;

- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices;

- addressed 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;

- expanded the types of entities eligible for the 340B drug discount program;

- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D; 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.

Other legislative changes have been proposed and adopted in the United States since the Affordable Care Act 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 will remain in effect through 2025 unless additional Congressional action is taken. In January 2013, then-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. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their commercial products, which has resulted in several Congressional inquiries and proposed bills designed to, among other things, reform government program reimbursement methodologies.

Legislative changes to or regulatory changes under the ACA remain possible and appear likely in the 115th U.S. Congress and under the Trump administration. The nature and extent of any legislative or regulatory changes to the ACA are uncertain at this time, particularly given the introduction of the American Health Care Act of 2017, or AHCA, which would repeal and replace key portions of the ACA. The AHCA was passed by the U.S. House of Representatives but remains subject to passage by the U.S. Senate. It is possible that the AHCA or other repeal and replacement initiatives, if enacted into law, could ultimately result in fewer individuals having health insurance coverage or in individuals having insurance coverage with less generous benefits. The scope of potential future legislation to repeal and replace ACA provisions is highly uncertain in many respects.

Legal Proceedings

We are not currently subject to any material legal proceedings.

Facilities

Our facilities consist of office and laboratory space of approximately 7,400 square feet in Cambridge, Massachusetts under an operating lease agreement that expires in May 2018. We expect to move into a new facility in 2018.

Employees

As of April 30, 2017, we had 14 full-time employees, including a total of seven employees with M.D. and/or Ph.D. degrees. Of the workforce, ten employees are directly engaged in research and development with the rest providing administrative, business and operations support. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider the relationship with our employees to be good. We also use outside consultants and contractors with unique expertise and skills for limited engagements. As of April 30, 2017, we utilized multiple outside consultants or contractors that represented approximately seven full-time equivalents to supplement our full-time workforce.

MANAGEMENT

The following table sets forth the name, age as of April 30, 2017 and position of each of our executive officers and directors.

Name	Age	Position
Executive Officers		
Joseph A. Yanchik III	53	President and Chief Executive Officer and Director
Manuel C. Aivado, M.D., Ph.D.	47	Senior Vice President, Chief Medical Officer
Kira A. Nelson	48	Vice President, Finance and Operations
Non-Employee Directors		
Scott B. Kapnick	58	Chairman of the Board of Directors
Reinhard J. Ambros, Ph.D.	61	Director
Brian M. Gallagher, Jr., Ph.D.	47	Director
John H. McArthur, Ph.D.	82	Director
Armen B. Shanafelt, Ph.D.	58	Director
Caleb Winder	45	Director

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

Executive Officers

Joseph A. Yanchik III has served as our President and Chief Executive Officer and as a member of our board of directors since January 2006. From June 2005 until September 2006, Mr. Yanchik served as a venture partner at Apple Tree Partners, a life sciences investment firm, and from June 2005 until March 2008, he served as chief executive officer of Tokai Pharmaceuticals, Inc., or Tokai, a biopharmaceutical company focused on prostate cancer treatment. Mr. Yanchik has served on the board of directors of Tokai since August 2005. Previously, Mr. Yanchik served as vice president of corporate development at Mendel Biotechnology, Inc., an agricultural biotechnology company, and was the founder and chief business officer of Poetic Genetics, Inc., a gene therapy company. Prior to that, Mr. Yanchik specialized in corporate and securities law at Cahill Gordon & Reindel and Venture Law Group. Mr. Yanchik received a B.B.A. from Loyola College and a J.D. from the Villanova University School of Law. We believe Mr. Yanchik is qualified to serve on our board of directors due to his service as our President and Chief Executive Officer and his extensive knowledge of our company and industry.

Manuel C. Aivado, M.D., Ph.D. has served as our Senior Vice President, Chief Medical Officer since September 2014. From March 2012 until September 2014, Dr. Aivado served as vice president of clinical development and pharmacovigilance at Taiho Oncology, Inc., a pharmaceutical company. From October 2006 until March 2012, Dr. Aivado served as senior medical director in the clinical development group at GlaxoSmithKline, Inc., a global pharmaceutical company. In addition, Dr. Aivado was an instructor in medicine at Beth Israel Deaconess Medical Center/Harvard Medical School. Prior to his industry experience, Dr. Aivado practiced clinical medicine in Germany for ten years, during which time he was awarded the Dr. Mildred Scheel cancer research scholarship award in 2002. Dr. Aivado is a German board-certified physician for internal medicine, hematology and medical oncology, and he received an M.D. and Ph.D. from the Medical School of the University of Dusseldorf, in Germany.

Kira A. Nelson, CPA has served as our Vice President, Finance and Operations since April 2015. From February 2013 to April 2015, Ms. Nelson served as our Director of Accounting and Finance. From March 2002 to February 2013, Ms. Nelson was a finance and accounting consultant to companies in various industries, including biotechnology, providing accounting and finance services. From 1998 to March 2002, Ms. Nelson held various positions at Omtool, Ltd., a developer of software solutions, ultimately serving as chief financial officer,

secretary and treasurer. From 1997 to 1998, Ms. Nelson served as a senior financial analyst at Discreet Logic. Ms. Nelson began her career at Arthur Andersen LLP, where she became a certified public accountant. Ms. Nelson received a B.A. from the College of the Holy Cross.

Non-Employee Directors

Scott B. Kapnick has served as a member of our board of directors since April 2011 and as Chairman of our board of directors since November 2013. Mr. Kapnick has served as chief executive officer of HPS Investment Partners, LLC, a global investment platform with a focus on non-investment grade credit, since 2007 when he founded the firm. From July 2013 to March 2016, Mr. Kapnick also served as chief executive officer of Highbridge Capital Management, LLC, a global alternative investment management organization. Before joining Highbridge, Mr. Kapnick spent twenty-one years at Goldman Sachs, a global investment banking, securities and investment management firm, including serving as a management committee member, partner and co-head of global investment banking at Goldman Sachs from 2001 to 2006 and as co-chief executive officer of Goldman Sachs International from 2005 to 2006. Mr. Kapnick is a member of the Council on Foreign Relations. Mr. Kapnick received a B.A. from Williams College and holds a combined J.D./M.B.A. from the University of Chicago. We believe Mr. Kapnick is qualified to serve on our board of directors due to his extensive investment and financial experience.

Reinhard J. Ambros, Ph.D. has served as a member of our board of directors since June 2013. Since August 2005, Dr. Ambros has served as global head of Novartis Venture Funds, a venture fund that invests in life sciences companies. He previously served as head of group strategic planning for Novartis Corporation, a multinational pharmaceutical company, from 2001 until 2005, and as global head of business development and licensing for cardiovascular and metabolic diseases at Novartis Pharma AG. Dr. Ambros received an M.S. from the University of Regensburg, Germany, and a Ph.D. in medicinal chemistry and pharmacology from the University of Regensburg, Germany. We believe Dr. Ambros is qualified to serve on our board of directors due to his management experience in the biotechnology sector and his service on other boards of directors.

Brian M. Gallagher, Jr., Ph.D. has served as a member of our board of directors since December 2010. Since May 2010, Dr. Gallagher has served as a partner at S.R. One, Limited, the corporate venture capital arm of GlaxoSmithKline. From July 2008 until May 2010, Dr. Gallagher worked at Sirtris Pharmaceuticals, Inc., a biotechnology company that was acquired by GlaxoSmithKline in 2008. Prior to that, Dr. Gallagher was with Alantos Pharmaceuticals, Inc., a pharmaceutical company which was acquired by Amgen, Inc., a multinational biopharmaceutical company, in 2007. Dr. Gallagher received a B.S. from the University of Massachusetts and an M.S. and Ph.D. from the University of Michigan. We believe Dr. Gallagher is qualified to serve on our board of directors due to his investment and operations experience in the life sciences industry.

John H. McArthur, Ph.D. has served as a member of our board of directors since April 2011. Since 1995, Dr. McArthur has served as the George F. Baker professor of business administration emeritus and dean emeritus at Harvard Business School. From 1980 until 1995, he served as dean of the faculty at Harvard Business School. Prior to that, Dr. McArthur was a member of the faculty at Harvard Business School since 1962. Since 1999, Dr. McArthur has served as a member of the board of directors of Koç Holding, A.S., a multinational industrial conglomerate. From 1995 to 2005, Dr. McArthur served as senior advisor to the president of The World Bank. Dr. McArthur formerly served as chair of Brigham and Women’s Hospital. He received a B.C. from the University of British Columbia and an M.B.A. and Ph.D. from Harvard Business School. We believe Dr. McArthur is qualified to serve on our board of directors due to his extensive experience on multinational corporate boards and understanding of and expertise in business management and corporate governance.

Armen B. Shanafelt, Ph.D. has served as a member of our board of directors since November 2013. Since April 2009, he has served as a partner at Lilly Ventures, one of the venture capital arms of Eli Lilly and Company, a global pharmaceutical company. Prior to joining Lilly Ventures, Dr. Shanafelt served as the chief scientific officer of the biotechnology division at Eli Lilly and Company. Prior to joining Eli Lilly, he was a

research fellow and director of research at Roche Diagnostics Corporation, a global diagnostics company, and held several leadership positions in the biotechnology division at Bayer Corporation, a multinational chemical and healthcare corporation. Dr. Shanafelt currently serves on the boards of directors of two publicly traded biopharmaceutical companies, Aeglea BioTherapeutics, Inc. and Protagonist Therapeutics, Inc. Dr. Shanafelt received a B.S. from Pacific Lutheran University and a Ph.D. from the University of California, Berkeley. We believe Dr. Shanafelt is qualified to serve on our board of directors due to his significant background in pharmaceutical research and development and his experience in life sciences investing.

Caleb Winder has served as a member of our board of directors since December 2014. He has served as a managing director of Excel Venture Management, or Excel, a venture capital firm that focuses on life science technologies, since March 2014, served as a director of Excel from November 2010 to February 2014, and served as vice president of Excel from January 2007 to October 2010. Prior to this, Mr. Winder was a principal at Biotechonomy, a life sciences research and investment firm, where he financed and managed several entrepreneurial ventures. Mr. Winder received a B.A. from Colby College and an M.B.A. from Babson College. We believe Mr. Winder is qualified to serve on our board of directors due to his investment experience in the life sciences sector.

Board Composition and Election of Directors

Board Composition

Our board of directors currently consists of eight members. Our directors hold office until their successors have been elected and qualified or until the earlier of their resignation or removal.

Our certificate of incorporation and bylaws that will become effective as of the closing date of this offering provide that the authorized number of directors may be changed only by resolution of our board of directors. Our certificate of incorporation and bylaws will also provide that our directors may be removed only for cause by the affirmative vote of the holders of at least 75% of our shares of capital stock present in person or by proxy and entitled to vote, and that any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office.

In accordance with the terms of our certificate of incorporation and bylaws that will become effective as of the closing date of this offering, our board of directors will be divided into three classes, class I, class II and class III, with members of each class serving staggered three-year terms. Upon the closing of this offering, the members of the classes will be divided as follows:

- the class I directors will be , and , and their term will expire at the annual meeting of stockholders to be held in 2018;
- the class II directors will be , and , and their term will expire at the annual meeting of stockholders to be held in 2019; and
- the class III directors will be and , and their term will expire at the annual meeting of stockholders to be held in 2020.

Upon the expiration of the term of a class of directors, directors in that class will be eligible to be elected for a new three-year term at the annual meeting of stockholders in the year in which their term expires.

We have no formal policy regarding board diversity. Our priority in selection of board members is identification of members who will further the interests of our stockholders through his or her established record of professional accomplishment, the ability to contribute positively to the collaborative culture among board members, knowledge of our business and understanding of the competitive landscape.

Director Independence

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

In 2017, our board of directors undertook a review of the composition of our board of directors and its committees and the independence of each director. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board of directors has determined that is an "independent director" as defined under applicable NASDAQ rules, including, in the case of all the members of our audit committee, the independence criteria set forth in Rule 10A-3 under the Exchange Act, and in the case of all the members of our compensation committee, the independence criteria set forth in Rule 10C-1 under the Exchange Act. In making such determination, our board of directors considered the relationships that each such non-employee director has with our company and all other facts and circumstances that our board of directors deemed relevant in determining his or her independence, including the beneficial ownership of our capital stock by each non-employee director. Mr. Yanchik is not an independent director under these rules because he is our President and Chief Executive Officer.

There are no family relationships among any of our directors or executive officers.

Board Committees

Our board of directors has established an audit committee, a compensation committee and a nominating and corporate governance committee. Each of these committees will operate under a charter that has been approved by our board of directors. The composition of each committee will be effective as of the date of this prospectus.

Audit Committee

The members of our audit committee are , and , and is the chair of the audit committee. Effective as of the date of this prospectus, our audit committee's responsibilities will include:

- appointing, approving the compensation of, and assessing the independence of our registered public accounting firm;

- overseeing the work of our independent registered public accounting firm, including through the receipt and consideration of reports from that firm;
- reviewing and discussing with management and our independent registered public accounting firm our annual and quarterly financial statements and related disclosures;
- monitoring our internal control over financial reporting, disclosure controls and procedures and code of business conduct and ethics;
- overseeing our internal audit function, if any;
- discussing our risk assessment and risk management policies;
- establishing policies regarding hiring employees from our independent registered public accounting firm and procedures for the receipt and retention of accounting related complaints and concerns;
- meeting independently with our internal auditing staff, if any, our independent registered public accounting firm and management;
- reviewing and approving or ratifying any related person transactions; and
- preparing the audit committee report required by the SEC rules.

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

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

Compensation Committee

The members of our compensation committee are and , and is the chair of the compensation committee. Effective as of the date of this prospectus, our compensation committee's responsibilities will include:

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

We believe that the composition of our compensation committee will meet the requirements for independence under current NASDAQ and SEC rules and regulations.

Nominating and Corporate Governance Committee

The members of our nominating and corporate governance committee are , and , and is the chair of the nominating and corporate governance committee. Effective as of the date of this prospectus, our nominating and corporate governance committee's responsibilities will include:

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

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

Compensation Committee Interlocks and Insider Participation

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

Code of Business Conduct and Ethics

We plan to adopt a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions, which will be effective upon the closing of this offering. Following this offering, we will post a copy of the code on the Corporate Governance section of our website. If we make any substantive amendments to, or grant any waivers from, the code of business conduct and ethics for any officer or director, we will disclose the nature of such amendment or waiver on our website or in a current report on Form 8-K.

EXECUTIVE COMPENSATION

This section describes the material elements of compensation awarded to, earned by or paid to each of our named executive officers in 2015 and 2016. We are an "emerging growth company," within the meaning of the JOBS Act, and have elected to comply with the reduced compensation disclosure requirements available to emerging growth companies under the JOBS Act. Our named executive officers for 2016 were Joseph A. Yanchik III, Manuel C. Aivado and Evan Lippman. This section also provides qualitative information regarding the manner and context in which compensation is awarded to and earned by our named executive officers and is intended to place in perspective the data presented in the tables and narrative that follow.

Summary Compensation Table

The following table sets forth information regarding compensation awarded to, earned by or paid to our named executive officers during 2015 and 2016.

Name and Principal Position	Year	Salary ($)	Bonus ($)(1)	Option Awards ($)(2)	All Other Compensation ($)	Total ($)
Joseph A. Yanchik III(3)	2016	425,200	239,175	—	214(4)	664,589
President and Chief Executive Officer	2015	406,800	162,720	1,242,967	216(4)	1,812,703
Manuel C. Alves Aivado, M.D., Ph.D.	2016	371,000	162,313	—	66,848(5)	600,161
Senior Vice President, Chief Medical Officer	2015	355,000	106,500	453,178	51,237(6)	965,915
Evan Lippman(7)	2016	334,600	—	—	19,518(8)	354,118
Former Senior Vice President, Chief Financial Officer and Chief Business Officer	2015	320,100	111,030(9)	423,328	216(10)	854,674

(1) The amounts reported in the "Bonus" column represent discretionary annual cash bonuses awarded to our named executive officers.

(2) The amounts reported in the "Options Awards" column reflect the aggregate grant date fair value of share-based compensation awarded during the year computed in accordance with the provisions of Financial Accounting Standards Board Accounting Standards Codification, or ASC, Topic 718. See Note 9 to our financial statements appearing at the end of this prospectus regarding assumptions underlying the valuation of equity awards.

(3) Mr. Yanchik serves as a member of our board of directors but does not receive any additional compensation for his service as a director.

(4) Consists of the cost to us of a life insurance premium paid for Mr. Yanchik.

(5) Consists of $42,895 in travel expenses, $23,739 in tax gross-ups for the payment of taxes and $214 for the cost to us of a life insurance premium paid for Dr. Aivado.

(6) Consists of $38,167 in travel expenses, $12,854 in tax gross-ups for the payment of taxes and $216 for the cost to us of a life insurance premium paid for Dr. Aivado.

(7) Mr. Lippman joined us as Senior Vice President, Chief Financial Officer and Chief Business Officer in January 2015. Mr. Lippman resigned effective December 31, 2016.

(8) Consists of a $19,304 paid to Mr. Lippman for accrued vacation in connection with Mr. Lippman's resignation effective December 31, 2016 and $214 for the cost to us of a life insurance premium paid for Mr. Lippman.

(9) Includes a one-time $15,000 transition bonus payment to Mr. Lippman in connection with the commencement of his employment with us.

(10) Consists of the cost to us of a life insurance premium paid for Mr. Lippman.

Narrative to Summary Compensation Table

In 2016, we paid annual base salaries of $425,200 to Mr. Yanchik, $371,000 to Dr. Aivado and $334,600 to Mr. Lippman. We use base salaries to recognize the experience, skills, knowledge and responsibilities required of all our employees, including our named executive officers. None of our named executive officers is currently party to an employment agreement or other agreement or arrangement that provides for automatic or scheduled increases in base salary.

We do not have a formal performance-based bonus plan. From time to time, our board of directors has approved discretionary annual cash bonuses to our named executive officers with respect to their prior year performance. Mr. Yanchik and Dr. Aivado earned cash bonuses of $239,175 and $162,313, respectively, for services performed during 2016. Mr. Lippman resigned effective December 31, 2016 and did not receive a bonus for services performed during 2016.

Although we do not have a formal policy with respect to the grant of equity incentive awards to our named executive officers, or any formal equity ownership guidelines applicable to them, we believe that equity grants provide our named executive officers with a strong link to our long-term performance, create an ownership culture and help to align the interests of our named executive officers and our stockholders. In addition, we believe that equity grants with a time-based vesting feature promote executive retention because this feature incents our named executive officers to remain in our employment during the vesting period. Accordingly, our board of directors periodically reviews the equity incentive compensation of our named executive officers and from time to time may grant equity incentive awards to them in the form of stock options. In June 2015, the board of directors granted options to purchase 3,272,600 shares of common stock to Mr. Yanchik. In March 2015, we granted Dr. Aivado options to purchase 1,250,000 shares of our common stock and Mr. Lippman options to purchase 1,167,664 shares of our common stock. Our named executive officers did not receive any option grants in 2016. In March 2017, the board of directors granted options to purchase 1,580,000 shares of common stock to Mr. Yanchik. In March 2017, the board of directors granted options to purchase 1,430,000 shares of common stock to Dr. Aivado. Each of the options granted is subject to service-based vesting.

Outstanding Equity Awards at 2016 Year End

The following table sets forth information regarding outstanding equity awards held by our named executive officers as of December 31, 2016:

Name	Number of Securities Underlying Unexercised Options Exercisable (#)	Number of Securities Underlying Unexercised Options Unexercisable (#)	Option Exercise Price ($/share)	Option Expiration Date
Joseph A. Yanchik III	50,440(1)	—	0.13	6/25/2019
	59,611(2)	—	0.13	6/25/2019
	1,388,930(3)	—	0.13	6/25/2019
	1,227,225(4)	2,045,375(4)	0.55	6/18/2025
Manuel C. Alves Aivado, M.D., Ph.D.	703,125(5)	546,875(5)	0.51	3/10/2025
Evan Lippman	559,506(6)	— (7)	0.51	3/31/2017

(1) These options were granted on June 25, 2009 and were fully vested on the date of grant.

(2) These options were granted on June 25, 2009 and vested as to 3.8462% of the shares in equal monthly installments through September 1, 2011.

(3) These options were granted on June 25, 2009 and vested as to 2.0833% of the shares in equal monthly installments through July 1, 2013.

(4) These options were granted on June 18, 2015 and vest as to 2.0833% of the shares in equal monthly installments through June 18, 2019.

(5) These options were granted on March 10, 2015 and vested as to 25% of the shares on September 1, 2015 and vest thereafter as to 2.0833% of the shares in equal monthly installments through September 1, 2018.

(6) These options were granted on March 10, 2015 and vested as to 25% of the shares on January 1, 2016 and were eligible to vest thereafter as to 2.0833% of the shares in equal monthly installments through January 1, 2019.

(7) All unvested options were forfeited on December 31, 2016 upon Mr. Lippman's resignation. Mr. Lippman exercised options to purchase 147,000 shares of common stock in March 2017. The balance of his vested options were forfeited as of April 1, 2017.

Agreements with Our Named Executive Officers

Employment Agreements, Severance and Change in Control Agreements

Joseph A. Yanchik III

In March 2008, we entered into an employment agreement with Mr. Yanchik. The employment agreement establishes Mr. Yanchik's title, his base salary, his eligibility for an annual bonus, and his eligibility for benefits made available to employees generally and also provides for certain benefits upon termination of his employment under specified conditions. Our board of directors has determined that Mr. Yanchik is eligible to receive an annual bonus of up to 40% of his base salary. Mr. Yanchik's employment is at will.

Under the terms of the employment agreement, if Mr. Yanchik's employment is terminated by us without cause or by Mr. Yanchik for good reason, each as defined in his employment agreement, and subject to Mr. Yanchik's execution of a general release of potential claims against us, we have agreed to continue to pay his then-current base salary for a period of 12 months, premiums for continuation health coverage under COBRA for up to 12 months, a performance-based bonus pro-rated based on Mr. Yanchik's target bonus percentage and his achievement of certain milestones to be agreed upon by him and us for the calendar year in which his employment was terminated, as determined by our board in its sole discretion, and to accelerate vesting by six months of any restricted stock or stock options held by Mr. Yanchik.

In addition, if Mr. Yanchik's employment is terminated by us without cause or by Mr. Yanchik for good reason within one year following a change of control, as defined in the stock option agreement evidencing the options granted to Mr. Yanchik in June 2015, these options will accelerate in full.

Manuel C. Aivado

In July 2014, in connection with our appointment of Dr. Aivado as our Senior Vice President, Chief Medical Officer, we entered into an employment agreement with Dr. Aivado. The employment agreement establishes Dr. Aivado's title, his base salary, his eligibility for an annual bonus, and his eligibility for benefits made available to employees generally and also provides for certain benefits upon termination of his employment under specified conditions. Dr. Aivado was also entitled to receive a one-time transition bonus of $50,000,

payable within thirty days of his commencement of employment, and reimbursement of up to $3,750 per month for travel and living accommodations in order to commute to and live in the Boston area. Dr. Aivado's employment is at will. In March 2015, we granted Dr. Aivado options to purchase 1,250,000 shares of our common stock, which are subject to service-based vesting.

Under the terms of the employment agreement, if Dr. Aivado's employment is terminated by us without cause or by Dr. Aivado for good reason, each as defined in his employment agreement, and subject to Dr. Aivado's execution of a general release of potential claims against us, we have agreed to continue to pay his then-current base salary for a period of 12 months and premiums for continuation health coverage under COBRA for up to 12 months.

In addition, if Dr. Aivado's employment is terminated by us without cause or by Dr. Aivado for good reason within one year following a change of control, as defined in the stock option agreement evidencing the options granted to Dr. Aivado in March 2015, these options will accelerate in full.

Evan Lippman

In December 2014, in connection with our appointment of Mr. Lippman as our Senior Vice President, Chief Financial Officer and Chief Business Officer, we entered into an employment agreement with Mr. Lippman. Under the employment agreement, Mr. Lippman commenced employment with us on January 1, 2015. Mr. Lippman's employment agreement established his title, his base salary, his eligibility for an annual bonus of up to 30% of his base salary, and his eligibility for benefits made available to employees generally and also provides for certain benefits upon termination of his employment under specified conditions. Pursuant to Mr. Lippman's employment agreement, in March 2015, we granted Mr. Lippman an option to purchase 1,167,664 shares of our common stock, which was subject to service-based vesting. Mr. Lippman resigned effective December 31, 2016.

Other Agreements

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

Stock Option and Other Compensation Plans

The four equity incentive plans described in this section are our 2006 stock incentive plan, as amended to date, or the 2006 plan, our 2016 stock incentive plan, or the 2016 plan, our 2017 stock incentive plan, or the 2017 plan, and our 2017 employee stock purchase plan, or the 2017 ESPP. Prior to this offering, we granted awards to eligible participants under the 2006 plan and the 2016 plan. Following the closing of this offering, we expect to grant awards to eligible participants only under the 2017 plan and the 2017 ESPP.

2006 Stock Incentive Plan, as amended

The 2006 plan was first adopted by our board of directors and first approved by our stockholders in October 2006. Our 2006 plan was amended in December 2006, November 2007, March 2008, May 2009, April 2010, November 2013 and October 2014. Under the 2006 plan, as amended, our employees, officers, directors, consultants and advisors were eligible to receive awards; however, only employees were eligible for incentive stock option grants. In accordance with the terms of the 2006 plan, our board of directors, or a committee

appointed by our board, administered the 2006 plan and, subject to any limitations in the 2006 plan, selected the recipients of awards and determined:

- the number of shares of common stock covered by options and the dates upon which those options became exercisable;
- the type of options granted;
- the exercise prices of options;
- the duration of options; and
- the number of shares of common stock subject to any restricted stock or other stock-based awards and the terms and conditions of those awards, including the issue price, conditions for repurchase or forfeiture and repurchase price.

If our board of directors delegated authority to an executive officer to grant awards under the 2006 plan, the executive officer had the power to make awards to employees, directors, consultants and advisors, except officers or executive officers. Our board of directors fixed the terms of the awards granted by such executive officer, including the exercise price of such awards, and the maximum number of shares subject to awards that such executive officer made.

In the event of a reorganization event, as defined in the 2006 plan, our board had the right to take any one or more of the following actions as to all or any outstanding awards on such terms as the board determined:

- provide that all outstanding awards would be assumed, or substantially equivalent awards would be substituted, by the acquiring or succeeding corporation or an affiliate thereof;
- upon written notice to a participant, provide that all of the participant's unexercised awards would become exercisable in full and terminate immediately prior to the consummation of such reorganization event, unless exercised by the participant within a specified period following the date of such notice;
- provide that all outstanding awards would become realizable or deliverable, or restrictions applicable to an award would lapse, in whole or in part, prior to or upon such reorganization event;
- in the event of a reorganization event pursuant to which holders of shares of our common stock received a cash payment for each share surrendered in the reorganization event, which we refer to as the acquisition price, make or provide for a cash payment to the participants with respect to each award held by a participant equal to (a) the acquisition price times the number of shares of our common stock subject to the participant's awards to the extent the exercise price of such awards did not exceed the acquisition price minus (b) the aggregate exercise price of all such outstanding awards, in exchange for the termination of such options or other awards;
- in connection with a liquidation or dissolution, provide that awards would convert into the right to receive liquidation proceeds (if applicable, net of the exercise price thereof); and
- provide for any combination of the foregoing.

The 2006 plan expired by its terms in October 2016. As of April 30, 2017, there were options to purchase an aggregate of 8,557,900 shares of common stock outstanding under the 2006 plan at a weighted average exercise price of $0.43 per share.

2016 Stock Incentive Plan

The 2016 plan was adopted by our board of directors and approved by our stockholders in December 2016. The 2016 plan provides for the grant of incentive stock options, nonqualified stock options, restricted stock awards, restricted stock units, stock appreciation rights and other stock-based awards. Our employees, officers, directors, consultants and advisors are eligible to receive awards under the 2016 plan; however, incentive stock options may only be granted to our employees. Our board of directors, or a committee appointed by our board, administers the 2016 plan and, subject to any limitations set forth in the 2016 plan, will select the recipients of awards and determine:

- the number of shares of common stock covered by options and the dates upon which those options become exercisable;
- the type of options to be granted;
- the exercise prices of options;
- the duration of options; and
- the number of shares of common stock subject to any restricted stock or other stock-based awards and the terms and conditions of those awards, including the issue price, conditions for repurchase or forfeiture and repurchase price.

If our board of directors delegates authority to an executive officer to grant awards under the 2016 plan, the executive officer has the power to make awards to employees and officers, except executive officers. Our board of directors will fix the terms of the awards to be granted by such executive officer, including the exercise price of such awards, and the maximum number of shares subject to awards that such executive officer may make.

The maximum number of shares of common stock authorized for issuance under the 2016 plan is equal to the sum of 7,583,595 shares plus such additional number of shares of common stock (up to 9,757,648 shares) as is equal to the number of shares of common stock subject to awards granted under the 2006 plan which awards expire, terminate or are otherwise surrendered, canceled, forfeited or repurchased by us at their original issuance price pursuant to a contractual repurchase right (subject, however, in the case of incentive stock options to any limitations of the Internal Revenue Code). Our board of directors may amend, suspend, or terminate the 2016 plan at any time.

Upon the occurrence of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spinoff, or other similar change in capitalization or event, or any dividend or distribution to holders of our common stock other than an ordinary cash dividend, under the terms of the 2016 plan, we are required to equitably adjust (or make substitute awards, if applicable), in the manner determined by our board of directors:

- the number and class of securities available under the 2016 plan;
- the number and class of securities and exercise price per share of each outstanding option;
- the share and per-share provisions and the measurement price of each outstanding stock appreciation right;
- the number of shares subject to and the repurchase price per share subject to each outstanding restricted stock award; and

- the share and per-share-related provisions and the purchase price, if any, of each outstanding other stock-based award.

Upon the occurrence of a merger or consolidation of our company with or into another entity as a result of which all of our common stock is converted into or exchanged for the right to receive cash, securities, or other property or is cancelled; any transfer or disposition of all of our common stock for cash, securities, or other property pursuant to a share exchange or other transaction; or a liquidation or dissolution of our company, our board of directors may, on such terms as our board of directors determines (except to the extent specifically provided otherwise in an applicable award agreement or other agreement between us and the plan participant), take any one or more of the following actions pursuant to the 2016 plan, as to some or all outstanding awards, other than restricted stock awards:

- provide that awards shall be assumed, or substantially equivalent awards shall be substituted, by the acquiring or succeeding corporation (or an affiliate thereof);

- upon written notice to a plan participant, provide that the participant's unexercised awards will terminate immediately prior to the consummation of such transaction unless exercised by the participant (to the extent then exercisable) within a specified period;

- provide that outstanding awards shall become exercisable, realizable or deliverable, or restrictions applicable to an award shall lapse, in whole or in part, prior to or upon such transaction;

- in the event of a transaction under the terms of which holders of common stock will receive upon consummation thereof a cash payment for each share surrendered in the transaction, make or provide for a cash payment to a plan participant;

- provide that, in connection with a liquidation of dissolution of the company, awards shall convert into the right to receive liquidation proceeds; or

- any combination of the foregoing.

Our board of directors is not obligated under the 2016 plan to treat all awards, all awards held by a participant, or all awards of the same type, identically.

Upon the occurrence of any corporate transaction described above, other than our liquidation or dissolution, our repurchase and other rights under each outstanding restricted stock award will continue for the benefit of our successor and will, unless our board of directors determines otherwise, apply to the cash, securities, or other property which our common stock was converted into or exchanged for in the transaction in the same manner and to the same extent as they applied to the common stock subject to the restricted stock award; provided, however, that the board may provide termination or deemed satisfaction of such repurchase or other rights under the restricted stock award agreement, either initially or by amendment, or provide for forfeiture of such restricted stock if issued at no cost. Upon our liquidation or dissolution, except to the extent specifically provided to the contrary in the restricted stock award agreement or any other agreement between the plan participant and us, all restrictions and conditions on all restricted stock awards then outstanding will automatically be deemed terminated or satisfied.

Our board of directors, in its sole discretion, may accelerate the exercisability of any option or time at which any restrictions shall lapse or be removed from any restricted stock award, as the case may be.

As of April 30, 2017, there were 4,385,000 shares of common stock outstanding under the 2016 plan at a weighted average exercise price of $0.58 per share, and 4,219,259 shares of common stock were available for future issuance under the 2016 plan. On and after the effective date of the 2017 plan described below, we will grant no further stock options or other awards under the 2016 plan.

2017 Stock Incentive Plan

We expect our board of directors to adopt, and our stockholders to approve, the 2017 plan, which will become effective immediately prior to the closing of this offering. The 2017 plan provides for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, awards of restricted stock, restricted stock units and other stock-based awards. Upon the closing of this offering, the number of shares of our common stock that will be reserved for issuance under the 2017 plan will be (1) ; plus (2) the number of shares (up to shares) equal to the sum of the number of shares of our common stock then available for issuance under the 2016 plan and the number of shares of our 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 us at their original issuance price pursuant to a contractual repurchase right; plus (3) an annual increase, to be added on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2018 and continuing until, and including, the fiscal year ending December 31, 2027, equal to the lower of shares of our common stock, % of the number of shares of our common stock outstanding on the first day of such fiscal year and an amount determined by our board of directors.

Our employees, officers, directors, consultants and advisors will be eligible to receive awards under the 2017 plan; however, incentive stock options may only be granted to our employees.

Pursuant to the terms of the 2017 plan, our board of directors, or a committee delegated by our board of directors, administers the 2017 plan and, subject to any limitations set forth in the 2017 plan, will select the recipients of awards and determine:

- the number of shares of common stock covered by options and the dates upon which those options become exercisable;
- the type of options to be granted;
- the exercise price of options, which price must be at least equal to the fair market value of our common stock on the date of grant;
- the duration of options, which may not be in excess of ten years;
- the methods of payment of the exercise price of options; and
- the number of shares of our common stock subject to and the terms of any stock appreciation rights, awards of restricted stock, restricted stock units and other stock-based awards and the terms and conditions of such awards, including the issue price, conditions for repurchase, repurchase price and performance conditions (though the measurement price of stock appreciation rights must be at least equal to the fair market value of our common stock on the date of grant and the duration of such awards may not be in excess of ten years), if any.

If our board of directors delegates authority to an executive officer to grant awards under the 2017 plan, the executive officer will have the power to make awards to all of our employees, except executive officers. Our board of directors will fix the terms of the awards to be granted by such executive officer, including the exercise price of such awards (or a formula for establishing such price), and the maximum number of shares subject to awards that such executive officer may make.

In the event of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spin-off or other similar change in capitalization or event, or any dividend or distribution to holders of our common stock other than an ordinary cash dividend, we are required by the 2017 plan to make equitable adjustments (or make substitute awards, if applicable), in a manner determined by our board, to:

- the number and class of securities available under the 2017 plan;
- the share counting rules under the 2017 plan;
- the number and class of securities and exercise price per share of each outstanding option;
- the share and per-share provisions and measurement price of each outstanding stock appreciation right;
- the number of shares and the repurchase price per share subject to each outstanding restricted stock award or restricted stock unit award; and
- the share and per-share related provisions and purchase price, if any, of any outstanding other stock-based award.

Upon a merger or other reorganization event, as defined in our 2017 plan, our board of directors, may, on such terms as our board determines, except to the extent specifically provided otherwise in an applicable award agreement or other agreement between the participant and us, take any one or more of the following actions pursuant to the 2017 plan, as to some or all outstanding awards, other than restricted stock awards:

- provide that all outstanding awards will be assumed or substantially equivalent awards will be substituted by the successor corporation or an affiliate thereof;
- upon written notice to a participant, provide that the participant's unvested and/or unexercised options or other awards will terminate immediately prior to the consummation of such transaction unless exercised by the participant;
- provide that outstanding awards will become exercisable, realizable or deliverable, or restrictions applicable to an award will lapse, in whole or in part, prior to or upon the reorganization event;
- in the event of a reorganization event pursuant to which holders of our common stock will receive a cash payment for each share surrendered in the reorganization event, make or provide for a cash payment to the participants with respect to each award held by a participant equal to (1) the number of shares of our common stock subject to the vested portion of the award (after giving effect to any acceleration of vesting that occurs upon or immediately prior to such reorganization event) multiplied by (2) the excess, if any, of the cash payment for each share surrendered in the reorganization event over the exercise, measurement or purchase price of such award and any applicable tax withholdings, in exchange for the termination of such award;
- provide that, in connection with a liquidation or dissolution, awards convert into the right to receive liquidation proceeds, net of exercise, measurement or purchase price thereof, if applicable, and any applicable tax withholdings; or
- any combination of the foregoing.

Our board of directors is not obligated by the 2017 plan to treat all awards, all awards held by a participant, or all awards of the same type, identically.

In the case of certain restricted stock units, no assumption or substitution is permitted, and the restricted stock units will instead be settled in accordance with the terms of the applicable restricted stock unit agreement.

Upon the occurrence of a reorganization event other than a liquidation or dissolution, the repurchase and other rights under each outstanding restricted stock award will continue for the benefit of the successor company and will, unless our board of directors may otherwise determine, apply to the cash, securities or other property which our common stock is converted into or exchanged for pursuant to the reorganization event, unless our board provided for the termination or deemed satisfaction of such repurchase or other rights under the restricted stock award agreement or any other agreement between the participant and us. Upon the occurrence of a reorganization event involving a liquidation or dissolution, all restrictions and conditions on each outstanding restricted stock award will automatically be deemed terminated or satisfied, unless otherwise provided in the agreement evidencing the restricted stock award or in any other agreement between the participant and us.

Our board of directors may at any time provide that any award under the 2017 plan shall become immediately exercisable in whole or in part, free of some or all restrictions or conditions, or otherwise realizable in whole or in part, as the case may be.

Except with respect to certain actions requiring stockholder approval under the Internal Revenue Code or the rules of The NASDAQ Stock Market, our board of directors may amend, modify or terminate any outstanding award under the 2017 plan, including but not limited to, substituting therefor another award of the same or a different type, changing the date of exercise or realization, and converting an incentive stock option into a nonstatutory stock option, subject to certain participant consent requirements. Unless our stockholders approve such action, the 2017 plan provides that we may not, except as otherwise permitted in connection with a change in capitalization or reorganization event:

- amend any outstanding stock option or stock appreciation right granted under the 2017 plan to provide an exercise or measurement price per share that is lower than the then-current exercise or measurement price per share of such outstanding award;
- cancel any outstanding option or stock appreciation right, whether or not granted under the 2017 plan, and grant in substitution therefor new awards under the 2017 plan, other than substitute awards permitted in connection with a merger or consolidation of an entity with us or our acquisition of property or stock of another entity, covering the same or a different number of shares of our common stock and having an exercise or measurement price per share lower than the then-current exercise or measurement price per share of the cancelled award;
- cancel in exchange for a cash payment any outstanding option or stock appreciation right with an exercise or measurement price per share above the then-current fair market value of our common stock; or
- take any other action that constitutes a “repricing” within the meaning of the rules of The NASDAQ Stock Market.

No award may be granted under the 2017 plan after , 2027. Our board of directors may amend, suspend or terminate the 2017 plan at any time, except that stockholder approval will be required to comply with applicable law or stock market requirements.

2017 Employee Stock Purchase Plan

We expect our board of directors to adopt, and our stockholders to approve, the 2017 ESPP, which will become effective immediately prior to the closing of this offering. The 2017 ESPP will be administered by our board of directors or by a committee appointed by our board of directors. The 2017 ESPP initially provides

participating employees with the opportunity to purchase up to an aggregate of shares of our common stock. The number of shares of our common stock reserved for issuance under the 2017 ESPP will automatically increase on the first day of each fiscal year, commencing on January 1, 2018 and ending on December 31, 2028, in an amount equal to the least of shares of our common stock, % of the total number of shares of our common stock outstanding on the first day of the applicable year, and an amount determined by our board of directors.

All of our employees or employees of any designated subsidiary, as defined in the 2017 ESPP, are eligible to participate in the 2017 ESPP, provided that:

- such person is customarily employed by us or a designated subsidiary for more than 20 hours a week and for more than five months in a calendar year;
- such person has been employed by us or by a designated subsidiary for at least six months prior to enrolling in the 2017 ESPP; and
- such person was our employee or an employee of a designated subsidiary on the first day of the applicable offering period under the 2017 ESPP.

No employee may purchase shares of our common stock under the 2017 ESPP and any of our other employee stock purchase plans in excess of $25,000 of the fair market value of our common stock, as of the date of the option grant, in any calendar year. In addition, no employee may purchase shares of our common stock under the 2017 ESPP that would result in the employee owning 5% or more of the total combined voting power or value of our stock or the stock of any of our subsidiaries.

We expect to make one or more offerings to our eligible employees to purchase stock under the 2017 ESPP beginning at such time as our board of directors may determine. Each offering will consist of a six-month offering period during which payroll deductions will be made and held for the purchase of our common stock at the end of the offering period. Our board of directors may, at its discretion, choose a different period of not more than 12 months for offerings.

On the commencement date of each offering period, each eligible employee may authorize up to a maximum of 15% of his or her compensation to be deducted by us during the offering period. Each employee who continues to be a participant in the 2017 ESPP on the last business day of the offering period will be deemed to have exercised an option to purchase from us the number of whole shares of our common stock that his or her accumulated payroll deductions on such date will pay for, not in excess of the maximum numbers set forth above. Under the terms of the 2017 ESPP, the purchase price shall be determined by our board of directors for each offering period and will be at least 85% of the applicable closing price of our common stock. If our board of directors does not make a determination of the purchase price, the purchase price will be 85% of the lesser of the closing price of our common stock on the first business day of the offering period or on the last business day of the offering period.

An employee who is not a participant on the last day of the offering period is not entitled to purchase shares under the 2017 ESPP, and the employee's accumulated payroll deductions will be refunded. An employee's rights under the 2017 ESPP terminate upon voluntary withdrawal from an offering under the 2017 ESPP at any time, or when the employee ceases employment for any reason.

We will be required to make equitable adjustments to the number and class of securities available under the 2017 ESPP, the share limitations under the 2017 ESPP, and the purchase price for an offering period under the 2017 ESPP to reflect stock splits, reverse stock splits, stock dividends, recapitalizations, combinations of shares, reclassifications of shares, spin-offs and other similar changes in capitalization or events or any dividends or distributions to holders of our common stock other than ordinary cash dividends.

In connection with a merger or other reorganization event, as defined in the 2017 ESPP, our board of directors or a committee of our board of directors may take any one or more of the following actions as to outstanding options to purchase shares of our common stock under the 2017 ESPP on such terms as our board or committee determines:

- provide that options shall be assumed, or substantially equivalent options shall be substituted, by the acquiring or succeeding corporation or an affiliate thereof;
- upon written notice to employees, provide that all outstanding options will be terminated immediately prior to the consummation of such reorganization event and that all such outstanding options will become exercisable to the extent of accumulated payroll deductions as of a date specified by our board or committee in such notice, which date shall not be less than ten days preceding the effective date of the reorganization event;
- upon written notice to employees, provide that all outstanding options will be cancelled as of a date prior to the effective date of the reorganization event and that all accumulated payroll deductions will be returned to participating employees on such date;
- in the event of a reorganization event under the terms of which holders of our common stock will receive upon consummation thereof a cash payment for each share surrendered in the reorganization event, change the last day of the offering period to be the date of the consummation of the reorganization event and make or provide for a cash payment to each employee equal to (1) the cash payment for each share surrendered in the reorganization event times the number of shares of our common stock that the employee's accumulated payroll deductions as of immediately prior to the reorganization event could purchase at the applicable purchase price, where the acquisition price is treated as the fair market value of our common stock on the last day of the applicable offering period for purposes of determining the purchase price and where the number of shares that could be purchased is subject to the applicable limitations under the 2017 ESPP minus (2) the result of multiplying such number of shares by the purchase price; and/or
- provide that, in connection with our liquidation or dissolution, options shall convert into the right to receive liquidation proceeds net of the purchase price thereof.

Our board of directors may at any time, and from time to time, amend or suspend the 2017 ESPP or any portion thereof. We will obtain stockholder approval for any amendment if such approval is required by Section 423 of the Internal Revenue Code. Further, our board of directors may not make any amendment that would cause the 2017 ESPP to fail to comply with Section 423 of the Internal Revenue Code. The 2017 ESPP may be terminated at any time by our board of directors. Upon termination, we will refund all amounts in the accounts of participating employees.

401(k) Retirement Plan

We maintain a 401(k) retirement plan that is intended to be a tax-qualified defined contribution plan under Section 401(k) of the Internal Revenue Code. In general, all of our employees are eligible to participate, beginning on the first day of the month following commencement of their employment. The 401(k) plan includes a salary deferral arrangement pursuant to which participants may elect to reduce their current compensation by up to the statutorily prescribed limit, equal to $18,000 in 2017, and have the amount of the reduction contributed to the 401(k) plan. Currently, we do not match employee contributions.

Limitations on Liability and Indemnification

As permitted by Delaware law, we expect our board of directors and stockholders to adopt provisions in our certificate of incorporation, which will become effective as of the closing date of this offering, that limit or

eliminate the personal liability of our directors. Our certificate of incorporation, which will become effective as of the closing date of this offering, limits the personal liability of directors for breach of fiduciary duty to the maximum extent permitted by the General Corporation Law of the State of Delaware and provides that no director will have personal liability to us or to our stockholders for monetary damages for breach of fiduciary duty. However, these provisions do not eliminate or limit the liability of any of our directors:

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

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

In addition, our certificate of incorporation, which will become effective as of the closing date of this offering, provides that we must indemnify our directors and officers and we must advance expenses, including attorneys' fees, to our directors and officers in connection with legal proceedings, subject to very limited exceptions.

We maintain a general liability insurance policy that covers specified liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers. In addition, we expect to enter into indemnification agreements with each of our officers and directors prior to the completion of this offering. These indemnification agreements will require us, among other things, to indemnify each such director or officer for some expenses, including attorneys' fees, judgments, fines and settlement amounts, incurred by him or her in any action or proceeding arising out of his or her service as one of our directors or officers.

Some of our non-employee directors may, through their relationships with their employers, be insured or indemnified against specified liabilities incurred in their capacities as members of our board of directors.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, executive officers or persons controlling us, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

Rule 10b5-1 Sales Plans

Our directors and executive officers may adopt written plans, known as Rule 10b5-1 plans, in which they will contract with a broker to buy or sell shares of our common stock on a periodic basis. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the director or officer when entering into the plan, without further direction from the director or officer. The director or officer may amend or terminate the plan in some circumstances. Our directors and executive officers may also buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material, nonpublic information.

Director Compensation

The following table sets forth information regarding compensation earned by our non-employee directors during 2016.

Name	Fees Earned or Paid in Cash ($)	Total ($)(1)
Scott B. Kapnick	7,500	7,500
Reinhard J. Ambros, Ph.D.	—	—
Brian M. Gallagher, Jr., Ph.D.	—	—
Seth L. Harrison, M.D.(2).	—	—
John H. McArthur, Ph.D.	10,000	10,000
Armen B. Shanafelt, Ph.D.	—	—
Caleb Winder	—	—

(1) No options were granted to directors in 2016. As of December 31, 2016, the aggregate number of shares of our common stock subject to each non-employee director's outstanding option awards was as follows: Mr. Kapnick, 277,761 shares, and Dr. McArthur, 247,761 shares.

(2) Dr. Harrison resigned as a director effective April 1, 2017.

We currently do not have a formal non-employee director compensation policy. We pay Mr. Kapnick and Dr. McArthur $2,500 for each board of directors meeting they attend. Such amounts earned in 2016 are reflected in the table above. No options were granted to directors in 2016. In 2015, we granted options to purchase 100,000 shares and 70,000 shares of common stock to Mr. Kapnick and Dr. McArthur, respectively, with an exercise price of $0.51 per share. These options vest over three years, with one-third of the shares of common stock underlying each option vesting annually.

None of our other non-employee directors receives any compensation. We reimburse our non-employee directors for reasonable travel and out-of-pocket expenses incurred in connection with attending board of directors and committee meetings. The compensation that we pay to our President and Chief Executive Officer is discussed earlier in this "Executive Compensation" section.

Our board of directors intends to approve a compensation policy for our non-employee directors that will become effective as of the closing date of this offering. This policy will be intended to provide a total compensation package that enables us to attract and retain qualified and experienced individuals to serve as directors and to align our directors' interests with those of our stockholders.

TRANSACTIONS WITH RELATED PERSONS

Since January 1, 2014, we have engaged in the following transactions in which the amount involved exceeded $120,000 and any of our directors, executive officers or beneficial holders of more than 5% of any class of our voting securities, or any of their affiliates, had a material interest. We believe that all of these transactions were on terms comparable to terms that could have been obtained from unrelated third parties.

Series E-1 Preferred Stock Financing

In October 2014, we entered into a Series E-1 preferred stock purchase agreement for the sale of up to 24,264,705 shares of Series E-1 preferred stock in one or more closings at a price per share of $1.36. In October 2014, we issued and sold an aggregate of 14,558,823 shares of our Series E-1 preferred stock at a price per share of $1.36, for an aggregate purchase price of approximately $19.8 million. The following table sets forth the number of shares of our Series E-1 preferred stock purchased by our directors, executive officers and 5% stockholders and their affiliates and the aggregate purchase price paid for such shares.

Name	Shares of Series E-1 Preferred Stock Purchased	Aggregate Purchase Price
Apple Tree Partners II—Annex, L.P.	1,816,152	$ 2,469,967
Novartis BioVentures Ltd.	1,376,297	1,871,764
Lilly Ventures Fund I LLC	992,647	1,350,000
S.R. One, Limited	765,833	1,041,533
Scott B. Kapnick	759,678	1,033,162
Excel Medical Fund, L.P.	692,164	941,343
Roche Finance Ltd	382,916	520,766
Total	6,785,687	$ 9,228,535

In January 2016, in the second tranche closing, we issued and sold an aggregate of 9,705,882 shares of our Series E-1 preferred stock at a price per share of $1.36, for an aggregate purchase price of approximately $13.2 million. The following table sets forth the number of shares of our Series E-1 preferred stock purchased by our directors, executive officers and 5% stockholders and their affiliates and the aggregate purchase price paid for such shares.

Name	Shares of Series E-1 Preferred Stock Purchased	Aggregate Purchase Price
Apple Tree Partners II—Annex, L.P.	1,210,768	$ 1,646,644
Novartis BioVentures Ltd.	917,532	1,247,844
Lilly Ventures Fund I LLC	661,764	899,999
S.R. One, Limited	510,556	694,356
Scott B. Kapnick	506,452	688,775
Excel Medical Fund, L.P.	461,442	627,561
Roche Finance Ltd	255,278	347,178
Total	4,523,792	$ 6,152,357

Series F Preferred Stock Financing

In December 2016, we entered into a Series F preferred stock purchase agreement for the sale of up to 29,411,764 shares of Series F preferred stock in one or more closings at a price per share of $1.36. In December 2016, we issued and sold an aggregate of 13,949,357 shares of our Series F preferred stock at a price per share of $1.36, for an aggregate purchase price of approximately $19.0 million. The following table sets forth the number of shares of our Series F preferred stock purchased by our directors, executive officers and 5% stockholders and their affiliates and the aggregate purchase price paid for such shares.

Name	Shares of Series F Preferred Stock Purchased	Aggregate Purchase Price
Novartis BioVentures Ltd.	3,705,882	$ 5,040,000
S.R. One, Limited	1,979,188	2,691,696
Lilly Ventures Fund I LLC	1,443,972	1,963,802
Excel Medical Fund, L.P.	1,083,119	1,473,042
Roche Finance Ltd	989,594	1,345,848
Scott B. Kapnick	487,776	663,375
Total	9,689,531	$ 13,177,763

In December 2016, pursuant to the Series F preferred stock purchase agreement, we issued an aggregate of 8,927,582 shares of our Series E-2 preferred stock and 16,567,108 shares of our Series E-3 preferred stock in exchange for an aggregate of 8,927,582 shares of our Series E preferred stock and 16,567,108 shares of our Series E-1 preferred stock, respectively. The following table sets forth the number of shares of Series E preferred stock and Series E-1 preferred stock exchanged by our directors, executive officers and 5% stockholders and their affiliates.

Name	Shares of Series E Preferred Stock Exchanged	Shares of Series E-2 Preferred Stock Received	Shares of Series E-1 Preferred Stock Exchanged	Shares of Series E-3 Preferred Stock Received
Novartis BioVentures Ltd.	2,644,558	2,644,558	2,293,829	2,293,829
S.R. One, Limited	1,471,551	1,471,551	1,276,389	1,276,389
Lilly Ventures Fund I LLC	1,907,373	1,907,373	1,654,411	1,654,411
Excel Medical Fund, L.P.	1,329,993	1,329,993	1,153,606	1,153,606
Roche Finance Ltd	735,775	735,775	638,194	638,194
Scott B. Kapnick	612,002	612,002	1,266,130	1,266,130
Total	8,701,252	8,701,252	8,282,559	8,282,559

Investor Rights Agreement

We are a party to an investor rights agreement, dated as of December 23, 2016, with holders of our preferred stock, including some of our directors and 5% stockholders and their affiliates and entities affiliated with our directors. The investor rights agreement provides these holders the right, following the completion of this offering, to demand that we file a registration statement or request that their shares be covered by a registration statement that we are otherwise filing. See “Description of Capital Stock—Registration Rights” for additional information regarding these registration rights.

Employment Agreements

See the “Executive Compensation—Agreements with Our Named Executive Officers” section of this prospectus for a further discussion of these arrangements.

Indemnification Agreements

Our certificate of incorporation that will become effective as of the closing date of this offering provides that we will indemnify our directors and officers to the fullest extent permitted by Delaware law. In addition, we plan to enter into indemnification agreements with each of our officers and directors that may be broader in scope than the specific indemnification provisions contained in the Delaware General Corporation Law. See “Executive Compensation—Limitation of Liability and Indemnification” for additional information regarding these agreements.

Policies and Procedures for Related Person Transactions

Our board of directors plans to adopt a written related person transaction policy, which will become effective as of the closing date of this offering, setting forth adopted written policies and procedures for the review of any transaction, arrangement or relationship in which we are a participant, the amount involved exceeds $120,000 and one of our executive officers, directors, director nominees or 5% stockholders, or their immediate family members, each of whom we refer to as a "related person," has a direct or indirect material interest.

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

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

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

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

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

- interests arising solely from the related person's position as an executive officer of another entity, whether or not the person is also a director of such entity, that is a participant in the transaction,

where (a) the related person and all other related persons own in the aggregate less than a 10% equity interest in such entity; (b) the related person and his or her immediate family members are not involved in the negotiation of the terms of the transaction and do not receive any special benefits as a result of the transaction; (c) the amount involved in the transaction equals less than the greater of $1 million or 2% of the annual gross revenues of the other entity that is a party to the transaction; and (d) the amount involved in the transaction equals less than 2% of our annual gross revenues; and

- a transaction that is specifically contemplated by provisions of our charter or bylaws.

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

PRINCIPAL STOCKHOLDERS

The following table sets forth information with respect to the beneficial ownership of our common stock as of April 30, 2017 by:

- each of our directors;
- each of our named executive officers;
- all of our directors and executive officers as a group; and
- each person, or group of affiliated persons, who is known by us to beneficially own more than 5% of our common stock.

The column entitled "Percentage of Shares Beneficially Owned—Before Offering" is based on a total of 108,881,951 shares of our common stock outstanding as of April 30, 2017, assuming the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 104,435,674 shares of our common stock upon the closing of this offering. The column entitled "Percentage of Shares Beneficially Owned—After Offering" is based on shares of our common stock to be outstanding after this offering, including the shares of our common stock that we are selling in this offering, but not including any additional shares issuable upon exercise of outstanding options or any exercise by the underwriters of their option to purchase additional shares.

Beneficial ownership is determined in accordance with the rules and regulations of the SEC and includes voting or investment power with respect to our common stock. Shares of our common stock subject to options that are currently exercisable or exercisable within 60 days after April 30, 2017 are considered outstanding and beneficially owned by the person holding the options for the purpose of calculating the percentage ownership of that person but not for the purpose of calculating the percentage ownership of any other person. Except as otherwise noted, the persons and entities in this table have sole voting and investment power with respect to all of the shares of our common stock beneficially owned by them, subject to community property laws, where applicable. Except as otherwise set forth below, the address of the beneficial owner is c/o Aileron Therapeutics, Inc., 281 Albany Street, Cambridge, MA 02139.

Name of Beneficial Owner	Shares Beneficially Owned	Percentage of Shares Beneficially Owned Before Offering	Percentage of Shares Beneficially Owned After Offering
5% Stockholders			
Entities affiliated with Apple Tree Partners(1) 230 Park Avenue, Suite 2800 New York, NY 10169	24,399,156	22.4%	
Novartis BioVentures Ltd.(2) PO Box HM 2899 Hamilton HM LX Bermuda	22,631,671	20.8	
S.R. One, Limited(3) 161 Washington Street Eight Tower Bridge, Suite 500 Conshohocken, PA 19428-2077	11,508,898	10.6	
Excel Medical Fund, L.P.(4) Prudential Tower, Suite 2825 800 Boylston Street Boston, MA 02199	9,500,768	8.7	
Lilly Ventures Fund I LLC(5) 115 W. Washington Street Suite 1680—South Indianapolis, IN 46204	8,396,641	7.7	
Roche Finance Ltd(6) Grenzacherstrasse 122 4070 Basel Switzerland	5,792,909	5.3	
Named Executive Officers and Directors			
Joseph A. Yanchik III(7)	4,464,196	4.0	
Manuel C. Aivado, M.D., Ph.D.(8)	948,750	*	
Evan Lippman(9)	147,000	*	
Scott B. Kapnick(10)	3,176,602	2.9	
Reinhard J. Ambros, Ph.D.(2)	22,631,671	20.8	
Brian M. Gallagher, Jr., Ph.D.(3)	11,508,898	10.6	
John H. McArthur, Ph.D.(11)	224,428	*	
Armen B. Shanafelt, Ph.D.(5)	8,396,641	7.7	
Caleb Winder	—	—	
All Current Executive Officers and Directors as a Group (9 persons)(12)	51,576,082	45.3	

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

(1) Consists of (i) 2,500 shares of common stock and 17,879,996 shares of common stock underlying shares of redeemable convertible preferred stock held by Apple Tree Partners II, L.P. and (ii) 6,516,660 shares of

common stock underlying shares of redeemable convertible preferred stock held by Apple Tree Partners II—Annex, L.P. Dr. Seth L. Harrison, a former member of our board of directors, is a principal of the general partner of each of Apple Tree Partners II, L.P. and Apple Tree Partners II—Annex, L.P., and Dr. Harrison disclaims beneficial ownership of the shares held by each of Apple Tree Partners II, L.P. and Apple Tree Partners II—Annex, L.P., except to the extent of his pecuniary interest therein. Dr. Harrison has sole voting and investment power over the shares held by Apple Tree Partners II, L.P. and Apple Tree Partners II—Annex, L.P.

(2) Consists of 22,631,671 shares of common stock underlying shares of redeemable convertible preferred stock held by Novartis BioVentures Ltd., a Bermuda corporation. The board of directors of Novartis BioVentures Ltd. has sole voting and investment power over such shares. None of the members of its board of directors has individual voting or investment power with respect to such shares and each disclaims beneficial ownership of such shares. Dr. Reinhard J. Ambros, a member of our board of directors, is an employee of a corporation that is affiliated with Novartis BioVentures Ltd. Dr. Ambros disclaims beneficial ownership of the shares held by Novartis BioVentures Ltd., except to the extent of his pecuniary interest arising as a result of his employment by such affiliate of Novartis BioVentures Ltd. Novartis BioVentures Ltd. is an indirectly owned subsidiary of Novartis AG.

(3) Consists of 11,508,898 shares of common stock underlying shares of redeemable convertible preferred stock held by S.R. One, Limited, an indirect wholly owned subsidiary of GlaxoSmithKline plc. Dr. Brian Gallagher, a member of our board of directors, is a partner of S.R. One, Limited and disclaims beneficial ownership of the shares held by S.R. One, Limited, except to the extent of his pecuniary interest therein.

(4) Consists of 9,500,768 shares of common stock underlying shares of redeemable convertible preferred stock held by Excel Medical Fund, L.P. Excel Medical Ventures, LLC is the general partner of Excel Medical Fund, L.P. Steven R. Gullans, Frederick R. Blume and Juan Enriquez, the Managing Directors of Excel Medical Ventures, LLC, may be deemed to share voting and dispositive power with respect to all shares held by Excel Medical Fund, L.P. Each of the individuals and entities listed above expressly disclaims beneficial ownership of the securities listed above except to the extent of any pecuniary interest therein.

(5) Consists of 8,396,641 shares of common stock underlying shares of redeemable convertible preferred stock held by Lilly Ventures Fund I LLC, or LVFI. LV Management Group, LLC, or LVMG, is the management company for LVFI and as such may be deemed to indirectly beneficially own the shares held by LVFI. LVMG's voting and dispositive decisions with respect to the shares held by LVFI are made by LVMG's management committee, which consists of Ed Torres, Dr. Steve Hall and Armen B. Shanafelt, a member of our board of directors. Each of the individuals and entities listed above expressly disclaims beneficial ownership of the shares held by LVFI, except to the extent of his or its pecuniary interest therein.

(6) Consists of (1) 5,754,448 shares of common stock underlying shares of redeemable convertible preferred stock held by Roche Finance Ltd and (2) 38,461 shares of common stock held by Genentech, Inc. Roche Finance Ltd exercises voting and investment control over such shares.

(7) Consists of (i) 1,230,165 shares of common stock and (ii) 3,234,031 shares of common stock underlying options that are exercisable as of April 30, 2017 or will become exercisable within 60 days after such date.

(8) Consists of 948,750 shares of common stock underlying options that are exercisable as of April 30, 2017 or will become exercisable within 60 days after such date.

(9) Consists of 147,000 shares of common stock.

(10) Consists of (i) 95,774 shares of common stock (ii) 2,836,400 shares of common stock underlying shares of preferred stock and (iii) 244,428 shares of common stock underlying options that are exercisable as of April 30, 2017 or will become exercisable within 60 days after such date.

(11) Consists of 224,428 shares of common stock underlying options that are exercisable as of April 30, 2017 or will become exercisable within 60 days after such date.

(12) Includes 4,876,533 shares of common stock underlying options that are exercisable as of April 30, 2017 or will become exercisable within 60 days after such date.

DESCRIPTION OF CAPITAL STOCK

General

Following the closing of this offering, our authorized capital stock will consist of shares of common stock, par value $0.001 per share, and shares of preferred stock, par value $0.001 per share, all of which preferred stock will be undesignated. The following description of our capital stock and provisions of our restated certificate of incorporation and amended and restated bylaws are summaries and are qualified by reference to the certificate of incorporation and the bylaws that will become effective as of the closing date of this offering. We have filed copies of these documents as exhibits to our registration statement of which this prospectus forms a part. The descriptions of the common stock and preferred stock reflect changes to our capital structure that will occur upon the closing of this offering.

Common Stock

As of April 30, 2017, we had outstanding 108,911,951 shares of common stock, assuming the automatic conversion of all outstanding shares of our preferred stock into common stock upon the closing of this offering, which were held of record by 76 stockholders.

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. An election of directors by our stockholders will be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Other matters shall be decided by the affirmative vote of our stockholders having a majority in voting power of the votes cast by the stockholders present or represented and voting on such matter, except as otherwise disclosed below. Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of outstanding preferred stock.

In the event of our liquidation or dissolution, the holders of common stock are entitled to receive proportionately all assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock. Holders of common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Preferred Stock

Under the terms of our certificate of incorporation that will become effective as of the closing date of this offering, our board of directors is authorized to issue shares of preferred stock in one or more series without stockholder approval. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock.

The purpose of authorizing our board of directors to issue preferred stock and determine its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions, future financings and other corporate purposes, could have the effect of making it more difficult for a third party to acquire, or could discourage a third party from seeking to acquire, a majority of our outstanding voting stock. Upon the closing of this offering, there will be no shares of preferred stock outstanding, and we have no present plans to issue any shares of preferred stock.

Stock Options

As of April 30, 2017, options to purchase 12,942,900 shares of our common stock at a weighted average exercise price of $0.48 per share were outstanding, of which options to purchase 5,906,721 shares of our common stock were exercisable, at a weighted average exercise price of $0.39 per share.

Registration Rights

Our investor rights agreement, or the Investor Rights Agreement, provides certain holders of our preferred stock, including some of our directors and 5% stockholders and their respective affiliates and entities affiliated with our directors, the right, following the completion of this offering, to require us to register these shares under the Securities Act under specified circumstances as described below. After registration pursuant to these rights, these shares will become freely tradable without restriction under the Securities Act.

Demand Registration Rights

Beginning 180 days after the closing of this offering, subject to specified limitations set forth in the Investor Rights Agreement, at any time the holder or holders of at least thirty percent of senior preferred registrable securities, as defined in the Investor Rights Agreement, acting together, may demand in writing that we register at least twenty percent of the outstanding registrable securities, as defined in the Investor Rights Agreement, under the Securities Act or any lesser percentage so long as the total amount of registrable shares requested to be registered has an anticipated aggregate offering price to the public of least $10.0 million. We are not obligated to file a registration statement pursuant to this demand provision on more than two occasions, subject to specified exceptions.

In addition, at any time after we become eligible to file a registration statement on Form S-3 under the Securities Act, subject to specified limitations, a holder or holders of the senior preferred registrable securities may demand in writing that we register on Form S-3 all or part of the registrable securities held by them so long as the total amount of registrable shares requested to be registered has an anticipated aggregate offering price to the public of least $1.0 million.

Incidental Registration Rights

If, at any time after the closing of this offering, we propose to file a registration statement to register any of our common stock under the Securities Act, either for our own account or for the account of any of our stockholders that are not holders of registrable securities, and on a form that would also permit the registration of registrable securities, the holders of our registrable securities are entitled to notice of registration and, subject to specified exceptions, we will be required to use our best efforts to register the registrable securities then held by them that they request that we register.

Expenses of Registration

Pursuant to the Investor Rights Agreement, we are required to pay all registration expenses, including registration fees, printing expenses, fees and disbursements of our counsel and accountants and reasonable fees and disbursements not to exceed $30,000 of one counsel representing the selling stockholders, other than any underwriting discounts and commissions, related to any demand or incidental registration.

The Investor Rights Agreement contains customary cross-indemnification provisions, pursuant to which we are obligated to indemnify the selling stockholders in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions in the registration statement attributable to them.

Anti-Takeover Effects of Delaware Law and Our Charter and Bylaws

Delaware law contains, and upon the completion of this offering our certificate of incorporation and our bylaws will contain, provisions that could have the effect of delaying, deferring or discouraging another party from acquiring control of us. These provisions, which are summarized below, are expected to discourage

coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors.

Staggered Board; Removal of Directors

Upon the completion of this offering, our certificate of incorporation and bylaws will divide our board of directors into three classes with staggered three-year terms. In addition, a director will only be able to be removed for cause and only by the affirmative vote of the holders of at least 75% of the votes that all of our stockholders would be entitled to cast in an annual election of directors. Any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, will only be able to be filled by vote of a majority of our directors then in office. The classification of our board of directors and the limitations on the removal of directors and filling of vacancies could make it more difficult for a third party to acquire, or discourage a third party from seeking to acquire, control of our company.

Stockholder Action by Written Consent; Special Meetings

Upon the completion of this offering, our certificate of incorporation will provide that any action required or permitted to be taken by our stockholders must be effected at a duly called annual or special meeting of such holders and may not be effected by any consent in writing by such holders. Upon the completion of this offering, our certificate of incorporation and bylaws will also provide that, except as otherwise required by law, special meetings of our stockholders can only be called by our chairman of the board, our Chief Executive Officer or our board of directors.

Advance Notice Requirements for Stockholder Proposals

Upon the completion of this offering, our bylaws will establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of stockholders, including proposed nominations of persons for election to our board of directors. Stockholders at an annual meeting will only be able to consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of our board of directors or by a stockholder of record on the record date for the meeting who is entitled to vote at the meeting and who has delivered timely written notice in proper form to our secretary of the stockholder's intention to bring such business before the meeting. These provisions could have the effect of delaying until the next stockholder meeting stockholder actions that are favored by the holders of a majority of our outstanding voting securities.

Delaware Business Combination Statute

Upon the completion of this offering, we will be subject to Section 203 of the General Corporation Law of the State of Delaware. Subject to certain exceptions, Section 203 prevents a publicly held Delaware corporation from engaging in a "business combination" with any "interested stockholder" for three years following the date that the person became an interested stockholder, unless the interested stockholder attained such status with the approval of our board of directors or unless the business combination is approved in a prescribed manner. A "business combination" includes, among other things, a merger or consolidation involving us and the "interested stockholder" and the sale of more than 10% of our assets. In general, an "interested stockholder" is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person.

Amendment of Certificate of Incorporation and Bylaws

The General Corporation Law of the State of Delaware provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or bylaws, unless a corporation's certificate of incorporation or bylaws, as the case may be,

requires a greater percentage. Effective as of the closing date of this offering, our bylaws may be amended or repealed by a majority vote of our board of directors or by the affirmative vote of the holders of at least 75% of the votes that all of our stockholders would be entitled to cast in any annual election of directors. In addition, the affirmative vote of the holders of at least 75% of the votes that all of our stockholders would be entitled to cast in any annual election of directors is required to amend or repeal or to adopt any provisions inconsistent with any of the provisions of our certificate of incorporation described above under "—Staggered Board; Removal of Directors" and "—Stockholder Action by Written Consent; Special Meetings."

Exclusive Forum Selection

Effective as of the closing date of this offering, our certificate of incorporation will provide 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) shall be the sole and exclusive forum for (1) any derivative action or proceeding brought on behalf of our company, (2) 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, (3) any action asserting a claim against our company arising pursuant to any provision of the General Corporation Law of the State of Delaware or our certificate of incorporation or bylaws, or (4) any action asserting a claim against our company governed by the internal affairs doctrine. Although our certificate of incorporation contains the choice of forum provision described above, it is possible that a court could rule that such a provision is inapplicable for a particular claim or action or that such provision is unenforceable.

Listing on The NASDAQ Global Market

We have applied to have our common stock listed on The NASDAQ Global Market under the symbol "ALRN."

Authorized but Unissued Shares

The authorized but unissued shares of common stock and preferred stock are available for future issuance without stockholder approval, subject to any limitations imposed by the listing requirements of The NASDAQ Global Market. These additional shares may be used for a variety of corporate finance transactions, acquisitions and employee benefit plans. The existence of authorized but unissued and unreserved common stock and preferred stock could make it more difficult or discourage an attempt to obtain control of us by means of a proxy contest, tender offer, merger or otherwise.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock will be Computershare Trust Company, N.A.

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our common stock, and an active trading market for our common stock may not develop or be sustained after this offering. Future sales of substantial amounts of our common stock in the public market, including shares issued upon exercise of outstanding options or in the public market after this offering, or the anticipation of these sales, could adversely affect market prices prevailing from time to time and could impair our ability to raise capital through sales of our equity securities.

Based upon the 4,476,277 shares of our common stock that were outstanding on April 30, 2017, upon the closing of this offering, we will have outstanding shares of our common stock, after giving effect to the issuance of shares of our common stock in this offering and the conversion of all outstanding shares of our preferred stock into 104,435,674 shares of common stock upon the closing of this offering, and assuming no exercise by the underwriters of their option to purchase additional shares and no exercise of options outstanding as of April 30, 2017.

Of the shares to be outstanding immediately after the closing of this offering, we expect that the shares to be sold in this offering (assuming that the underwriters do not exercise their option to purchase additional shares), will be freely tradable without restriction or further registration under the Securities Act unless purchased by our "affiliates," as that term is defined in Rule 144 under the Securities Act, or Rule 144, whose sales would be subject to the Rule 144 resale restrictions described below, other than the holding period requirement.

The remaining 108,911,951 shares of our common stock outstanding after this offering will be "restricted securities" under Rule 144, and we expect that substantially all of these restricted securities will be subject to the 180-day lock-up period under the lock-up agreements as described below. These restricted securities may be sold in the public market only if registered or pursuant to an exemption from registration, such as Rule 144 or Rule 701 under the Securities Act.

Rule 144

In general, under Rule 144, beginning 90 days after the date of this prospectus, any person who is not our affiliate and has not been our affiliate at any time during the preceding three months and has held their shares for at least six months, including the holding period of any prior owner other than one of our affiliates, may sell shares without restriction, subject to the availability of current public information about us. In addition, under Rule 144, any person who is not our affiliate and has not been our affiliate at any time during the preceding three months and has held their shares for at least one year, including the holding period of any prior owner other than one of our affiliates, would be entitled to sell an unlimited number of shares immediately upon the closing of this offering without regard to whether current public information about us is available.

Beginning 90 days after the date of this prospectus, a person who is our affiliate or who was our affiliate at any time during the preceding three months may sell any unrestricted securities, as well as restricted securities that the person has beneficially owned for at least six months, including the holding period of any prior owner other than one of our affiliates, under Rule 144. Affiliates selling restricted or unrestricted securities may sell a number of shares within any three-month period that does not exceed the greater of:

- 1% of the number of shares of our common stock then outstanding, which will equal approximately shares immediately after this offering; and
- the average weekly trading volume of our common stock on The NASDAQ Global Market during the four calendar weeks preceding the filing of a Notice of Proposed Sale of Securities Pursuant to Rule 144 with respect to the sale.

Sales under Rule 144 by our affiliates are also subject to manner of sale provisions and notice requirements and to the availability of current public information about us.

Upon expiration of the 180-day lock-up period described below, approximately shares of our common stock will be eligible for sale under Rule 144, including shares eligible for resale immediately upon the closing of this offering as described above. We cannot estimate the number of shares of our common stock that our existing stockholders will elect to sell under Rule 144.

Rule 701

In general, under Rule 701 of the Securities Act, any of our employees, consultants or advisors, other than our affiliates, who purchased shares from us in connection with a qualified compensatory stock plan or other written agreement is eligible to resell these shares 90 days after the date of this prospectus in reliance on Rule 144, but without compliance with the holding period requirements of Rule 144 and without regard to the volume of such sales or the availability of public information about us. Subject to the 180-day lock-up period described below, approximately shares of our common stock will be eligible for sale in accordance with Rule 701.

Lock-Up Agreements

We, each of our executive officers and directors and the holders of our outstanding stock have agreed that, without the prior written consent of Merrill Lynch, Pierce, Fenner & Smith Incorporated and Jefferies LLC, on behalf of the underwriters, we and they will not, subject to limited exceptions, during the period ending 180 days after the date of this prospectus:

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant for the sale of, or otherwise dispose of or transfer any shares of our common stock or any securities convertible into or exchangeable or exercisable for our common stock;

- exercise any right with respect to the registration of any shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock, or with respect to the filing of any registration statement in connection therewith under the Securities Act; or

- enter into any swap or any other agreement or any transaction that transfers, in whole or in part, the economic consequence of ownership of our common stock, whether any transaction described above is to be settled by delivery of our common stock or such other securities, in cash or otherwise.

Registration Rights

Subject to the lock-up agreements described above, upon the closing of this offering, the holders of an aggregate of 104,576,635 shares of our common stock will be entitled to various rights with respect to the registration of these shares under the Securities Act. Registration of these shares under the Securities Act would result in these shares becoming fully tradable without restriction under the Securities Act immediately upon the effectiveness of the registration. See “Description of Capital Stock—Registration Rights” for additional information. Shares covered by a registration statement will be eligible for sale in the public market upon the expiration or release from the terms of lock-up agreements applicable to such shares.

Stock Options

As of April 30, 2017, we had outstanding options to purchase 12,942,900 shares of our common stock, of which options to purchase 5,906,721 shares were vested and exercisable. Following this offering, we intend to file one or more registration statements on Form S-8 under the Securities Act to register all of the shares of our common stock subject to outstanding options under the 2006 plan and the 2016 plan and options and other awards issuable pursuant to the 2017 plan and the 2017 ESPP. Shares covered by these registration statements will then be eligible for sale in the public markets, subject to vesting restrictions, any applicable lock-up agreements described above and Rule 144 limitations applicable to affiliates.

MATERIAL U.S. FEDERAL INCOME AND ESTATE TAX CONSIDERATIONS FOR NON-U.S. HOLDERS OF COMMON STOCK

The following is a discussion of material U.S. federal income and estate tax considerations relating to the ownership and disposition of our common stock by a non-U.S. holder. For purposes of this discussion, the term "non-U.S. holder" means a beneficial owner (other than a partnership or other entity that is treated as a partnership for U.S. federal income tax purposes) of our common stock that is not, for U.S. federal income tax purposes:

- an individual who is a citizen or resident of the United States;
- a corporation, or other entity treated as a corporation for U.S. federal income tax purposes, created or organized in or under the laws of the United States or of any political subdivision of the United States;
- an estate the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust if (1) a U.S. court is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have authority to control all substantial decisions of the trust or (2) the trust has a valid election in effect under applicable U.S. Treasury Regulations to be treated as a U.S. person.

This discussion does not address the tax treatment of partnerships or other entities that are pass-through entities for U.S. federal income tax purposes or persons who hold their common stock through partnerships or other pass-through entities. A partner in a partnership or other pass-through entity that will hold our common stock should consult his, her or its tax advisor regarding the tax consequences of the ownership and disposition of our common stock through a partnership or other pass-through entity, as applicable.

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, which we refer to as the Code, final, temporary and proposed U.S. Treasury Regulations promulgated thereunder, current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus and all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any change could alter the tax consequences to non-U.S. holders described in this prospectus. There can be no assurance that the Internal Revenue Service, or the IRS, will not challenge one or more of the tax consequences described in this prospectus.

We assume in this discussion that each non-U.S. holder holds shares of our common stock as a "capital asset" within the meaning of Section 1221 of the Code (generally, property held for investment). This discussion does not address all aspects of U.S. federal income and estate taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder's individual circumstances nor does it address any aspects of U.S. state, local or non-U.S. taxes, the alternative minimum tax, or the Medicare tax on net investment income. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

- financial institutions;
- brokers or dealers in securities;
- tax-exempt organizations;
- pension plans;
- owners that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment or who have elected to mark securities to market;

- insurance companies;
- controlled foreign corporations;
- passive foreign investment companies;
- non-U.S. governments; and
- certain U.S. expatriates.

THIS DISCUSSION IS FOR INFORMATION ONLY AND IS NOT, AND IS NOT INTENDED TO BE, LEGAL OR TAX ADVICE. PROSPECTIVE INVESTORS SHOULD CONSULT THEIR TAX ADVISORS REGARDING THE U.S. FEDERAL, STATE, LOCAL, ESTATE AND NON-U.S. INCOME AND OTHER TAX CONSIDERATIONS OF ACQUIRING, HOLDING AND DISPOSING OF OUR COMMON STOCK.

Distributions

As discussed under "Dividend Policy" above, we do not expect to make cash dividends to holders of our common stock in the foreseeable future. If we make distributions in respect of our common stock, those distributions generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles, subject to the tax treatment described in this section. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder's investment, up to the holder's tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below under the heading "Gain on Sale, Exchange or Other Taxable Disposition of Our Common Stock." Any such distributions will also be subject to the discussions below under the headings "Information Reporting and Backup Withholding" and "FATCA."

Subject to the discussion below on effectively connected income, dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States, and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements (generally including provision of a valid IRS Form W-8ECI (or applicable successor form) certifying that the dividends are effectively connected with the non-U.S. holder's conduct of a trade or business within the United States). However, such U.S. effectively connected income, net of specified deductions and credits, is taxed in the hands of the non-U.S. holder at the same graduated U.S. federal income tax rates as would apply if such holder were a U.S. person (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is classified as a corporation for U.S. federal income tax purposes may also, under certain circumstances, be subject to an additional "branch profits tax" at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence.

A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder's country of residence generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or successor form) and satisfy applicable certification and other requirements. Non-U.S. holders are urged to consult their tax advisors regarding their entitlement to benefits under a relevant income tax treaty and the specific methods available to them to satisfy these requirements.

A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim for a refund with the IRS.

Gain on Sale, Exchange or Other Taxable Disposition of Our Common Stock

Subject to the discussions below under the headings "Information Reporting and Backup Withholding" and "FATCA," a non-U.S. holder generally will not be subject to U.S. federal income tax or withholding tax on any gain realized upon such non-U.S. holder's sale, exchange or other disposition of our common stock unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a trade or business in the United States, and, if an applicable income tax treaty so provides, the gain is attributable to a permanent establishment or fixed base maintained by the non-U.S. holder in the United States; in these cases, the non-U.S. holder generally will be taxed on a net income basis at the graduated U.S. federal income tax rates applicable to U.S. persons, and, if the non-U.S. holder is a foreign corporation, an additional branch profits tax at a rate of 30% (or a lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence) may also apply;

- the non-U.S. holder is a non-resident alien present in the United States for 183 days or more in the taxable year of the disposition and certain other requirements are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence) on the net gain derived from the disposition, which may be offset by certain U.S.-source capital losses of the non-U.S. holder, if any; or

- we are or have been, at any time during the five-year period preceding such disposition (or the non-U.S. holder's holding period, if shorter) a "U.S. real property holding corporation" unless our common stock is regularly traded on an established securities market and the non-U.S. holder held no more than 5% of our outstanding common stock, directly or indirectly, during the shorter of the five-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. Generally, a corporation is a "U.S. real property holding corporation" if the fair market value of its "U.S. real property interests" (as defined in the Code and applicable regulations) equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we believe that we are not currently, and we do not anticipate becoming, a "U.S. real property holding corporation" for U.S. federal income tax purposes. No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rule described above.

Information Reporting and Backup Withholding

The gross amount of the distributions on our common stock paid to each non-U.S. holder and the tax withheld, if any, with respect to such distributions must be reported annually to the IRS and to such holder. Non-U.S. holders generally will have to comply with specific certification procedures to establish that the holder is not a U.S. person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to dividends on our common stock. Generally, a holder will comply with such procedures if it provides a properly executed IRS Form W-8BEN or W-8BEN-E (or other applicable Form W-8), or otherwise meets documentary evidence requirements for establishing that it is a non-U.S. holder, or otherwise establishes an exemption. Dividends paid to non-U.S. holders subject to withholding of U.S. federal income tax, as described above under "Distributions," will generally be exempt from U.S. backup withholding.

Information reporting and backup withholding generally will apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or non-U.S., unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their tax advisors regarding the application of the information reporting and backup withholding rules to them.

Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is timely filed with the IRS.

FATCA

Provisions of the Code commonly known as the Foreign Account Tax Compliance Act, or FATCA, generally impose a 30% withholding tax on dividends on, and gross proceeds from the sale or disposition of, our common stock if paid to a foreign entity unless (i) if the foreign entity is a "foreign financial institution," the foreign entity undertakes certain due diligence, reporting, withholding, and certification obligations, (ii) if the foreign entity is not a "foreign financial institution," the foreign entity identifies certain of its U.S. investors, if any, or (iii) the foreign entity is otherwise exempt under FATCA.

Withholding under FATCA generally (1) applies to payments of dividends on our common stock and (2) will apply to payments of gross proceeds from a sale or other disposition of our common stock made after December 31, 2018. An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this section. Under certain circumstances, a non-U.S. holder may be eligible for refunds or credits of the tax. Non-U.S. holders should consult their tax advisors regarding the possible implications of FATCA on their investment in our common stock.

Federal Estate Tax

Shares of our common stock that are owned or treated as owned by an individual who is not a citizen or resident of the United States (as specially defined for U.S. federal estate tax purposes) at the time of death are considered U.S. situs assets and will be included in the individual's gross estate for U.S. federal estate tax purposes. Such shares, therefore, may be subject to U.S. federal estate tax, unless an applicable estate tax or other treaty provides otherwise.

The preceding discussion of material U.S. federal tax considerations is for information only. It is not legal or tax advice. Prospective investors should consult their tax advisors regarding the particular U.S. federal, state, local and non-U.S. tax consequences of purchasing, holding and disposing of our common stock, including the consequences of any proposed changes in applicable laws.

UNDERWRITING

Merrill Lynch, Pierce, Fenner & Smith Incorporated and Jefferies LLC are acting as representatives of each of the underwriters named below. Subject to the terms and conditions set forth in an underwriting agreement among us and the underwriters, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the number of shares of common stock set forth opposite its name below.

Underwriter	Number of Shares
Merrill Lynch, Pierce, Fenner & Smith Incorporated	
Jefferies LLC	
William Blair & Company, L.L.C.	
Canaccord Genuity Inc.	
Total	

Subject to the terms and conditions set forth in the underwriting agreement, the underwriters have agreed, severally and not jointly, to purchase all of the shares sold under the underwriting agreement if any of these shares are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the nondefaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make in respect of those liabilities.

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the shares, and other conditions contained in the underwriting agreement, such as the receipt by the underwriters of officers' certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commissions and Discounts

The representatives have advised us that the underwriters propose initially to offer the shares to the public at the public offering price set forth on the cover page of this prospectus and to dealers at that price less a concession not in excess of $ per share. After the initial offering, the public offering price, concession or any other term of the offering may be changed.

The following table shows the public offering price, underwriting discount and proceeds before expenses to us. The information assumes either no exercise or full exercise by the underwriters of their option to purchase additional shares.

	Per Share	Without Option	With Option
Public offering price	$	$	$
Underwriting discount	$	$	$
Proceeds, before expenses, to us	$	$	$

The expenses of the offering, not including the underwriting discount, are estimated at $ and are payable by us. We have also agreed to reimburse the underwriters for certain of their expenses, in an amount of up to $, as set forth in the underwriting agreement.

Option to Purchase Additional Shares

We have granted an option to the underwriters, exercisable for 30 days after the date of this prospectus, to purchase up to additional shares at the public offering price, less the underwriting discount. If the underwriters exercise this option, each will be obligated, subject to conditions contained in the underwriting agreement, to purchase a number of additional shares proportionate to that underwriter's initial amount reflected in the above table.

No Sales of Similar Securities

We, each of our executive officers and directors and the holders of our outstanding stock have agreed not to sell or transfer any shares of common stock or securities convertible into or exchangeable or exercisable for common stock, for 180 days after the date of this prospectus without first obtaining the written consent of Merrill Lynch, Pierce, Fenner & Smith Incorporated and Jefferies LLC. Specifically, we and these other persons have agreed, with certain limited exceptions, not to directly or indirectly:

- offer, pledge, sell or contract to sell any common stock;
- sell any option or contract to purchase any common stock;
- purchase any option or contract to sell any common stock;
- grant any option, right or warrant for the sale of any common stock;
- otherwise dispose of or transfer any common stock;
- exercise any right with respect to the filing of a registration statement related to the common stock; or
- enter into any swap or other agreement that transfers, in whole or in part, the economic consequence of ownership of any common stock whether any such swap or transaction is to be settled by delivery of shares or other securities, in cash or otherwise.

This lock-up provision applies to common stock and to securities convertible into or exchangeable or exercisable for common stock. It also applies to common stock owned now or acquired later by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition

NASDAQ Global Market Listing

We expect the shares to be approved for listing on The NASDAQ Global Market, subject to notice of issuance, under the symbol "ALRN".

Determination of Offering Price

Before this offering, there has been no public market for our common stock. The initial public offering price will be determined through negotiations between us and the representatives. In addition to prevailing market conditions, the factors to be considered in determining the initial public offering price are:

- the valuation multiples of publicly traded companies that the representatives believe to be comparable to us;
- our financial information;

- the history of, and the prospects for, our company and the industry in which we compete;
- an assessment of our management, its past and present operations, and the prospects for, and timing of, our future revenues;
- the present state of our development; and
- the above factors in relation to market values and various valuation measures of other companies engaged in activities similar to ours.

An active trading market for the shares may not develop. It is also possible that after the offering the shares will not trade in the public market at or above the initial public offering price.

The underwriters do not expect to sell more than 5% of the shares in the aggregate to accounts over which they exercise discretionary authority.

Price Stabilization, Short Positions and Penalty Bids

Until the distribution of the shares is completed, SEC rules may limit underwriters and selling group members from bidding for and purchasing our common stock. However, the representatives may engage in transactions that stabilize the price of the common stock, such as bids or purchases to peg, fix or maintain that price.

In connection with the offering, the underwriters may purchase and sell our common stock in the open market. These transactions may include short sales, purchases on the open market to cover positions created by short sales and stabilizing transactions. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering. “Covered” short sales are sales made in an amount not greater than the underwriters’ option to purchase additional shares described above. The underwriters may close out any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option granted to them. “Naked” short sales are sales in excess of such option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of our common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of shares of common stock made by the underwriters in the open market prior to the completion of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Similar to other purchase transactions, the underwriters’ purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. The underwriters may conduct these transactions on The NASDAQ Global Market, in the over-the-counter market or otherwise.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. In addition, neither we nor any of the underwriters make any representation that the representatives will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Electronic Distribution

In connection with the offering, certain of the underwriters or securities dealers may distribute prospectuses by electronic means, such as e-mail.

Other Relationships

Some of the underwriters and their affiliates have engaged in, and may in the future engage in, investment banking and other commercial dealings in the ordinary course of business with us or our affiliates. They have received, or may in the future receive, customary fees and commissions for these transactions.

In addition, in the ordinary course of their business activities, the underwriters and their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Notice to Prospective Investors in Canada

The common stock may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the shares of common stock must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Notice to Prospective Investors in the European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a "Relevant Member State"), with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State, no offer of shares that are the subject of the offering contemplated by this prospectus may be made to the public in that Relevant Member State other than:

(a) to any legal entity which is a "qualified investor" as defined in the Prospectus Directive;

(b) to fewer than 150 natural or legal persons (other than "qualified investors" as defined in the Prospectus Directive), per Relevant Member State, subject to obtaining the prior consent of the representatives of the underwriters; or

(c) in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of shares shall result in a requirement for us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive or a supplemental prospectus pursuant to Article 16 of the Prospectus Directive.

Each person in a Relevant Member State who initially acquires any shares or to whom any offer is made will be deemed to have represented, warranted and agreed to and with the representatives of the underwriters and us that it is a "qualified investor" within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive. In the case of any shares being offered to a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, each such financial intermediary will also be deemed to have represented, warranted and agreed that the shares acquired by it in this offering have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to offering those shares to the public, other than their offer or resale in a Relevant Member State to "qualified investors" as so defined or in circumstances in which the prior consent of the representatives of the underwriters has been obtained to each such proposed offer or resale.

We, the underwriters and their affiliates will rely upon the truth and accuracy of the foregoing representations, warranties and agreements.

This prospectus has been prepared on the basis that any offer of shares in any Relevant Member State will be made pursuant to an exemption under the Prospectus Directive from the requirement to publish a prospectus for offers of shares. Accordingly any person making or intending to make an offer in that Relevant Member State of shares which are the subject of the offering contemplated in this prospectus may only do so in circumstances in which no obligation arises for us or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive in relation to such offer. Neither we nor the underwriters have authorized, nor do they authorize, the making of any offer of shares in circumstances in which an obligation arises for us or the underwriters to publish a prospectus for such offer.

For the purposes of the above provisions, the expression "an offer of shares to the public" in relation to any shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe for the shares, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State. The expression "Prospectus Directive" means Directive 2003/71/EC (as amended, including by Directive 2010/73/EU), and includes any relevant implementing measure in the Relevant Member State.

Notice to Prospective Investors in the United Kingdom

In addition, in the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are "qualified investors" (as defined in the Prospectus Directive) (i) who have professional experience in matters relating to investments falling within Article 19 (5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the "Order") and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as "relevant persons"). This document must not be acted on or relied on in the United Kingdom by persons who are not relevant persons. In the United Kingdom, any investment or investment activity to which this document relates is only available to, and will be engaged in with, relevant persons.

Notice to Prospective Investors in Switzerland

The shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange ("SIX") or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the

Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the shares or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, the company, or the shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority, and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes ("CISA"). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares.

Notice to Prospective Investors in the Dubai International Financial Centre

This prospectus relates to an Exempt Offer in accordance with the Offered Securities Rules of the Dubai Financial Services Authority ("DFSA"). This prospectus is intended for distribution only to persons of a type specified in the Offered Securities Rules of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus nor taken steps to verify the information set forth herein and has no responsibility for the prospectus. The shares to which this prospectus relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the shares offered should conduct their own due diligence on the shares. If you do not understand the contents of this prospectus you should consult an authorized financial advisor.

Notice to Prospective Investors in Australia

No placement document, prospectus, product disclosure statement or other disclosure document has been lodged with the Australian Securities and Investments Commission ("ASIC"), in relation to the offering. This prospectus does not constitute a prospectus, product disclosure statement or other disclosure document under the Corporations Act 2001 (the "Corporations Act"), and does not purport to include the information required for a prospectus, product disclosure statement or other disclosure document under the Corporations Act.

Any offer in Australia of the shares may only be made to persons (the "Exempt Investors") who are "sophisticated investors" (within the meaning of section 708(8) of the Corporations Act), "professional investors" (within the meaning of section 708(11) of the Corporations Act) or otherwise pursuant to one or more exemptions contained in section 708 of the Corporations Act so that it is lawful to offer the shares without disclosure to investors under Chapter 6D of the Corporations Act.

The shares applied for by Exempt Investors in Australia must not be offered for sale in Australia in the period of 12 months after the date of allotment under the offering, except in circumstances where disclosure to investors under Chapter 6D of the Corporations Act would not be required pursuant to an exemption under section 708 of the Corporations Act or otherwise or where the offer is pursuant to a disclosure document which complies with Chapter 6D of the Corporations Act. Any person acquiring shares must observe such Australian on-sale restrictions.

This prospectus contains general information only and does not take account of the investment objectives, financial situation or particular needs of any particular person. It does not contain any securities recommendations or financial product advice. Before making an investment decision, investors need to consider whether the information in this prospectus is appropriate to their needs, objectives and circumstances, and, if necessary, seek expert advice on those matters.

Notice to Prospective Investors in Hong Kong

The securities have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or (b) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance. No advertisement, invitation or document relating to the securities has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the Securities and Futures Ordinance and any rules made under that Ordinance.

Notice to Prospective Investors in Japan

The securities have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948, as amended) and, accordingly, will not be offered or sold, directly or indirectly, in Japan, or for the benefit of any Japanese Person or to others for re-offering or resale, directly or indirectly, in Japan or to any Japanese Person, except in compliance with all applicable laws, regulations and ministerial guidelines promulgated by relevant Japanese governmental or regulatory authorities in effect at the relevant time. For the purposes of this paragraph, "Japanese Person" shall mean any person resident in Japan, including any corporation or other entity organized under the laws of Japan.

Notice to Prospective Investors in Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of Non-CIS Securities may not be circulated or distributed, nor may the Non-CIS Securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the "SFA"), (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275, of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the Non-CIS Securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

(a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

(b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the Non-CIS Securities pursuant to an offer made under Section 275 of the SFA except:

(a) to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;

(b) where no consideration is or will be given for the transfer;

(c) where the transfer is by operation of law;

(d) as specified in Section 276(7) of the SFA; or

(e) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

LEGAL MATTERS

The validity of the shares of our common stock offered hereby is being passed upon for us by Wilmer Cutler Pickering Hale and Dorr LLP. Certain legal matters relating to this offering will be passed upon for the underwriters by Latham & Watkins LLP.

EXPERTS

The financial statements as of December 31, 2015 and 2016 and for each of the two years in the period ended December 31, 2016 included in this prospectus have been so included in reliance on the report (which contains an explanatory paragraph relating to the Company's requirement for additional financing to fund future operations) of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the shares of our common stock we are offering to sell. This prospectus, which constitutes part of the registration statement, does not include all of the information contained in the registration statement and the exhibits, schedules and amendments to the registration statement. Some items are omitted in accordance with the rules and regulations of the SEC. For further information with respect to us and our common stock, we refer you to the registration statement and to the exhibits, schedules and amendments to the registration statement. Statements contained in this prospectus about the contents of any contract, agreement or other document filed as an exhibit are not necessarily complete, and, in each instance, we refer you to the copy of the contract, agreement or other document filed as an exhibit to the registration statement. Each of these statements is qualified in all respects by this reference.

You may read and copy the registration statement of which this prospectus is a part at the SEC's public reference room, which is located at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You can request copies of the registration statement by writing to the Securities and Exchange Commission and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the SEC's public reference room. In addition, the SEC maintains an Internet website, which is located at *www.sec.gov*, that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC. You may access the registration statement of which this prospectus is a part at the SEC's Internet website.

Upon completion of this offering, we will be subject to the information reporting requirements of the Securities Exchange Act of 1934, and we will file reports, proxy statements and other information with the SEC. We intend to furnish our stockholders with annual reports containing financial statements certified by an independent registered public accounting firm. We also maintain a website at www.aileronrx.com. The information contained on, or that can be accessed through, our website is not a part of, and is not incorporated into, this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

INDEX TO FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

In our opinion, the accompanying balance sheets and the related statements of operations and comprehensive loss, of redeemable convertible preferred stock and stockholders' deficit and of cash flows present fairly, in all material respects, the financial position of Aileron Therapeutics, Inc. as of December 31, 2015 and 2016, 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. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits. We conducted our audits of these statements in accordance with the standards of the Public Company Accounting Oversight Board (United States) and in accordance with auditing standards generally accepted in the United States of America. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

As discussed in Note 1 to the financial statements, the Company will require additional financing to fund future operations. Management's plans in regard to this matter are described in Note 1.

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts
April 14, 2017

AILERON THERAPEUTICS, INC.
BALANCE SHEETS

(In thousands, except share and per share data)

	December 31, 2015	December 31, 2016	March 31, 2017 (unaudited)	Pro Forma March 31, 2017 (unaudited)
Assets				
Current assets:				
Cash and cash equivalents	$ 3,768	$ 20,715	$ 8,029	$ 8,029
Investments	—	—	7,265	7,265
Prepaid expenses and other current assets	258	333	663	663
Restricted cash	—	25	25	25
Total current assets	4,026	21,073	15,982	15,982
Property and equipment, net	351	107	123	123
Restricted cash	63	63	63	63
Other assets	—	778	782	782
Deferred offering costs	1,500	—	205	205
Total assets	$ 5,940	$ 22,021	$ 17,155	$ 17,155
Liabilities, Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)				
Current liabilities:				
Accounts payable	$ 641	$ 1,971	$ 1,035	$ 1,035
Accrued expenses and other current liabilities	1,908	2,100	1,836	1,836
Total current liabilities	2,549	4,071	2,871	2,871
Deferred rent	29	11	4	4
Total liabilities	2,578	4,082	2,875	2,875
Commitments and contingencies (Note 12)				
Redeemable convertible preferred stock (Series A, A-1, B, C-1, C-2, D, D-1, E, E-1, E-2, E-3 and F), $0.01 par value; 91,681,662 shares authorized at December 31, 2015 and 151,557,293 shares authorized at December 31, 2016 and March 31, 2017 (unaudited); 81,975,780, 105,631,019 and 106,114,520 shares issued and outstanding at December 31, 2015 and 2016 and March 31, 2017 (unaudited), respectively; aggregate liquidation preference of $130,053 and $130,711 at December 31, 2016 and March 31, 2017 (unaudited), respectively; no shares issued and outstanding, pro forma at March 31, 2017 (unaudited)	97,681	129,745	130,391	—
Stockholders' equity (deficit):				
Common stock, $0.001 par value; 109,000,000 shares authorized at December 31, 2015 and 143,500,000 shares authorized at December 31, 2016 and March 31, 2017 (unaudited); 4,235,448, 4,297,193 and 4,446,277 shares issued and outstanding at December 31, 2015 and 2016 and March 31, 2017 (unaudited), respectively; 108,881,951 shares issued and outstanding, pro forma at March 31, 2017 (unaudited)	4	4	4	109
Additional paid-in capital	1,896	2,532	2,784	133,070
Accumulated deficit	(96,219)	(114,342)	(118,899)	(118,899)
Total stockholders' equity (deficit)	(94,319)	(111,806)	(116,111)	14,280
Total liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)	$ 5,940	$ 22,021	$ 17,155	$ 17,155

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,		Three Months Ended March 31,	
	2015	2016	2016	2017
			(unaudited)	
Revenue	$ —	$ —	$ —	$ —
Operating expenses:				
Research and development	7,832	10,276	2,493	2,942
General and administrative	5,059	7,893	1,446	1,647
Total operating expenses	12,891	18,169	3,939	4,589
Loss from operations	(12,891)	(18,169)	(3,939)	(4,589)
Interest and other income	13	46	14	32
Net loss	(12,878)	(18,123)	(3,925)	(4,557)
Accretion of redeemable convertible preferred stock to redemption value	(71)	(75)	(18)	(20)
Net loss attributable to common stockholders	$ (12,949)	$ (18,198)	$ (3,943)	$ (4,577)
Net loss per share attributable to common stockholders—basic and diluted	$ (3.25)	$ (4.26)	$ (0.93)	$ (1.06)
Weighted average common shares outstanding—basic and diluted	3,981,886	4,270,092	4,238,305	4,300,331
Pro forma net loss per share attributable to common stockholders—basic and diluted (unaudited)		$ (0.19)		$ (0.04)
Pro forma weighted average common shares outstanding—basic and diluted (unaudited)		94,392,508		108,456,749
Net loss	$ (12,878)	$ (18,123)	$ (3,925)	$ (4,557)
Other comprehensive loss:				
Unrealized gain (loss) on investments, net of tax of $0	(4)	—	7	—
Total other comprehensive income (loss)	(4)	—	7	—
Comprehensive loss	$ (12,882)	$ (18,123)	$ (3,918)	$ (4,557)

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

AILERON THERAPEUTICS, INC.
STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' DEFICIT

(In thousands, except share data)

	Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Total Stockholders' Deficit
	Shares	Amount	Shares	Par Value				
Balances at December 31, 2014	81,975,780	$ 97,610	3,839,281	$ 4	$ 1,289	$ 4	$ (83,341)	$ (82,044)
Exercise of stock options	—	—	396,167	—	52	—	—	52
Stock-based compensation expense	—	—	—	—	626	—	—	626
Accretion of redeemable convertible preferred stock to redemption value	—	71	—	—	(71)	—	—	(71)
Unrealized loss on investments	—	—	—	—	—	(4)	—	(4)
Net loss	—	—	—	—	—	—	(12,878)	(12,878)
Balances at December 31, 2015	81,975,780	97,681	4,235,448	4	1,896	—	(96,219)	(94,319)
Issuance of Series E-1 redeemable convertible preferred stock, net of issuance costs of $17	9,705,882	13,183	—	—	—	—	—	—
Issuance of Series F redeemable convertible preferred stock, net of issuance costs of $165	13,949,357	18,806	—	—	—	—	—	—
Exercise of stock options	—	—	61,745	—	23	—	—	23
Stock-based compensation expense	—	—	—	—	688	—	—	688
Accretion of redeemable convertible preferred stock to redemption value	—	75	—	—	(75)	—	—	(75)
Net loss	—	—	—	—	—	—	(18,123)	(18,123)
Balances at December 31, 2016	105,631,019	129,745	4,297,193	4	2,532	—	(114,342)	(111,806)
Issuance of Series F redeemable convertible preferred stock, net of issuance costs of $32	483,501	626	—	—	—	—	—	—
Exercise of stock options	—	—	149,084	—	75	—	—	75
Stock-based compensation expense	—	—	—	—	197	—	—	197
Accretion of redeemable convertible preferred stock to redemption value	—	20	—	—	(20)	—	—	(20)
Net loss	—	—	—	—	—	—	(4,557)	(4,557)
Balances at March 31, 2017 (unaudited)	106,114,520	$130,391	4,446,277	$ 4	$ 2,784	$ —	$ (118,899)	$ (116,111)

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

AILERON THERAPEUTICS, INC.
STATEMENTS OF CASH FLOWS

(In thousands)

	Year Ended December 31,		Three Months Ended March 31,	
	2015	2016	2016	2017
			(unaudited)	
Cash flows from operating activities:				
Net loss	$(12,878)	$(18,123)	$ (3,925)	$ (4,557)
Adjustments to reconcile net loss to net cash used in operating activities:				
Depreciation and amortization expense	325	232	67	22
Stock-based compensation expense	626	688	163	197
Change in deferred rent	(21)	(18)	(20)	(7)
Loss on disposal of property and equipment	—	12	—	—
Write-off of deferred offering costs	—	1,500	—	—
Changes in operating assets and liabilities:				
Prepaid expenses and other current assets	(109)	(75)	50	(330)
Other assets	—	(778)	—	(4)
Accounts payable	(237)	1,215	68	(829)
Accrued expenses and other current liabilities	584	333	(151)	(444)
Net cash used in operating activities	(11,710)	(15,014)	(3,748)	(5,952)
Cash flows from investing activities:				
Purchases of property and equipment	(94)	—	—	(38)
Purchases of investments	(2,368)	(12,634)	(10,391)	(7,265)
Proceeds from sales or maturities of investments	12,378	12,634	—	—
Changes in restricted cash	713	(25)	(1)	—
Net cash provided by (used in) investing activities	10,629	(25)	(10,392)	(7,303)
Cash flows from financing activities:				
Proceeds from issuance of redeemable convertible preferred stock, net of issuance costs	(91)	32,143	13,198	494
Proceeds from exercise of stock options	52	23	2	75
Payments of initial public offering costs	(1,320)	(180)	(117)	—
Net cash provided by (used in) financing activities	(1,359)	31,986	13,083	569
Net increase (decrease) in cash and cash equivalents	(2,440)	16,947	(1,057)	(12,686)
Cash and cash equivalents at beginning of period	6,208	3,768	3,768	20,715
Cash and cash equivalents at end of period	$ 3,768	$ 20,715	$ 2,711	$ 8,029
Supplemental disclosure of non-cash financing activities:				
Accretion of redeemable convertible preferred stock to redemption value	$ 71	$ 75	$ 18	$ 20
Issuance costs for redeemable convertible preferred stock included in accounts payable and accrued expenses	$ —	$ 154	$ 14	$ 23
Deferred offering costs included in accounts payable and accrued expenses	$ 180	$ —	$ 223	$ 205

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

AILERON THERAPEUTICS, INC.
NOTES TO 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 therapeutics called stapled peptides. The Company's lead product candidate, ALRN-6924, targets the tumor suppressor p53 for the treatment of a wide variety of cancers. ALRN-6924 reactivates p53-mediated tumor suppression by targeting the two primary p53 suppressor proteins, MDMX and MDM2. ALRN-6924 was in multiple clinical trials as of December 31, 2016 and March 31, 2017.

The Company was incorporated under the laws of the State of Delaware in August 2001 as Renegade Therapeutics, Inc. and commenced its principal operations in 2006. In February 2007, the Company amended its certificate of incorporation to change its name to Aileron Therapeutics, Inc.

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 employees and consultants.

The Company's financial statements have been prepared on the basis of continuity of operations, realization of assets and the satisfaction of liabilities in the ordinary course of business. Through December 31, 2016 and March 31, 2017 (unaudited), the Company has funded its operations with proceeds from the sale of redeemable convertible preferred stock and, to a lesser extent, payments received in connection with a collaboration agreement. The Company has incurred losses and negative cash flows from operations and had an accumulated deficit of $114,342 as of December 31, 2016 and $118,899 as of March 31, 2017 (unaudited). The Company expects to continue to generate losses for the foreseeable future. As of April 14, 2017, the date of issuance of the financial statements for the year ended December 31, 2016, the Company expected that its cash and cash equivalents of $20,715 as of December 31, 2016, together with gross proceeds of $658 the Company received from its sale of Series F preferred stock in February 2017 (see Note 15), would be sufficient to fund its operating expenses and capital expenditure requirements through at least 12 months from the issuance date of those financial statements.

As of May 26, 2017 (unaudited), the date of issuance of the interim financial statements for the three months ended March 31, 2017, the Company expects that its cash, cash equivalents and investments of $15,294 as of March 31, 2017 (unaudited) will be sufficient to funds its operating expenses and capital expenditure requirements through at least 12 months from the issuance date of the interim financial statements. The future viability of the Company beyond that point is dependent on its ability to raise additional capital to finance its operations. Although the Company has been successful in raising capital in the past, there is no assurance that it will be successful in obtaining such additional financing on terms acceptable to the Company, if at all.

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The Company is seeking to complete an initial public offering of its common stock. Upon the closing of a qualified public offering on specified terms, the Company's outstanding redeemable convertible preferred stock will automatically convert into shares of common stock (see Note 7).

In the event the Company does not complete an initial public offering, the Company expects to seek additional funding through private financings, debt financings, collaboration agreements, strategic alliances and licensing arrangements. The Company may not be able to obtain financing on acceptable terms, or at all, and the Company may not be able to enter into collaboration arrangements. 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 will be required to delay, reduce and/or eliminate research and development programs or future commercialization efforts, which could adversely affect its business prospects. Although management continues to pursue these plans, there is no assurance that the Company will be successful in obtaining sufficient funding on terms acceptable to the Company to fund continuing operations, if at all.

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

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.

Unaudited Interim Financial Information

The accompanying balance sheet as of March 31, 2017, the statements of operations and comprehensive loss and of cash flows for the three months ended March 31, 2016 and 2017, and the statement of redeemable convertible preferred stock and stockholders' deficit for the three months ended March 31, 2017 are unaudited. The unaudited interim financial statements have been prepared on the same basis as the audited annual financial statements and, in the opinion of management, reflect all adjustments, which include only normal recurring adjustments, necessary for the fair statement of the Company's financial position as of March 31, 2017 and the results of its operations and cash flows for the three months ended March 31, 2016 and 2017. The financial data and other information disclosed in these notes related to the three months ended March 31, 2016 and 2017 are unaudited. The results for the three months ended March 31, 2017 are not necessarily indicative of results to be expected for the year ending December 31, 2017, any other interim periods, or any future year or period.

Unaudited Pro Forma Information

The accompanying unaudited pro forma balance sheet as of March 31, 2017 has been prepared to give effect to the automatic conversion of all outstanding shares of redeemable convertible preferred stock into 104,435,674 shares of common stock as if the Company's proposed initial public offering had occurred on March 31, 2017.

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In the accompanying statements of operations and comprehensive loss, unaudited pro forma basic and diluted net loss per share attributable to common stockholders for the year ended December 31, 2016 and the three months ended March 31, 2017 have been prepared to give effect to the automatic conversion of all outstanding shares of redeemable convertible preferred stock into shares of common stock as if the Company's proposed initial public offering had occurred on the later of January 1, 2016 or the issuance date of the redeemable convertible preferred stock.

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, commercial paper and corporate notes, are stated at fair value.

Restricted Cash

As of December 31, 2016 and March 31, 2017 (unaudited), current restricted cash consisted of $25 of cash deposited in a separate restricted bank account as a security deposit for the Company's corporate credit cards. As of December 31, 2015 and 2016 and March 31, 2017 (unaudited), non-current restricted cash consisted of $63 of cash deposited in a separate restricted bank account as a security deposit for the lease of the Company's facilities.

Investments

The Company classifies its available-for-sale 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' 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 statement 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 statement 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

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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 risk. 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 will be expensed immediately as a charge to operating expenses in the statement of operations and comprehensive loss.

As of December 31, 2015, the Company had recorded $1,500 of deferred offering costs in contemplation of a probable 2016 equity financing. The Company determined in June 2016 that the equity financing was no longer

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probable of being consummated and, at that time, recorded general and administrative expense of $1,500 in the statement of operations and comprehensive loss to write-off the deferred offering costs that had been capitalized.

As of December 31, 2016, the Company had not recorded any deferred offering costs. As of March 31, 2017 (unaudited), the Company recorded $205 of deferred offering costs in contemplation of an initial public offering of its common stock.

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
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

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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.

For stock-based awards granted to non-employees, compensation expense is recognized over the period during which services are rendered by such non-employees until completed. At the end of each financial reporting period prior to the completion of the service, the fair value of these awards is remeasured using the then-current fair value of the Company's common stock and updated assumption inputs in the Black-Scholes option-pricing model. The Company classifies stock-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 Company recognizes compensation expense for only the portion of awards that are expected to vest. In developing a forfeiture rate estimate, the Company has considered its historical experience to estimate pre-vesting forfeitures for awards with service-based vesting conditions. The impact of a forfeiture rate adjustment will be recognized in full in the period of adjustment, and if the actual forfeiture rate is materially different from the Company's estimate, the Company may be required to record adjustments to stock-based compensation expense in future periods.

The 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.

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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' 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

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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 entitles the holders of such shares to participate in dividends but contractually does 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 Issued Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board ("FASB") issued Accounting Standard Update ("ASU") No. 2014-09, *Revenue from Contracts with Customers (Topic 606)* ("ASU 2014-09"), which supersedes existing revenue recognition guidance under GAAP. The standard's core principle is that a company will recognize revenue when it transfers promised goods or services to customers in an amount that reflects the consideration to which the company expects to be entitled in exchange for those goods or services. The standard defines a five-step process to achieve this principle, and will require companies to use more judgment and make more estimates than under the current guidance. The Company expects that these judgments and estimates will include identifying performance obligations in the customer contract, estimating the amount of variable consideration to include in the transaction price and allocating the transaction price to each separate performance obligation. ASU 2014-09 also requires additional disclosure about the nature, amount, timing and uncertainty of revenue and cash flows arising from customer contracts. In August 2015, the FASB issued ASU No. 2015-14, *Revenue from Contracts with Customers (Topic 606): Deferral of the Effective Date*, which delays the effective date of ASU 2014-09 such that the standard is effective for public entities for annual periods beginning after December 15, 2017 and for interim periods within those fiscal years. Early adoption of the standard is permitted for annual periods beginning after December 15, 2016. In March 2016, the FASB issued ASU No. 2016-08, *Revenue from Contracts with Customers (Topic 606): Principal versus Agent Considerations* ("ASU 2016-08"), which further clarifies the implementation guidance on principal versus agent considerations in ASU 2014-09. In April 2016, the FASB issued ASU No. 2016-10, *Revenue from Contracts with Customers (Topic 606): Identifying Performance Obligations and Licensing* ("ASU 2016-10"), clarifying the implementation guidance on identifying performance obligations and licensing. Specifically, the amendments in this update reduce the cost and complexity of identifying promised goods or services and improve the guidance for determining whether promises are separately identifiable. The amendments in this update also provide implementation guidance on determining whether an entity's promise to grant a license provides a customer with either a right to use the entity's intellectual property (which is satisfied at a point in time) or a right to access the entity's intellectual property (which is satisfied over time). In May 2016, the FASB issued ASU No. 2016-12, *Revenue from Contracts with Customers (Topic 606): Narrow-Scope Improvements and Practical Expedients* ("ASU 2016-12"), which clarifies the objective of the collectability criterion, presentation of taxes collected from customers, non-cash consideration, contract modifications at transition, completed contracts at transition and how guidance in ASU 2014-09 is retrospectively applied. ASU 2016-08, ASU 2016-10 and ASU 2016-12 have the same effective dates and transition requirements as ASU 2014-09. The adoption of these standards is not expected to have an impact on the Company's financial position, results of operations or cash flows as the Company does not currently have any revenue-generating arrangements.

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In August 2014, the FASB issued ASU No. 2014-15, *Presentation of Financial Statements—Going Concern (Subtopic 205-40): Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern* ("ASU 2014-15"). This update is intended to define management's responsibility to evaluate whether there is substantial doubt about an organization's ability to continue as a going concern within one year of the date of issuance of the entity's financial statements and to provide related footnote disclosures in certain circumstances. This guidance is effective for fiscal years ending after December 15, 2016 and for interim periods thereafter. Early adoption is permitted. The Company adopted ASU 2014-15 as of the required effective date of December 31, 2016. The Company performed a working capital analysis as of December 31, 2016 to determine whether or not this disclosure was appropriate and concluded that additional disclosure was not required per the updated guidance.

In November 2015, the FASB issued ASU No. 2015-17, *Income Taxes (Topic 740): Balance Sheet Classification of Deferred Taxes* ("ASU 2015-17"). ASU 2015-17 requires deferred tax liabilities and assets to be classified as noncurrent in the balance sheet. ASU 2015-17 is required to be adopted for annual periods beginning after December 15, 2016, including interim periods within that annual period, with early adoption permitted. The amendment may be applied either prospectively to all deferred tax liabilities and assets or retrospectively to all periods presented. The Company elected to early adopt ASU 2015-17 prospectively in the three months ended December 31, 2015, and its adoption had no impact on the Company's financial position, results of operations or cash flows.

In January 2016, the FASB issued ASU No. 2016-01, *Financial Instruments-Overall: Recognition and Measurement of Financial Assets and Financial Liabilities*. The ASU affects the accounting for equity investments, financial liabilities under the fair value option, and the presentation and disclosure requirements for financial instruments. In addition, it includes a clarification related to the valuation allowance assessment when recognizing deferred tax assets resulting from unrealized losses on available-for-sale debt securities. The standard is effective for public entities for annual periods beginning after December 15, 2017 and for interim periods within those fiscal years. Entities can early adopt the provision to record changes in the fair value of financial liabilities under the fair value option resulting from instrument-specific credit risk separately in other comprehensive income. Early adoption of this provision can be elected for all financial statements for annual and interim periods that have not yet been issued (for public business entities) or that have not yet been made available for issuance. The adoption of this standard is not expected to have a material impact on the Company's financial position, results of operations or cash flows.

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 currently evaluating the potential impact that the adoption of ASU 2016-02 will have on its financial statements.

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In March 2016, the FASB issued ASU No. 2016-09, *Compensation—Stock Compensation* ("ASU 2016-09"), which amends ASC Topic 718, *Compensation—Stock Compensation*. The new standard identifies areas for simplification involving several aspects of accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities, an option to recognize gross stock compensation expense with actual forfeitures recognized as they occur, as well as certain classifications on the statements of cash flows. The standard is effective for annual periods beginning after December 15, 2016 and for interim periods within those fiscal years. The Company adopted ASU 2016-09 on the required effective date of January 1, 2017. The Company elected to maintain its existing policy to estimate forfeitures when determining periodic stock-based compensation expense. The adoption of the other provisions of ASU 2016-09 had no impact on the Company's financial position, results of operations or cash flows.

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows: Classification of Certain Cash Receipts and Cash Payments* ("ASU 2016-15"). This guidance addresses the presentation and classification of certain cash receipts and cash payments in the statement of cash flows. The standard is effective for annual periods beginning after December 15, 2017 and for interim periods within those fiscal years. Early adoption is permitted. The Company is currently evaluating the potential impact that the adoption of ASU 2016-15 will have on its financial statements.

In November 2016, the FASB issued ASU No. 2016-18, *Restricted Cash* ("ASU 2016-18"). The new standard requires restricted cash and restricted cash equivalents be included with cash and cash equivalents when reconciling the total beginning and ending amounts for the periods shown on the statement of cash flows. The new standard is effective for annual periods beginning after December 15, 2017 and for interim periods within those fiscal years. Early adoption is permitted. The Company is currently evaluating the potential impact that the adoption of ASU 2016-18 will have on its financial statements.

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, 2015 using:			
	Level 1	Level 2	Level 3	Total
Cash equivalents:				
Money market funds	$ 2,898	$ —	$ —	$ 2,898
	$ 2,898	$ —	$ —	$ 2,898

	Fair Value Measurements as of December 31, 2016 using:			
	Level 1	Level 2	Level 3	Total
Cash equivalents:				
Money market funds	$20,016	$ —	$ —	$20,016
	$20,016	$ —	$ —	$20,016

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	Fair Value Measurements as of March 31, 2017 using:			
	Level 1	Level 2	Level 3	Total
		(unaudited)		
Cash equivalents:				
Money market funds	$5,729	$ —	$ —	$ 5,729
Corporate notes	—	1,525	—	1,525
Investments:				
Corporate notes	—	325	—	325
Commerical paper	—	6,940	—	6,940
	$5,729	$8,790	$ —	$14,519

As of December 31, 2015 and 2016, the Company's cash equivalents were invested in money market funds and were valued based on Level 1 inputs. As of March 31, 2017 (unaudited), 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, 2015 and 2016 and the three months ended March 31, 2016 and 2017 (unaudited), there were no transfers between Level 1, Level 2 and Level 3.

4. Investments

As of December 31, 2015 and 2016, the Company had no available-for-sale investments. As of March 31, 2017 (unaudited), the fair value of available-for-sale investments by type of security was as follows:

	March 31, 2017			
	Amortized Cost	Gross Unrealized Gain	Gross Unrealized Loss	Fair Value
		(unaudited)		
Investments:				
Corporate notes	$ 325	$ —	$ —	$ 325
Commercial paper	6,940	—	—	6,940
	$ 7,265	$ —	$ —	$7,265

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5. Property and Equipment, Net

Property and equipment, net consisted of the following:

	December 31, 2015	December 31, 2016	March 31, 2017 (unaudited)
Laboratory equipment	$ 1,240	$ 1,240	$ 1,240
Leasehold improvements	559	559	559
Computer equipment and software	343	331	369
Furniture and fixtures	71	71	71
	2,213	2,201	2,239
Less: Accumulated depreciation and amortization	(1,862)	(2,094)	(2,116)
	$ 351	$ 107	$ 123

Depreciation and amortization expense for the years ended December 31, 2015 and 2016 was $325 and $232, respectively, and for the three months ended March 31, 2016 and 2017 (unaudited) was $67 and $22, respectively. During the year ended December 31, 2016, assets with a cost of $12 were disposed of for no proceeds, resulting in a loss of $12. No assets were disposed of during the year ended December 31, 2015 or the three months ended March 31, 2016 and 2017 (unaudited).

6. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following:

	December 31, 2015	December 31, 2016	March 31, 2017 (unaudited)
Payroll and payroll-related costs	$ 774	$ 899	$ 305
External research and development services	491	723	673
Professional fees	467	322	665
Other	176	156	193
	$1,908	$2,100	$ 1,836

7. Redeemable Convertible Preferred Stock

As of December 31, 2016 and March 31, 2017 (unaudited), the Company's certificate of incorporation, as amended and restated, authorized the Company to issue 151,557,293 shares of $0.01 par value preferred stock.

The Company has issued 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"), together the "Redeemable Preferred Stock". The Redeemable Preferred Stock is classified outside of stockholders' deficit because the shares contain redemption features that are not solely within the control of the Company.

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In October 2014, the Company issued 14,558,823 shares of Series E-1 redeemable convertible preferred stock (the "Series E-1 preferred stock") at a price of $1.36 per share, resulting in proceeds of $19,674, net of issuance costs of $126.

In January 2016, the Company issued 9,705,882 shares of Series E-1 preferred stock at a price of $1.36 per share, resulting in proceeds of $13,183, net of issuance costs of $17.

In December 2016, the Company issued 13,949,357 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 $18,806, net of issuance costs of $165. As part of the Series F preferred stock purchase agreement, the investors agreed to purchase an additional 8,192,477 shares of Series F preferred stock at a price of $1.36 per share upon the Company achieving specified clinical milestones (the "second tranche closing") for an aggregate purchase price of $11,142. In February 2017, the Company amended the Series F preferred stock purchase agreement to permit the sale of up to 758,458 additional shares of Series F preferred stock. In February 2017, pursuant to the amended Series F preferred stock purchase agreement, the Company issued 483,501 shares of Series F preferred stock at a price of $1.36 per share, resulting in proceeds of $626, net of issuance costs of $32. The purchasers of Series F preferred stock in this February 2017 closing agreed to purchase an additional 274,957 shares of Series F preferred stock at a price of $1.36 per share in the second tranche closing, which increased the aggregate number of shares of Series F preferred stock to be purchased in the second tranche closing to 8,467,434 shares for an aggregate purchase price of $11,516. The Company determined that the future tranche obligations of the Series F preferred stock purchase agreement, as amended, do not meet the definition of a freestanding financial instrument because, while separately exercisable, they were not legally detachable. Further, the Company determined that the embedded future tranche obligations did not require bifurcation for accounting purposes as they are clearly and closely related to the economic characteristics and risks of the initial preferred shares and would not qualify as a derivative on a standalone basis.

Pursuant to the terms of the amended Series F preferred stock purchase agreement, if the second tranche closing has not occurred 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 will 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 may be waived in whole or in part by the Company's board of directors. As of December 31, 2016 and May 26, 2017, the specified clinical milestones had not been achieved and the second tranche closing had not occurred.

In December 2016, pursuant to the Series F preferred stock purchase agreement, holders of 8,927,582 shares of Series E redeemable convertible preferred stock (the "Series E preferred stock") that participated in the Series F preferred stock financing elected to convert their shares of Series E preferred stock into 8,927,582 shares of Series E-2 preferred stock, and holders of 16,567,108 shares of Series E-1 preferred stock that participated in the Series F preferred stock financing elected to convert their shares of Series E-1 preferred stock into 16,567,108 shares of Series E-3 redeemable convertible preferred stock (the "Series E-3 preferred stock"). Holders of Series E preferred stock and Series E-1 preferred stock that did not participate in the Series F preferred stock financing were not entitled to convert their shares into Series E-2 preferred stock and Series E-3 preferred stock, respectively. In February 2017, 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 December 2016 and February 2017 represented modifications of these securities for accounting purposes; however, the

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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.

As of each balance sheet date, Redeemable Preferred Stock consisted of the following:

	December 31, 2015				
	Preferred Shares Authorized	Preferred Shares Issued and Outstanding	Carrying Value	Liquidation Preference	Common Stock Issuable Upon Conversion
Series A preferred stock	1,250,000	1,250,000	$ 1,250	$ 1,250	125,000
Series A-1 preferred stock	615,384	615,384	800	800	61,538
Series B preferred stock	3,706,056	3,706,056	1,506	1,506	3,706,056
Series C-1 preferred stock	5,934,050	5,934,050	6,995	7,000	5,934,050
Series C-2 preferred stock	8,689,144	8,689,144	10,246	10,250	8,689,144
Series D preferred stock	34,142,865	34,142,865	40,256	40,276	34,142,865
Series D-1 preferred stock	363,636	363,636	2,000	2,000	363,636
Series E preferred stock	12,715,822	12,715,822	14,918	15,000	12,715,822
Series E-1 preferred stock	24,264,705	14,558,823	19,710	19,800	14,558,823
	91,681,662	81,975,780	$97,681	$ 97,882	80,296,934

	December 31, 2016				
	Preferred Shares Authorized	Preferred Shares Issued and Outstanding	Carrying Value	Liquidation Preference	Common Stock Issuable Upon Conversion
Series A preferred stock	1,250,000	1,250,000	$ 1,250	$ 1,250	125,000
Series A-1 preferred stock	615,384	615,384	800	800	61,538
Series B preferred stock	3,706,056	3,706,056	1,506	1,506	3,706,056
Series C-1 preferred stock	5,934,050	5,934,050	6,997	7,000	5,934,050
Series C-2 preferred stock	8,689,144	8,689,144	10,248	10,250	8,689,144
Series D preferred stock	34,142,865	34,142,865	40,263	40,276	34,142,865
Series D-1 preferred stock	363,636	363,636	2,000	2,000	363,636
Series E preferred stock	12,715,822	3,788,240	4,453	4,469	3,788,240
Series E-1 preferred stock	24,264,705	7,697,597	10,446	10,469	7,697,597
Series E-2 preferred stock	9,226,082	8,927,582	10,493	10,531	8,927,582
Series E-3 preferred stock	21,237,785	16,567,108	22,483	22,531	16,567,108
Series F preferred stock	29,411,764	13,949,357	18,806	18,971	13,949,357
	151,557,293	105,631,019	$ 129,745	$ 130,053	103,952,173

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	March 31, 2017 (unaudited)				
	Preferred Shares Authorized	Preferred Shares Issued and Outstanding	Carrying Value	Liquidation Preference	Common Stock Issuable Upon Conversion
Series A preferred stock	1,250,000	1,250,000	$ 1,250	$ 1,250	125,000
Series A-1 preferred stock	615,384	615,384	800	800	61,538
Series B preferred stock	3,706,056	3,706,056	1,506	1,506	3,706,056
Series C-1 preferred stock	5,934,050	5,934,050	6,997	7,000	5,934,050
Series C-2 preferred stock	8,689,144	8,689,144	10,248	10,250	8,689,144
Series D preferred stock	34,142,865	34,142,865	40,263	40,276	34,142,865
Series D-1 preferred stock	363,636	363,636	2,000	2,000	363,636
Series E preferred stock	12,715,822	3,788,240	4,454	4,469	3,788,240
Series E-1 preferred stock	24,264,705	3,285,832	4,460	4,469	3,285,832
Series E-2 preferred stock	9,226,082	8,927,582	10,496	10,531	8,927,582
Series E-3 preferred stock	21,237,785	20,978,873	28,474	28,531	20,978,873
Series F preferred stock	29,411,764	14,432,858	19,443	19,629	14,432,858
	151,557,293	106,114,520	$ 130,391	$ 130,711	104,435,674

The holders of the Redeemable Preferred Stock have the following rights and preferences:

Voting Rights

The holders of the Redeemable Preferred Stock are entitled to vote, together with the holders of common stock, on all matters submitted to stockholders for a vote and have the right to vote the number of shares equal to the number of whole shares of common stock into which such holders of Redeemable Preferred Stock could convert on the record date for determination of stockholders entitled to vote. In addition, holders of the Senior Preferred Stock, voting as a single class, are entitled to elect three directors of the Company. The holders of the Junior Preferred Stock, voting as a single class, are entitled to elect two directors of the Company.

Dividends

The holders of the Redeemable Preferred Stock, in order of preference, are entitled to receive noncumulative dividends when and if declared by the Company's board of directors. The Company may not declare, pay or set aside any dividends on shares of any other class or series of capital stock of the Company unless the holders of the Redeemable Preferred Stock then outstanding shall first receive, or simultaneously receive, a dividend on each outstanding share of Redeemable Preferred Stock in an amount at least equal to the greater of (i) $0.08 per share for Series A redeemable convertible preferred stock ("Series A preferred stock"), $0.104 per share for Series A-1 redeemable convertible preferred stock ("Series A-1 preferred stock"), $0.03251 per share for Series B redeemable convertible preferred stock ("Series B preferred stock"), $0.09437 per share for Series C-1 redeemable convertible preferred stock ("Series C-1 preferred stock"), $0.09437 per share for Series C-2 redeemable convertible preferred stock ("Series C-2 preferred stock"), $0.09437 per share for Series D redeemable convertible preferred stock ("Series D preferred stock"), Series E preferred stock and Series E-2 preferred stock, $0.40 per share for Series D-1 redeemable convertible preferred stock ("Series D-1 preferred stock"), and $0.1088 per share for Series E-1 preferred stock, Series E-3 preferred stock and Series F preferred stock and (ii) (A) in the case of a dividend on common stock or any class or series of

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stock that is convertible into common stock, that dividend per share of Redeemable Preferred Stock as would equal the product of (1) the dividend payable on each share of such class or series determined, if applicable, as if all shares of such class or series had been converted into common stock and (2) the number of shares of common stock issuable upon conversion of each share of Redeemable Preferred Stock, or (B) in the case of a dividend on any class or series that is not convertible into common stock, at a rate per share of Redeemable Preferred Stock determined by (1) dividing the amount of the dividend payable on each share of such class or series of capital stock by the Original Issue Price (as defined below) of such class or series of capital stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination of or other similar recapitalization affecting such shares) and (2) multiplying such fraction by an amount equal to the Original Issue Price of each series of Redeemable Preferred Stock. If the Company declares, pays or sets aside, on the same date, a dividend on shares of more than one class or series of capital stock of the Company, the dividend payable to the holders of the Redeemable Preferred Stock shall be calculated based upon the dividend on the class or series of capital stock that would result in the highest Redeemable Preferred Stock dividend. Stockholders are not entitled to any accruing dividends. No dividends have been declared or paid during the years ended December 31, 2015 or 2016 or the three months ended March 31, 2016 or 2017 (unaudited).

The Original Issue Price per share is $1.00 for Series A, $1.30 for Series A-1, $0.4064 for Series B, $1.179633 for Series C-1, $1.179633 for Series C-2, $1.179633 for Series D, $5.50 for Series D-1, $1.179633 for Series E, $1.36 for Series E-1, $1.179633 for Series E-2, $1.36 for Series E-3 and $1.36 for Series F preferred stock, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Redeemable Preferred Stock.

Liquidation Preference

In the event of any liquidation event, voluntary or involuntary, dissolution or winding up of the Company or Deemed Liquidation Event (as defined below), the holders of the then outstanding Series F preferred stock will be entitled to receive, prior and in preference to any distributions to the holders of the common stock and other preferred stock, $1.36 per share, plus any dividends declared but unpaid on the Series F preferred stock.

After the payment of all preferential amounts to the holders of Series F preferred stock, then, to the extent available, the holders of the Series E-2 and Series E-3 preferred stock will be paid $1.179633 per share and $1.36 per share, respectively, plus any dividends declared but unpaid on the Series E-2 and Series E-3 preferred stock, prior and in preference to any distributions to the holders of common stock, Series E, Series E-1, Series D and Series D-1 preferred stock, and Junior Preferred Stock.

After the payment of all preferential amounts to the holders of Series E-2 and Series E-3 preferred stock, then, to the extent available, the holders of the Series E preferred stock and the Series E-1 preferred stock will be entitled to receive, prior and in preference to any distributions to the holders of the common stock and other preferred stock, $1.179633 per share and $1.36 per share, respectively, plus any dividends declared but unpaid on the Series E and Series E-1 preferred stock, prior and in preference to any distributions to the holders of common stock, Series D and Series D-1 preferred stock, and Junior Preferred Stock.

After the payment of all preferential amounts to the holders of Series E and Series E-1 preferred stock, then, to the extent available, the holders of the Series D and Series D-1 preferred stock will be paid $1.179633 per share and $5.50 per share, respectively, plus any dividends declared but unpaid on the Series D and Series D-1 preferred stock, prior and in preference to any distributions to the holders of common stock and Junior Preferred Stock.

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After the payment of all preferential amounts to the holders of the Senior Preferred Stock, then, to the extent available, the holders of Series C-1 and Series C-2 preferred stock will be paid $1.179633 per share plus any dividends declared but unpaid on the Series C-1 and Series C-2 preferred stock, prior and in preference to any distributions to the holders of common stock and Series A, Series A-1 or Series B preferred stock.

After the payment of all preferential amounts to the holders of the Senior Preferred Stock and the Series C-1 and Series C-2 preferred stock, then, to the extent available, the holders of Series B preferred stock will be paid $0.4064 per share plus any dividends declared but unpaid on the Series B preferred stock, prior and in preference to any distributions to the holders of common stock and Series A or Series A-1 preferred stock.

After the payment of all preferential amounts to the holders of the Senior Preferred Stock, Series C-1, Series C-2 and Series B preferred stock, then, to the extent available, the holders of Series A and Series A-1 preferred stock will be paid $1.00 and $1.30 per share, respectively, plus any dividends declared but unpaid on the Series A and A-1 preferred stock prior and in preference to any distributions to the holders of common stock.

After payments have been made in full to the holders of the Redeemable Preferred Stock, then, to the extent available, the remaining amounts will be distributed among the holders of the shares of preferred stock and common stock, pro rata based on the number of shares held by each holder, treating for this purpose all such securities as if they had been converted to common stock immediately prior to such dissolution, liquidation or winding up of the Company.

Unless 55% of the holders of the Senior Preferred Stock, voting together as a single class, elect otherwise, a Deemed Liquidation Event shall include a merger or consolidation (other than one in which stockholders of the Company own a majority by voting power of the outstanding shares of the surviving or acquiring corporation) or a sale, lease, transfer, exclusive license, or other disposition of substantially all of the assets of the Company.

Conversion

Each share of Redeemable Preferred Stock is convertible, at the option of the holder, at any time, and without the payment of additional consideration, or will automatically be converted into shares of common stock at the applicable conversion ratio then in effect (i) upon the closing of a firm commitment underwritten public offering at a price per share to the public, which when multiplied by the total number of shares of common stock then outstanding or then issuable upon conversion of outstanding Redeemable Preferred Stock immediately prior to the consummation of the offering, exceeds $150,000 and with at least $50,000 of gross proceeds to the Company or (ii) upon the vote or written consent of the holders of at least 55% of the outstanding shares of the Senior Preferred Stock, voting together as a single class. All shares that are required to be surrendered per the provisions above will be deemed to have been retired and canceled and may not be reissued as shares of preferred stock.

The conversion ratio of each series of Redeemable Preferred Stock is determined by dividing the Original Issue Price of each series of preferred stock by the Conversion Price of each series. The Conversion Price is $10.00 for Series A, $13.00 for Series A-1, $0.4064 for Series B, $1.179633 for Series C-1, Series C-2, Series D, Series D-1, Series E and Series E-2, and $1.36 for Series E-1, Series E-3 and Series F. The Conversion Price is subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization and other adjustments as set forth in the Company’s certificate of incorporation, as amended and restated.

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Redemption Rights

At the written election of at least 55% of the holders of the Senior Preferred Stock, voting together as a single class, the shares of Redeemable Preferred Stock outstanding are redeemable, at any time on or after December 22, 2020, in three equal annual installments commencing 60 days after receipt of the required vote, in an amount equal to the Original Issue Price per share of each series of Redeemable Preferred Stock plus all declared but unpaid dividends thereon.

8. Common Stock

As of December 31, 2016 and March 31, 2017 (unaudited), the Company's certificate of incorporation, as amended and restated, authorized the Company to issue 143,500,000 shares of $0.001 par value common stock.

Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders. Common stockholders are entitled to receive dividends, as may be declared by the Company's board of directors, if any, subject to the preferential dividend rights of the Redeemable Preferred Stock. When dividends are declared on shares of common stock, the Company must declare at the same time a dividend payable to the holders of Redeemable Preferred Stock equivalent to the dividend amount they would receive if each preferred share were converted into common stock. The Company may not pay dividends to common stockholders until all dividends accrued or declared but unpaid on the Redeemable Preferred Stock have been paid in full. As of December 31, 2016 and March 31, 2017 (unaudited), no dividends had been declared.

As of December 31, 2016 and March 31, 2017 (unaudited), the Company had reserved 121,293,416 shares and 121,627,833 shares, respectively, for the conversion of outstanding shares of Redeemable Preferred Stock (see Note 7), the exercise of outstanding stock options and the number of shares remaining available for future grant under the Company's 2016 Stock Incentive Plan (see Note 9).

9. Stock-Based Awards

2016 Stock Incentive Plan

The Company's 2016 Stock Incentive Plan (the "2016 Plan") provides 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 is 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 are 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 generally vest over four years and expire after 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 2016 Plan was 17,341,243 shares and 17,192,159 shares as of December 31, 2016 and March 31, 2017 (unaudited), respectively, of which 8,191,754 shares and 3,806,754 shares remained available for future issuance as of December 31, 2016 and March 31, 2017 (unaudited), respectively.

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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.

Generally, the exercise price for stock options granted is not less than the fair value of common shares as determined by the board of directors as of the date of grant. The Company's board of directors values the Company's common stock, taking into consideration its most recently available valuation of common stock performed by third parties as well as additional factors which may have changed since the date of the most recent contemporaneous valuation through the date of grant.

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 2016 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 2016 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 were as follows, presented on a weighted average basis:

	Year Ended December 31,		Three Months Ended March 31, 2017
	2015	2016	(unaudited)
Risk-free interest rate	2.01%	1.37%	2.31%
Expected term (in years)	6.1	6.1	6.0
Expected volatility	80.5%	80.5%	79.8%
Expected dividend yield	0%	0%	0%

The Company did not grant any stock options to employees and directors during the three months ended March 31, 2016 (unaudited).

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Stock Options

The following table summarizes the Company's stock option activity since January 1, 2015:

	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value
Outstanding at December 31, 2014	6,454,356	$ 0.32	5.2	$ 1,048
Granted	6,565,264	0.53		
Exercised	(396,167)	0.13		
Forfeited	(2,946,805)	0.42		
Outstanding at December 31, 2015	9,676,648	$ 0.44	6.2	$ 4,333
Granted	293,000	0.47		
Exercised	(61,745)	0.38		
Forfeited	(758,414)	0.51		
Outstanding at December 31, 2016	9,149,489	$ 0.44	6.4	$ 1,297
Granted	4,385,000	0.58		
Exercised	(149,084)	0.50		
Forfeited	—	—		
Outstanding at March 31, 2017 (unaudited)	13,385,405	$ 0.48	7.4	$ 2,223
Options exercisable at December 31, 2016	5,822,677	$ 0.38	5.2	$ 1,136
Options vested and expected to vest at December 31, 2016	8,983,149	$ 0.44	6.3	$ 1,289
Options exercisable at March 31, 2017 (unaudited)	5,690,938	$ 0.38	5.7	$ 1,517
Options vested and expected to vest at March 31, 2017 (unaudited)	12,610,782	$ 0.48	7.6	$ 2,134

The weighted average grant-date fair value of stock options granted during the years ended December 31, 2015 and 2016 and the three months ended March 31, 2017 (unaudited) was $0.37, $0.33 and $0.45 per share, respectively.

The aggregate fair value of stock options that vested during the years ended December 31, 2015 and 2016 was $442 and $784, respectively, and during the three months ended March 31, 2016 and 2017 (unaudited) was $308 and $158, 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 years ended December 31, 2015 and 2016 was $300 and $12, respectively, and during the three months ended March 31, 2016 and 2017 (unaudited) was $0 and $22, respectively.

During the years ended December 31, 2015 and 2016 and the three months ended March 31, 2016 and 2017 (unaudited), the Company did not grant any stock options with performance-based vesting conditions.

During the years ended December 31, 2015 and 2016 and the three months ended March 31, 2016 (unaudited), the Company did not grant any stock options to non-employees in exchange for consulting services.

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During the three months ended March 31, 2017 (unaudited), the Company granted options to purchase 200,000 shares of common stock, at an exercise price of $0.58 per share, to non-employees in exchange for consulting services. As of December 31, 2015 and 2016, there were no outstanding unvested service-based stock options held by non-employees. As of March 31, 2017 (unaudited), there were outstanding unvested service-based stock options held by non-employees for the purchase of 200,000 shares of common stock.

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,		Three Months Ended March 31,	
	2015	2016	2016	2017
			(unaudited)	
Research and development expenses	$275	$219	$ 51	$ 75
General and administrative expenses	351	469	112	122
	$626	$688	$163	$197

As of December 31, 2016, the Company had an aggregate of $1,160 of unrecognized stock-based compensation expense, which is expected to be recognized over a weighted average period of 2.2 years. As of March 31, 2017 (unaudited), the Company had an aggregate of $2,922 of unrecognized stock-based compensation expense, which is expected to be recognized over a weighted average period of 3.3 years.

10. Net Loss per Share

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

	Year Ended December 31,		Three Months Ended March 31,	
	2015	2016	2016	2017
			(unaudited)	
Numerator:				
Net loss	$ (12,878)	$ (18,123)	$ (3,925)	$ (4,557)
Accretion of redeemable convertible preferred stock to redemption value	(71)	(75)	(18)	(20)
Net loss attributable to common stockholders	$ (12,949)	$ (18,198)	$ (3,943)	$ (4,577)
Denominator:				
Weighted average common shares outstanding—basic and diluted	3,981,886	4,270,092	4,238,305	4,300,331
Net loss per share attributable to common stockholders—basic and diluted	$ (3.25)	$ (4.26)	$ (0.93)	$ (1.06)

The Company's potential dilutive securities, which include stock options and redeemable convertible preferred stock, have been excluded from the computation of diluted net loss per share attributable to common

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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 common shares outstanding used to calculate both basic and diluted net loss per share attributable to common stockholders is the same. The following potential common shares, 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,		Three Months Ended March 31,	
	2015	2016	2016	2017
			(unaudited)	
Stock options to purchase common stock	9,676,648	9,149,489	9,671,648	13,385,405
Redeemable convertible preferred stock (as converted to common stock)	80,296,934	103,952,173	90,002,816	104,435,674
	89,973,582	113,101,662	99,674,464	117,821,079

11. Unaudited Pro Forma Net Loss per Share

The unaudited pro forma basic and diluted net loss per share attributable to common stockholders for the year ended December 31, 2016 and the three months ended March 31, 2017 gives effect to adjustments arising upon the closing of a qualified initial public offering. The unaudited pro forma net loss attributable to common stockholders used in the calculation of unaudited basic and diluted pro forma net loss per share attributable to common stockholders does not include the effects of the accretion of redeemable convertible preferred stock to redemption value because the calculation assumes that the conversion of the redeemable convertible preferred stock into common stock had occurred on the later of January 1, 2016 or the issuance date of the redeemable convertible preferred stock.

The unaudited pro forma basic and diluted weighted average common shares outstanding used in the calculation of unaudited pro forma basic and diluted net loss per share attributable to common stockholders for the year ended December 31, 2016 and the three months ended March 31, 2017 give effect to the automatic conversion upon a qualified initial public offering of all outstanding shares of redeemable convertible preferred stock as of March 31, 2017 into shares of common stock as if the conversion had occurred on the later of January 1, 2016 or the issuance date of the redeemable convertible preferred stock.

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Unaudited pro forma basic and diluted net loss per share attributable to common stockholders was calculated as follows:

	Year Ended December 31, 2016	Three Months Ended March 31, 2017
		(unaudited)
Numerator:		
Net loss attributable to common stockholders	$ (18,198)	$ (4,577)
Accretion of redeemable convertible preferred stock to redemption value	75	20
Pro forma net loss attributable to common stockholders	$ (18,123)	$ (4,557)
Denominator:		
Weighted average number of common shares outstanding	4,270,092	4,300,331
Pro forma adjustment for assumed conversion of redeemable convertible preferred stock to common stock upon the closing of the proposed initial public offering	90,122,416	104,156,418
Pro forma weighted average common shares outstanding—basic and diluted	94,392,508	108,456,749
Pro forma net loss attributable to common stockholders—basic and diluted	$ (0.19)	$ (0.04)

12. Commitments and Contingencies

Operating Leases

In February 2010, the Company entered into an operating lease agreement for office and laboratory space, which, as amended, expires in May 2018. Upon entering into the agreement, the Company was required to maintain a security deposit of $776, which was recorded as restricted cash in the Company's balance sheet. In connection with an amendment to the operating lease agreement in January 2015, the required security deposit was reduced from $776 to $63, and $713 of restricted cash was released to the Company.

In connection with an amendment to the operating lease agreement in June 2011, the landlord agreed to fund up to $752 in improvements to the leased facility, which was recorded as a liability and is being recognized as a reduction of rent expense over the remaining lease term.

As of December 31, 2016, future minimum lease payments due under the operating lease were $525 and $202 during the years ending December 31, 2017 and 2018, respectively.

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 $258 and $432 for the years ended December 31, 2015 and 2016, respectively, and $106 and $119 for the three months ended March 31, 2016 and 2017 (unaudited), respectively.

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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 stapled 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 annual license fees of $145 during the years ended December 31, 2015 and 2016 and the three months ended March 31, 2016 and 2017 (unaudited). In addition, the Company paid aggregate milestone payments of $150 during the year ended December 31, 2016 related to a specified milestone achieved in the Phase 2 clinical trial for one of its product candidates. As of December 31, 2016 and March 31, 2017 (unaudited), no additional milestones had been achieved and no liabilities for additional milestone payments had been recorded in the Company's financial statements. Through December 31, 2016 and March 31, 2017 (unaudited), the Company had made non-refundable cash payments, consisting of license and maintenance fees, milestone payments and sublicense fees, totaling $4,283 and $4,428, respectively.

As of December 31, 2016 and March 31, 2017 (unaudited), 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.

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Materia Agreement

In December 2006, the Company entered into a license agreement (the "Materia 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.

Under the Materia agreement, the Company is obligated to make aggregate milestone payments to Materia 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 Materia agreement requires the Company to pay annual license fees of $50. The Company incurred annual license fees of $50 and $50 during the years ended December 31, 2015 and 2016, respectively. The Company did not incur annual license fees during the three months ended March 31, 2016 or 2017 (unaudited). In addition, the Company paid Materia a milestone payment of $100 during the year ended December 31, 2016 related to the achievement of a specified regulatory milestone for one of its product candidates. As of December 31, 2016 and March 31, 2017 (unaudited), no additional milestones had been achieved and no liabilities for additional milestone payments had been 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 annual license fees of $50 and $50 during the years ended December 31, 2015 and 2016, respectively. The Company did not incur annual license fees during the three months ended March 31, 2016 or 2017 (unaudited).

As of December 31, 2015 and 2016 and March 31, 2017 (unaudited), no milestones had been achieved and no liabilities for milestone payments had been recorded in the Company's financial statements. As of December 31, 2016 and March 31, 2017 (unaudited), 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.

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Stanford Agreement

In May 2003, the Company entered into an exclusive license agreement with the Board of Trustees of the Leland Stanford Junior University ("Stanford"), which was amended and restated with non-exclusive terms in March 2006 (the "Stanford agreement"). The Stanford agreement granted the Company a non-exclusive license under specified patents, which gave the Company the rights to make and market licensed products for public use.

Under the agreement, the Company is obligated to make aggregate milestone payments to Stanford of up to $425 per licensed product upon achieving specified milestones. In addition, the Company is obligated to pay low single-digit royalties on net sales of each product developed under the agreement as well as a $25 non-refundable annual license maintenance fee. All such milestone payments, royalties and annual license maintenance fees payable may be reduced by a credit of $473 provided by Stanford.

As of December 31, 2015 and 2016 and March 31, 2017 (unaudited), no milestones had been achieved and no liabilities for milestone payments had been recorded in the Company's financial statements. As of December 31, 2016 and March 31, 2017 (unaudited), 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 written notice provided by either party to terminate 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 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, 2015 or 2016 or March 31, 2017 (unaudited).

13. Income Taxes

During the years ended December 31, 2015 and 2016 and the three months ended March 31, 2016 and 2017 (unaudited), the Company recorded no income tax provision due to the losses incurred, including recording no deferred income tax assets for the operating losses incurred in each period, due to its uncertainty of realizing a benefit from those items.

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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,	
	2015	2016
Federal statutory income tax rate	(34.0)%	(34.0)%
State taxes, net of federal benefit	(4.8)	(4.2)
Research and development tax credits	(1.7)	(1.4)
Write-off of deferred offering costs	—	3.1
Other permanent items	1.6	1.3
Change in deferred tax asset valuation allowance	38.9	35.2
Effective income tax rate	— %	— %

Net deferred tax assets as of December 31, 2015 and 2016 consisted of the following:

	December 31,	
	2015	2016
Deferred tax assets:		
Net operating loss carryforwards	$ 34,443	$ 41,948
Research and development tax credit carryforwards	2,170	2,392
Capitalized research and development expenses	2,466	755
Accrued expenses and reserves	153	457
Depreciation and amortization	70	124
Total deferred tax assets	39,302	45,676
Valuation allowance	(39,302)	(45,676)
Net deferred tax assets	$ —	$ —

As of December 31, 2016, the Company had net operating loss carryforwards for federal and state purposes of $107,256 and $103,808, respectively, which begin to expire in 2029 and 2030, respectively. As of December 31, 2016, the Company also had available research and development tax credit carryforwards for federal and state income tax purposes of $1,629 and $1,155, respectively, which begin to expire in 2025 and 2024, respectively. During the three months ended March 31, 2017 (unaudited), gross deferred tax assets increased by approximately $1,700 due to the operating loss incurred by the Company during that period. 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

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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, 2015 and 2016 and March 31, 2017 (unaudited). Management reevaluates the positive and negative evidence at each reporting period.

The increase in the valuation allowance for deferred tax assets during the years ended December 31, 2015 and 2016 related primarily to an increase in net operating loss carryforwards, partially offset by the reversal of temporary differences for capitalized research and development expenses. Changes in the valuation allowance were as follows:

	Year Ended December 31,	
	2015	2016
Valuation allowance at beginning of year	$(34,293)	$(39,302)
Increases recorded to income tax provision	(5,009)	(6,374)
Decreases recorded as a benefit to income tax provision	—	—
Valuation allowance at end of year	$(39,302)	$(45,676)

The Company has not recorded any amounts for unrecognized tax benefits as of December 31, 2015 and 2016 or March 31, 2017 (unaudited).

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 2013 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, 2015 and 2016, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Company's statements of operations and comprehensive loss.

14. 401(k) Plan

The Company has a 401(k) plan available for participating employees who meet certain eligibility requirements. Eligible employees may defer a portion of their salary as defined by the plan. Company contributions to the plan may be made at the discretion of the Company's board of directors. The Company has not elected to make any employer contributions for the years ended December 31, 2015 and 2016 and the three months ended March 31, 2016 and 2017 (unaudited).

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15. Subsequent Events

For its financial statements as of December 31, 2016 and for the year then ended, the Company evaluated subsequent events through April 14, 2017, the date on which those financial statements were available to be issued.

Sale of Series F Preferred Stock

In February 2017, the Company amended the Series F preferred stock purchase agreement to permit the sale of up to 758,458 additional shares of Series F preferred stock under the agreement. In February 2017, pursuant to the amended Series F preferred stock purchase agreement, the Company issued 483,501 shares of Series F preferred stock at a price of $1.36 per share (see Note 7), resulting in gross proceeds of $658. The purchasers of Series F preferred stock in this February 2017 closing also agreed to purchase an additional 274,957 shares of Series F preferred stock at a price of $1.36 per share in the second tranche closing, which increased the aggregate number of shares of Series F preferred stock to be purchased in the second tranche closing to 8,467,434 shares for an aggregate purchase price of $11,516 (see Note 7). In February 2017, 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 this 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.

16. Subsequent Events (unaudited)

For its interim financial statements as of March 31, 2017 and for the three months then ended, the Company evaluated subsequent events through May 26, 2017, the date on which those financial statements were issued.

Through and including , 2017, (the 25th day after the date of this prospectus), all dealers effecting transactions in the common stock, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to a dealer's obligation to deliver a prospectus when acting as an underwriter and with respect to an unsold allotment or subscription.

Shares

Common Stock

PROSPECTUS

BofA Merrill Lynch

Jefferies

William Blair

Canaccord Genuity

, 2017

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 13. Other Expenses of Issuance and Distribution.

The following table sets forth the expenses to be incurred in connection with the offering described in this Registration Statement, other than underwriting discounts and commissions, all of which will be paid by us. All amounts are estimates except the Securities and Exchange Commission's registration fee, the Financial Industry Regulatory Authority, Inc. filing fee and the NASDAQ listing fee.

	Amount
Securities and Exchange Commission registration fee	$ *
Financial Industry Regulatory Authority, Inc. filing fee	*
NASDAQ listing fee	*
Accountants' fees and expenses	*
Legal fees and expenses	*
Transfer Agent's fees and expenses	*
Printing and engraving expenses	*
Miscellaneous fees and expenses	*
Total expenses	$ *

* To be filed by amendment.

Item 14. Indemnification of Directors and Officers.

Section 102 of the General Corporation Law of the State of Delaware permits a corporation to eliminate the personal liability of its directors for monetary damages for a breach of fiduciary duty as a director, except where the director breached his or her duty of loyalty, failed to act in good faith, engaged in intentional misconduct or knowingly violated a law, authorized the payment of a dividend or approved a stock repurchase in violation of Delaware corporate law or obtained an improper personal benefit. Upon completion of this offering, our certificate of incorporation will provide that none of our directors shall be personally liable to us or our stockholders for monetary damages for any breach of fiduciary duty as a director, notwithstanding any provision of law imposing such liability, except to the extent that the General Corporation Law of the State of Delaware prohibits the elimination or limitation of liability of directors for breaches of fiduciary duty.

Section 145 of the General Corporation Law of the State of Delaware provides that a corporation has the power to indemnify a director, officer, employee, or agent of the corporation and certain other persons serving at the request of the corporation in related capacities against expenses (including attorneys' fees), judgments, fines and amounts paid in settlements actually and reasonably incurred by the person in connection with an action, suit or proceeding to which he or she is or is threatened to be made a party by reason of such position, if such person acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the corporation, and, in any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful, except that, in the case of actions brought by or in the right of the corporation, no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or other adjudicating court determines that, despite the adjudication of liability but in view of all of the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which the Court of Chancery or such other court shall deem proper.

Upon the completion of this offering, our certificate of incorporation will provide that we will indemnify each person who was or is a party or is threatened to be made a party or is involved in any threatened,

pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of us) by reason of the fact that he or she is or was, or has agreed to become, our director or officer, or is or was serving, or has agreed to serve, at our request as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (all such persons being referred to as an "Indemnitee"), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding and any appeal therefrom, if such Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, our best interests, and, with respect to any criminal action or proceeding, he or she had no reasonable cause to believe his or her conduct was unlawful. Our certificate of incorporation that will be effective as of the closing date of this offering also provides that we will indemnify any Indemnitee who was or is a party to an action or suit by or in the right of us to procure a judgment in our favor by reason of the fact that the Indemnitee is or was, or has agreed to become, our director or officer, or is or was serving, or has agreed to serve, at our request as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise, or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees) and, to the extent permitted by law, amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding, and any appeal therefrom, if the Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, our best interests, except that no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to us, unless a court determines that, despite such adjudication but in view of all of the circumstances, he or she is entitled to indemnification of such expenses. Notwithstanding the foregoing, to the extent that any Indemnitee has been successful, on the merits or otherwise, he or she will be indemnified by us against all expenses (including attorneys' fees) actually and reasonably incurred by him or her or on his or her behalf in connection therewith. If we do not assume the defense, expenses must be advanced to an Indemnitee under certain circumstances.

We plan to enter into indemnification agreements with each of our executive officers and directors. In general, these agreements provide that we will indemnify the director or executive officer to the fullest extent permitted by law for claims arising in his or her capacity as a director or executive officer of our company or in connection with their service at our request for another corporation or entity. The indemnification agreements also provide for procedures that will apply in the event that a director or executive officer makes a claim for indemnification and establish certain presumptions that are favorable to the director or executive officer.

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

The underwriting agreement we will enter into in connection with the offering of common stock being registered hereby provides that the underwriters will indemnify, under certain conditions, our directors and officers (as well as certain other persons) against certain liabilities arising in connection with such offering.

Insofar as the forgoing provisions permit indemnification of directors, executive officers, or persons controlling us for liability arising under the Securities Act of 1933, as amended, or the Securities Act, we have been informed that, in the opinion of the Securities and Exchange Commission, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

Item 15. Recent Sales of Unregistered Securities.

Set forth below is information regarding shares of our common stock and shares of our preferred stock issued, and stock options granted, by us within the past three years that were not registered under the Securities Act. Included is the consideration, if any, we received for such shares and options and information relating to the section of the Securities Act, or rule of the Securities and Exchange Commission, under which exemption from registration was claimed.

(a) Issuance of Shares of Preferred Stock.

In October 2014, we issued and sold an aggregate of 14,558,823 shares of our Series E-1 preferred stock at a purchase price per share of $1.36 for an aggregate purchase price of approximately $19,800,000. In January 2016, we issued and sold an aggregate of 9,705,882 shares of our Series E-1 preferred stock at a purchase price of $1.36 for an aggregate purchase price of approximately $13,200,000.

In December 2016, we issued and sold an aggregate of 13,949,357 shares of our Series F preferred stock at a purchase price of $1.36 for an aggregate purchase price of approximately $18,971,000.

In December 2016, we issued an aggregate of 8,927,582 shares of our Series E-2 preferred stock and 16,567,108 shares of our Series E-3 preferred stock in exchange for an aggregate of 8,927,582 shares of our Series E preferred stock and 16,567,108 shares of our Series E-1 preferred stock, respectively.

In February 2017, we issued and sold 483,501 shares of our Series F preferred stock at a purchase price per share of $1.36 per share for an aggregate purchase price of approximately $658,000, and a holder of 4,411,765 shares of our Series E-1 preferred stock exchanged these shares for 4,411,765 shares of our Series E-3 preferred stock.

All outstanding shares of Series F preferred stock will automatically convert into an aggregate of 14,432,858 shares of common stock upon completion of this offering. All outstanding shares of Series E-3 preferred stock will automatically convert into an aggregate of 20,978,873 shares of common stock upon completion of this offering. All outstanding shares of Series E-2 preferred stock will automatically convert into an aggregate of 8,927,582 shares of common stock upon completion of this offering. All outstanding shares of Series E-1 preferred stock will automatically convert into an aggregate of 3,285,832 shares of common stock upon completion of this offering

No underwriters were involved in the foregoing issuances of securities. The securities described in this section (a) of Item 15 were issued to investors in reliance upon the exemption from the registration requirements of the Securities Act, as set forth in Section 4(a)(2) under the Securities Act and Regulation D promulgated thereunder relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required. The recipients of securities in the transactions described above represented that they were accredited investors and were acquiring the securities for their own account for investment purposes only and not with a view to, or for sale in connection with, any distribution thereof and that they could bear the risks of the investment and could hold the securities for an indefinite period of time and appropriate legends were affixed to the instruments representing such securities issued in such transactions.

(b) Stock Option Grants and Option Exercises.

Between May 26, 2014 and May 26, 2017, we granted options to purchase an aggregate of 11,273,264 shares of common stock, with exercise prices ranging from $0.47 to $0.58 per share, to employees, directors, consultants and advisors pursuant to our 2006 stock incentive plan, as amended, and our 2016 stock incentive plan. Between May 26, 2014 and May 26, 2017, we issued an aggregate of 665,861 shares of common stock upon the exercise of options for aggregate consideration of $160,771.

No underwriters were involved in the foregoing issuances of securities. The issuances of stock options and the shares of our common stock issued upon the exercise of the options described in this paragraph (b) of Item 15 were issued pursuant to written compensatory plans or arrangements with our employees, directors, consultants and advisors, in reliance on the exemption provided by Rule 701 promulgated under the Securities Act, or pursuant to Section 4(a)(2) under the Securities Act, relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required. All recipients either received adequate information about us or had access, through employment or other relationships, to such information.

All of the securities described in paragraphs (a) and (b) of this Item 15 are deemed restricted securities for purposes of the Securities Act. All of the certificates representing such securities included appropriate legends setting forth that the securities have not been registered and the applicable restrictions on transfer.

Item 16. Exhibits and Financial Statement Schedules.

(a) Exhibits.

The exhibits to the registration statement are listed in the Exhibit Index attached hereto and incorporated by reference herein.

(b) Financial Statement Schedules.

No financial statement schedules are provided because the information called for is not required or is shown either in the financial statements or the related notes.

Item 17. Undertakings.

(a) The undersigned registrant hereby undertakes to provide to the underwriters at the closing specified in the underwriting agreement, certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.

(b) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

(c) The undersigned registrant hereby undertakes that:

(1) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.

(2) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Cambridge, Commonwealth of Massachusetts, on this day of , 2017.

AILERON THERAPEUTICS, INC.

By: _____
Joseph A. Yanchik III
President and Chief Executive Officer

Power of Attorney

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Joseph A. Yanchik III and Kira A. Nelson and each of them, his true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution for him and in his name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this registration statement, and any subsequent registration statements pursuant to Rule 462 of the Securities Act and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that each of said attorney-in-fact or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
_____ Joseph A. Yanchik III	President, Chief Executive Officer and Director (principal executive officer)	, 2017
_____ Kira A. Nelson	Vice President, Finance and Operations (principal financial and principal accounting officer)	, 2017
_____ Scott B. Kapnick	Chairman of the Board of Directors	, 2017
_____ Reinhard J. Ambros, Ph.D.	Director	, 2017
_____ Brian M. Gallagher, Jr., Ph.D.	Director	, 2017
_____ John H. McArthur, Ph.D.	Director	, 2017

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Signature	Title	Date
Armen B. Shanafelt, Ph.D.	Director	, 2017
Caleb Winder	Director	, 2017

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EXHIBIT INDEX

Exhibit Number	Description of Exhibit
1.1*	Form of Underwriting Agreement
3.1†	Tenth Amended and Restated Certificate of Incorporation of the Registrant
3.2†	Bylaws of the Registrant
3.3*	Form of Restated Certificate of Incorporation of the Registrant (to be effective upon the closing of this offering)
3.4*	Form of Amended and Restated Bylaws of the Registrant (to be effective upon the closing of this offering)
4.1*	Specimen stock certificate evidencing the shares of common stock
4.2†	Seventh Amended and Restated Investor Rights Agreement, dated as of December 23, 2016, among the Registrant and the other parties thereto
5.1*	Opinion of Wilmer Cutler Pickering Hale and Dorr LLP
10.1†	2006 Stock Incentive Plan, as amended
10.2†	Form of Incentive Stock Option Agreement under 2006 Stock Incentive Plan
10.3†	Form of Nonstatutory Stock Option Agreement under 2006 Stock Incentive Plan
10.4†	2016 Stock Incentive Plan
10.5†	Form of Incentive Stock Option Agreement under 2016 Stock Incentive Plan
10.6†	Form of Nonstatutory Stock Option Agreement under 2016 Stock Incentive Plan
10.7†	Form of Restricted Stock Agreement under 2016 Stock Incentive Plan
10.8*	2017 Stock Incentive Plan
10.9*	Form of Incentive Stock Option Agreement under 2017 Stock Incentive Plan
10.10*	Form of Nonstatutory Stock Option Agreement under 2017 Stock Incentive Plan
10.11*	2017 Employee Stock Purchase Plan
10.12*	Form of Director and Officer Indemnification Agreement
10.13+†	License Agreement, dated as of December 31, 2006, by and between the Registrant and Materia, Inc.
10.14+†	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.
10.15†	Lease Agreement, dated as of February 12, 2010, as amended on May 24, 2010, June 17, 2011 and August 25, 2014, between the Registrant and Massachusetts Institute of Technology
10.16†	Employment Agreement, dated as of March 1, 2008, between the Registrant and Joseph A. Yanchik III, as amended on December 31, 2008
10.17†	Employment Agreement, dated as of July 23, 2014, between the Registrant and Manuel Aivado
10.18†	Employment Agreement, dated as of December 18, 2014, between the Registrant and Evan Lippman
10.19†	Offer Letter, dated as of March 25, 2015, between the Registrant and Kira A. Nelson
23.1*	Consent of PricewaterhouseCoopers LLP, independent registered public accounting firm
23.2*	Consent of Wilmer Cutler Pickering Hale and Dorr LLP (included in Exhibit 5.1)
24.1	Power of Attorney (included on signature page)

* To be filed by amendment.

† Previously submitted.

\+ Confidential treatment requested as to certain portions, which portions have been omitted and filed separately with the Securities and Exchange Commission.