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As confidentially submitted to the Securities and Exchange Commission on February 4, 2016 as Amendment No. 1 to the Confidential Submission dated November 20, 2015, File No. 377-01218. This draft registration statement has not been publicly filed with the Securities and Exchange Commission and all information herein remains strictly confidential.

Registration No. 333-

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

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

SYROS PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware (State or other jurisdiction of incorporation or organization)	2834 (Primary Standard Industrial Classification Code Number)	45-3772460 (I.R.S. Employer Identification No.)
--------------------------------------------------------------------------------------	----------------------------------------------------------------------------	--------------------------------------------------------------

**620 Memorial Drive, Suite 300
Cambridge, Massachusetts 02139
(617) 744-1340**

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Nancy Simonian, M.D.
President and Chief Executive Officer
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620 Memorial Drive, Suite 300
Cambridge, Massachusetts 02139
(617) 744-1340

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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, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting 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

CALCULATION OF REGISTRATION FEE

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

- (1) In accordance with Rule 457(o) under the Securities Act of 1933, as amended, the number of shares being registered and the proposed maximum offering price per share are not included in this table.
- (2) Estimated solely for purposes of computing the amount of the registration fee pursuant to Rule 457(o) under the Securities Act of 1933, as amended. Includes the offering price of shares that the underwriters have the option to purchase to cover overallocments, if any.

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.

The information in this preliminary 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 preliminary prospectus is not an offer to sell these securities and it is not soliciting offers to buy these securities in any state or other jurisdiction where the offer or sale is not permitted.

PROSPECTUS (Subject to completion) Dated _____, 2016

Shares



Common Stock

This is the initial public offering of our common stock. We are offering _____ shares of our common stock. We have applied to list our common stock on The NASDAQ Global Market under the symbol "SYRS." We expect that the initial public offering price for our common stock will be between \$ _____ and \$ _____ per share.

We are an "emerging growth company" under applicable Securities and Exchange Commission rules and will be eligible for reduced public company disclosure requirements for this prospectus and future filings. See "Summary—Implications of Being an Emerging Growth Company."

Our business and investment in our common stock involve significant risks. These risks are described in the section titled "Risk Factors" beginning on page 12 of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.

	Per Share	Total
Initial public offering price	\$ _____	\$ _____
Underwriting discounts and commissions(1)	\$ _____	\$ _____
Proceeds, before expenses, to Syros Pharmaceuticals, Inc.	\$ _____	\$ _____

(1) We refer you to the section entitled "Underwriting" beginning on page 179 for additional information regarding total underwriting compensation.

The underwriters may also purchase up to an additional _____ shares from us at the initial public offering price, less the underwriting discounts and commissions, within 30 days from the date of this prospectus to cover overallotments.

The underwriters expect to deliver the shares against payment in New York, New York on or about _____, 2016.

Cowen and Company

Piper Jaffray

**JMP Securities
Wedbush PacGrow**

_____, 2016

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You should rely only on the information contained in this prospectus or in any free writing prospectus prepared by us or on our behalf. We have not, and the underwriters have not, authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not, and the underwriters are not, making an offer to sell these securities in any jurisdictions where the offer and sale is not permitted. You should assume that the information appearing in this prospectus is accurate only as of the date on the front cover of this prospectus. Our business, financial condition, results of operations and prospects may have changed since such date. Information contained on our website is not a part of this prospectus. Neither we nor any of the underwriters have 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. You are required to inform yourselves about, and to observe any restrictions relating to, this offering and the distribution of this prospectus outside of the United States.

SUMMARY

This summary highlights, and is qualified in its entirety by, the more detailed information and consolidated 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 consolidated financial statements and the related notes thereto included elsewhere in this prospectus and the "Risk Factors" section of this prospectus, before deciding to invest in our common stock.

Overview

We are a biopharmaceutical company applying a pioneering approach to discover and develop medicines that control the expression of genes, which we refer to as gene control, with the aim of treating cancer and other serious diseases. We have built a proprietary platform that provides a unique lens to systematically and efficiently identify crucial genes that become dysregulated in diseased cells and create medicines that return cells to a non-diseased state. We believe that our platform will allow us to create a pipeline of gene control medicines that will provide a profound and durable benefit for currently underserved patients. By focusing on genomically defined subsets of patients, we believe we can conduct efficient clinical trials with a higher likelihood of success. Using our platform, we have built a pipeline of gene control medicines and intend to submit two investigational new drug applications, or INDs, to the U.S. Food and Drug Administration, or FDA, in 2016. The first IND is for our lead product candidate, SY-1425 (tamibarotene), for which we intend to initiate a Phase 2 clinical trial in mid-2016, initially in a genomically defined subset of patients with acute myelogenous leukemia, or AML, and myelodysplastic syndromes, or MDS. The second IND is for our cyclin-dependent kinase 7, or CDK7, inhibitor program initially for the treatment of acute leukemias, for which we intend to initiate a Phase 1/2 clinical trial in the first half of 2017. Leveraging our platform, we are also generating a pipeline of novel preclinical drug candidates for genomically defined subsets of patients. Our goal is to build a fully integrated biopharmaceutical company based on our leadership position in gene control.

Our Focus—Gene Control Medicines

There are approximately 200 different cell types in a given individual. Despite having identical genomes, each of these cell types has a different function. For example, a skin cell functions differently from a muscle cell despite sharing the exact same DNA. A small number of genes are crucial for determining cell type and function. The coordinated activity, or expression, of these genes is referred to as the gene control program. By understanding gene control programs, we believe we have the ability to uncover the drivers of cell type and function in healthy and diseased cells. To understand the cell's gene control program, we use genomic tools to locate enhancers, which are specialized regions of DNA that are associated with specialized proteins that are involved in the expression of genes. We are focused on super-enhancers, a very small subset of enhancers where large amounts of specialized proteins congregate to control the expression of crucial genes responsible for cell type and function.

In disease, gene control programs are altered. Analysis of super-enhancers within diseased and healthy cells in specific patient segments enables us to systematically and efficiently identify disease-causing alterations in a cell's gene control program and pinpoint targets for therapeutic intervention.

The discovery and development of targeted therapies, in which the right drug is matched to the right patient, has dramatically improved the ability to treat certain cancers and other serious diseases. To date, however, virtually all of these efforts have focused on abnormal proteins resulting from genetic alterations found in regions of the genome that encode for proteins, which represent less than 2% of the entire genome. The identification of viable targets by sequencing the encoded regions of DNA has

been largely exhausted, and inhibiting proteins resulting from genetic alterations can often lead to drug resistance and limited durable clinical benefit, underscoring the need for new approaches.

Researchers have long believed that genomic alterations in non-coding regions of DNA, which account for the other 98% of the genome, play a key role in driving disease. But the scientific community has lacked the tools to study these regions of the genome, making these targets difficult to discover and drug. Gene control programs reside in these non-coding regions of the genome. Based on the work of our scientific founders, we have developed a proprietary platform that allows us to systematically and efficiently identify novel gene control targets, opening up a wide array of potential new drug targets in this largely untapped field of drug discovery and development.

The relatively few gene control medicines available are among the most important targeted therapies today and are widely used for approved indications, including estrogen receptor inhibitors for breast cancer and androgen receptor inhibitors for prostate cancer. In contrast to therapies that target a single abnormal protein, gene control medicines target the underlying coordinated expression of genes that contribute to disease. For this reason, we believe gene control medicines will allow us to influence multiple drivers of disease in a targeted fashion to achieve a profound and durable clinical benefit for patients.

Our Gene Control Platform

Our proprietary gene control platform consists of two fundamental pillars: mapping gene control programs and drugging gene control targets.

Mapping Gene Control Programs

Starting from human tissue samples, we compare diseased cells to normal cells and analyze the cells of different patient subsets within a disease to systematically and efficiently identify optimal points of therapeutic intervention and associated biomarkers for patient selection. We have invested significant resources in our tissue processing, genomics and computational biology capabilities to industrialize the production of maps of gene control programs to reveal the crucial genes in diseased cells. We have amassed one of the largest known datasets of these maps across a wide range of human diseases and cell types and have identified multiple novel disease targets and biomarkers. To date, we have mapped AML, breast cancer, renal cell carcinoma, polycystic kidney disease, spinal muscular atrophy and normal T-cells. We are in the process of mapping several other cancers, including ovarian, pancreatic, hepatocellular carcinoma, colorectal, lung and melanoma, as well as several other diseases including Alzheimer's disease and inflammatory disorders. Our long-term goal is to map all serious diseases where we believe patients who are currently underserved can benefit from gene control medicines.

Drugging Gene Control Targets

The specialized proteins responsible for gene expression include transcription factors, transcriptional kinases and other transcriptional and regulatory proteins. Transcription factors are proteins that bind directly to DNA sequences to control the transcription of genetic information from DNA. Transcription factors perform this function with other transcriptional and regulatory proteins, including transcriptional kinases. Because of the central role they play in gene control programs, these proteins are among the most promising and high-potential gene control targets for therapeutic intervention. These gene control targets have historically been difficult to drug; however, through our significant investments in developing proprietary assays, which are internally developed tests that we use to measure the biochemical and cellular activity of known and novel compounds against gene control targets, and in our capabilities in biochemistry, structural biology and medicinal chemistry, we believe we will be able to overcome challenges that have prevented others from systematically and successfully developing gene control medicines. We are building a pipeline of product candidates to

modulate gene control programs through two distinct approaches: internal efforts to discover novel drugs against these targets, and externally focused efforts to link existing drugs to novel genomically defined patient populations identified through our platform. These externally focused efforts could enable us to identify drugs that we may seek to in-license or acquire or use as a starting point for our own drug discovery programs, to accelerate our development path. By focusing on genomically defined subsets of patients who are most likely to respond, we believe we are positioning ourselves to rapidly achieve clinical proof-of-concept. With positive clinical results, we intend to apply for FDA Breakthrough Therapy designation and Fast Track designation which, if granted, could accelerate our clinical development path.

Our Clinical Programs

We are leveraging our platform to develop a pipeline of gene control product candidates. Our most advanced drug programs are summarized in the table below:

<u>Program</u>	<u>Initial Indications</u>	<u>Planned Milestones</u>	<u>Potential Indications</u>	<u>Syros Commercial Rights</u>
SY-1425 (RARA agonist)	AML and MDS	Submit IND in 1H 2016 Initiate Phase 2 clinical trial in mid-2016 Expected data readout in mid-2017	Breast cancer, acute promyelocytic leukemia (APL)	North America, Europe
CDK7 inhibitor	Acute leukemias	Submit IND in 2H 2016 Initiate Phase 1/2 clinical trial in 1H 2017	Small cell lung cancer, triple negative breast cancer, MYCN-amplified neuroblastoma	Worldwide

SY-1425

SY-1425 (tamibarotene) is an oral, potent and selective agonist, or activator, of the transcription factor RAR a. We leveraged our platform to map gene control programs in primary AML and breast cancer patient tissue samples and discovered that *RARA*, the gene that produces RARa, was associated with a super-enhancer in some patients' tumor but not in others. We are initially advancing SY-1425 into novel genomically defined patient populations in AML and MDS. We chose these initial indications due to high levels of observed efficacy of SY-1425 in our preclinical models, the significant unmet medical need of these patients and the potential for accelerated development. We intend to pursue additional indications, including breast cancer, in the near future. Through our platform, we have identified a biomarker for the *RARA* super-enhancer that we will use for patient selection.

We have exclusive North American and European commercial rights for SY-1425 in all human cancers under our license agreement with TMRC Co., Ltd. Tamibarotene is approved in Japan for the treatment of APL, a form of AML, in which tamibarotene has a well-characterized efficacy and safety profile. We intend to explore SY-1425 for the treatment of APL in North America and Europe.

Our Preclinical Data

We have conducted multiple preclinical studies of SY-1425 in AML and breast cancer. In a mouse model implanted with human AML cells with the *RARA* biomarker, known as a *RARA* biomarker-positive patient-derived xenograft, or PDX, model, SY-1425 was observed to have significant anti-tumor activity and prolonged survival in treated animals relative to untreated animals. In contrast, in a PDX model without the *RARA* biomarker, SY-1425 was not observed to have an effect on tumor control or survival. These data demonstrate a strong link between the *RARA* biomarker and sensitivity to SY-1425, and provide meaningful evidence that patients with the *RARA* biomarker will be promising candidates for treatment with SY-1425.

SY-1425 Clinical Development Plan

We plan to initiate a Phase 2 clinical trial in mid-2016 that will enroll genomically defined patients with the *RARA* biomarker with relapsed or refractory AML or high-risk relapsed or refractory MDS, AML patients who are elderly or unfit for treatment with standard therapies and low-risk transfusion-dependent MDS patients. We believe we will not be required to conduct a Phase 1 clinical trial of SY-1425 given the existing safety and efficacy data for the drug. We plan to select patients for this trial using the *RARA* biomarker. We believe patients whose tumors have this biomarker will be more likely to experience a profound and durable clinical benefit from treatment with SY-1425. We expect to have data from this study in mid-2017, or 12 months after the first patient is enrolled.

CDK7 Inhibitor Program

Our CDK7 inhibitor program is focused on cancers that are dependent on a high and constant expression of certain transcription factors for their growth and survival, a phenomenon known as transcriptional addiction. CDK7 is a transcriptional kinase that is associated with the super-enhancers controlling the expression of the transcription factors driving the cancer's growth and survival.

Inhibiting CDK7 preferentially lowers the expression of disease-driving transcription factors controlled by super-enhancers, resulting in the selective killing of cancer cells over normal cells. Preclinical studies using our CDK7 inhibitors demonstrated that transcriptionally addicted cancers are particularly sensitive to selective inhibition of CDK7, including AML, T-ALL, a form of acute lymphoblastic leukemia, or ALL, *MYCN*-amplified neuroblastoma, small cell lung cancer and triple negative breast cancer.

Our Preclinical Data

In preclinical studies, our selective CDK7 inhibitors were observed to have significant anti-tumor activity and to preferentially kill cancer cells over healthy cells in *in vivo* models of several aggressive and underserved cancers, including AML, ALL, *MYCN*-amplified neuroblastoma, small cell lung cancer and triple negative breast cancer. In addition, our CDK7 inhibitors were observed to have markedly fewer negative effects on healthy cells than pan-CDK inhibitors, which frequently cause blood cell death, or myelosuppression.

In cell-derived xenograft, or CDX, and PDX models of AML, mice treated with our CDK7 inhibitors experienced complete tumor regression, meaning that the percentage of leukemia cells in the blood was less than 1%. In fact, at the end of the 48-day dosing period, all treated mice remained alive and levels of human leukemia cells in the blood remained at less than 1%. In untreated mice, the cancer progressed, reaching levels of human leukemia cells of greater than 50% in blood and greater than 90% in tissues.

CDK7 Clinical Development Plan

We have generated several first-in-class potent and highly selective small molecule inhibitors of CDK7 with *in vivo* efficacy. We expect to select our development candidate and start IND-enabling activities in the first half of 2016. Our goal is to submit an IND in the second half of 2016 and to initiate a Phase 1/2 clinical trial in patients with acute leukemias, including AML and ALL, in the first half of 2017. We believe there is a well-defined path to clinical proof-of-concept in acute leukemias. We then plan to expand into a broader set of cancers using our gene control platform to identify patient subgroups with transcriptionally addicted cancers, such as small cell lung cancer, triple negative breast cancer and *MYCN*-amplified neuroblastoma.

Other Programs

We are using our platform to map gene control programs across additional cancers, inflammatory diseases and other diseases. Using these maps, we are creating a pipeline of novel preclinical drug candidates targeting transcriptional kinases, transcription factors and other transcriptional and regulatory proteins, as well as linking existing drugs to novel genomically defined patient populations.

Our Team

We were founded by leaders in the field of gene control from the Whitehead Institute for Biomedical Research at the Massachusetts Institute of Technology, or Whitehead, and the Dana-Farber Cancer Institute, or Dana-Farber, an affiliate of Harvard Medical School. Our management team consists of drug discovery, development and commercialization experts with experience in translating scientific discoveries into innovative treatments, including Avonex and Tysabri for multiple sclerosis, Velcade for hematological malignancies, Entyvio for ulcerative colitis, and Kalydeco and Orkambi for cystic fibrosis.

Our Financial Position

In January 2016, we announced the closing of a \$40 million preferred stock financing, which we believe will give us sufficient funding to reach a data readout for our SY-1425 program. To date, our investors include Flagship Ventures, ARCH Venture Partners, Fidelity Management and Research Company, Deerfield Management Company, Polaris Partners, WuXi PharmaTech, Redmile Group, Aisling Capital, Alexandria Venture Investments and Casdin Capital.

Our Strategy

Our mission is to transform the lives of patients through the creation of novel gene control medicines by building a fully integrated, leading biopharmaceutical company. To achieve this mission, we are executing on the following strategy:

- **Rapidly and efficiently advance our lead programs through clinical development.** We intend to enrich our trials with patients most likely to respond, which we believe will enable us to rapidly establish clinical proof-of-concept. Subject to encouraging clinical results, we intend to apply for Breakthrough Therapy designation and Fast Track designation.
- **Develop a robust pipeline of gene control product candidates.** We plan to continue to leverage our gene control platform to systematically and efficiently identify optimal therapeutic points of intervention in specific patient populations. We intend to generate a pipeline of gene control product candidates either through our internal drug discovery efforts or by linking existing drugs to novel patient populations.
- **Maintain our leadership position in the field of gene control.** Our long-term goal is to map all serious diseases where we believe currently underserved patients can benefit from gene control

medicines. We intend to use these maps to pinpoint crucial genes for disease and to validate the associated targets for therapeutic intervention.

- **Continue to foster a culture of innovation.** We are committed to pioneering science and leadership in gene control medicines. We will continue to foster an environment that encourages innovation, excellence and productivity and develops our team as leaders in the field of gene control.
- **Execute strategic collaborations to maximize value and extend the potential of our gene control platform across multiple disease areas.** We intend to engage in strategic collaborations for both our programs and our platform. For our programs, we are focused on partnerships that could expand our geographic reach and allow us to expand into additional indications. For our platform, we are seeking target and drug discovery collaborations that allow us to leverage our platform in cancers and other serious diseases beyond those that we can address on our own.

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, expect to incur significant and increasing losses for at least the next several years and may never achieve or maintain profitability.
- We have a limited operating history, no products approved for sale and no history of commercializing pharmaceutical products, which may make it difficult to evaluate the prospects for our future viability.
- We will need substantial additional funding, and if we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.
- Our approach to the discovery and development of product candidates based on our gene control platform is unproven, and we do not know whether or when we will be able to develop any products of commercial value.
- In the near term, we are dependent on the successful development and commercialization of our lead product candidate, SY-1425, and our CDK7 inhibitor program.
- Our gene control platform may fail to help us discover and develop additional potential product candidates.
- Clinical drug development involves a lengthy and expensive process and has an uncertain outcome.
- If clinical trials of any product candidates that we develop fail to demonstrate safety and efficacy, we may incur additional costs or experience delays in completing, or be unable to complete, the development and commercialization of these product candidates. A clinical trial of tamibarotene for the treatment of lung cancer conducted by a third party was terminated when data suggested the endpoint of progression-free survival for 18 months would not be reached.
- Adverse events or undesirable side effects caused by product candidates that we develop may be identified during development and could delay or prevent their marketing approval or limit their use. For example, SY-1425 is a retinoid, a class of compounds related to vitamin A that have been observed in certain circumstances to cause birth defects.
- We expect to rely on third parties to conduct clinical trials and certain aspects of our research and preclinical testing, to manufacture preclinical, clinical and commercial supplies of our product candidates and to develop our companion diagnostics.

- We are dependent on licenses with third parties for important intellectual property related to our business.
- If we are unable to obtain and maintain sufficient patent protection for our product candidates and gene control platform, including through existing and future licenses, or if the scope of the patent protection is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to commercialize our product candidates successfully may be adversely affected. We do not have composition of matter patent protection with respect to SY-1425.

Our Corporate Information

We were incorporated under the laws of the State of Delaware on November 9, 2011 under the name LS22, Inc. Our executive offices are located at 620 Memorial Drive, Suite 300, Cambridge, Massachusetts 02139, and our telephone number is (617) 744-1340. Our website address is www.syros.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.

Except as otherwise indicated herein or as the context otherwise requires, references in this prospectus to "Syros," "the company," "we," "us" and "our" refer to Syros Pharmaceuticals, Inc. and our wholly owned subsidiary Syros Securities Corporation.

The Syros logo, "Syros" and "Syros Pharmaceuticals" are our trademarks. 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. The trademarks, trade names and service marks appearing in this prospectus are the property of their respective owners.

Implications of Being an Emerging Growth Company

As a company with less than \$1.0 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. 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 consolidated financial statements and have not included all of the executive compensation related information that would be required if we were not an emerging growth company. The JOBS Act also provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. We have irrevocably elected not to avail ourselves of this exemption and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies. Because we intend to rely on certain disclosure and other requirements of the JOBS Act, the information contained herein may be different than the information you receive from other public companies in which you hold stock. In addition, it is possible that some investors will find our common stock less attractive as a result of our determination to avail ourselves of exemptions under the JOBS Act, which may result in a less active trading market for our common stock and higher volatility in our stock price. We will remain an emerging growth company until the earlier to occur of: (1) the last day of the fiscal year in which we have total annual gross revenues of \$1.0 billion or more; (2) the last day of the fiscal year following the fifth anniversary of the date of the closing of this offering; (3) the date on which we have issued more than \$1.0 billion in nonconvertible debt during the previous three years; or (4) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission.

THE OFFERING

Common stock offered by us	shares
Common stock to be outstanding immediately after this offering	shares, or shares if the underwriters exercise their option to purchase additional shares in full
Underwriters' option to purchase additional shares	shares
Use of proceeds	We estimate that we will receive net proceeds from this offering of 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 the underwriting discounts and commissions and estimated offering expenses payable by us. We intend to use the net proceeds from this offering to fund proof-of-concept readouts for our two lead drug candidates. In particular we intend to use the net proceeds from this offering to conduct a Phase 2 clinical trial of SY-1425, and, for our CDK7 inhibitor program, to launch IND-enabling activities and a Phase 1/2 clinical trial in acute leukemias, in each case including clinical research outsourcing, drug manufacturing, companion diagnostic development and internal personnel costs. We also intend to use a portion of the proceeds for new and ongoing research activities including our preclinical programs and our platform. The balance will be used 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	"SYRS"

The number of shares of our common stock to be outstanding after this offering is based on 9,549,721 shares of our common stock outstanding as of January 28, 2016 and 59,958,081 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:

- 8,350,322 shares of our common stock issuable upon the exercise of stock options outstanding as of January 28, 2016, at a weighted-average exercise price of \$1.02 per share;
- 526,420 shares of our common stock available for future issuance as of January 28, 2016 under our 2012 equity incentive plan; and

- 11,700,000 and 2,200,000 additional shares of our common stock that will become available for future issuance under our 2016 stock incentive plan and our 2016 employee stock purchase plan, respectively, each of which will become effective immediately prior to the closing of this offering, as well as any automatic increases in the number of shares of common stock reserved for future issuance under these plans.

Unless otherwise indicated, all information in this prospectus assumes:

- the filing and effectiveness of our restated certificate of incorporation and the adoption of our amended and restated bylaws, which will occur immediately prior to the closing of this offering;
- no exercise of the outstanding stock options described above;
- no exercise by the underwriters of their option to purchase up to _____ additional shares of our common stock to cover overallocments, if any; and
- the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 59,958,081 shares of our common stock upon the closing of this offering.

In addition, all information in this prospectus gives effect to a _____ -for- _____ reverse stock split of our capital stock, which became effective on _____, 2016.

SUMMARY CONSOLIDATED FINANCIAL INFORMATION

You should read the following summary consolidated financial data together with our consolidated financial statements and the related notes included elsewhere in this prospectus and the "Selected Consolidated 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, 2013 and 2014 from our audited consolidated financial statements included elsewhere in this prospectus. We have derived the statement of operations data for the nine months ended September 30, 2014 and 2015 and the balance sheet data as of September 30, 2015 from our unaudited consolidated financial statements included elsewhere in this prospectus, which have been prepared on the same basis as the audited consolidated financial statements. In the opinion of management, the unaudited consolidated financial data reflects all adjustments, consisting only of normal recurring adjustments, necessary for a fair presentation of the financial information as of and for the periods presented. 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,		Nine Months Ended	
	2013	2014	2014	2015
	(unaudited)			
	(in thousands, except share and per share data)			
Statements of Operations Data:				
Revenue	\$ —	\$ —	\$ —	\$ 317
Operating expenses:				
Research and development	6,266	10,923	7,901	16,030
General and administrative	2,367	2,512	1,843	3,418
Total operating expenses	8,633	13,435	9,744	19,448
Loss from operations	(8,633)	(13,435)	(9,744)	(19,131)
Other income (expense), net	(32)	4	2	2
Net loss and comprehensive loss	<u>\$ (8,665)</u>	<u>\$ (13,431)</u>	<u>\$ (9,742)</u>	<u>\$ (19,129)</u>
Net loss per share applicable to common stockholders—basic and diluted(1)	<u>\$ (2.25)</u>	<u>\$ (2.74)</u>	<u>\$ (1.93)</u>	<u>\$ (3.26)</u>
Weighted-average number of common shares used in net loss per share applicable to common stockholders—basic and diluted(1)	<u>4,110,716</u>	<u>5,718,844</u>	<u>5,599,543</u>	<u>6,997,532</u>
Pro forma net loss per share—basic and diluted (unaudited)(1)		<u>\$ (0.37)</u>		<u>\$ (0.36)</u>
Weighted-average number of common shares used in pro forma net loss per share—basic and diluted (unaudited)(1)		<u>35,901,743</u>		<u>54,250,987</u>

- (1) See Note 2 to our consolidated financial statements included elsewhere in this prospectus for a description of the method used to calculate basic and diluted net loss per share and unaudited pro forma basic and diluted net loss per share as well as the weighted-average number of common shares used in the calculation of the per share amounts.

The following table sets forth our summary consolidated balance sheet data as of September 30, 2015:

- on an actual basis;
- on a pro forma basis to give effect to (i) the completion of our Series B preferred stock financing in January 2016, in which we issued and sold an aggregate of 12,714,150 shares of our Series B preferred stock for an aggregate purchase price of \$40 million, (ii) the conversion of all outstanding shares of our preferred stock, including the Series B preferred stock sold in January 2016, into an aggregate of 59,958,081 shares of common stock and (iii) the change in our total stockholders' (deficit) equity resulting from the stock-based compensation expense associated with the vesting of 200,000 shares of restricted common stock and the vesting of performance-based option awards to purchase up to 222,706 shares of our common stock, each upon the closing of this offering; and
- on a pro forma as adjusted basis to give further effect to the 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 underwriting discounts and commissions and estimated offering expenses payable by us.

	September 30, 2015	
	Actual	Pro Forma As Adjusted(2)
(unaudited) (in thousands)		
Balance Sheet Data:		
Cash and cash equivalents	\$ 44,985	\$ 84,817
Working capital(1)	40,821	80,653
Total assets	50,042	89,874
Convertible preferred stock	82,013	—
Total stockholders' (deficit) equity	(38,180)	83,665

- (1) We define working capital as current assets less current liabilities. See our consolidated financial statements for further details regarding our current assets and current liabilities.
- (2) The pro forma as adjusted information presented in the summary consolidated balance sheet data is illustrative only and will change based on the actual initial public offering price and other terms of this offering determined at pricing. Each \$1.00 increase (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 (decrease) the pro forma as adjusted amount of each of cash and cash equivalents, working capital, total assets and total stockholders' (deficit) 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 underwriting discounts and commissions and estimated offering expenses payable by us. Each increase (decrease) of _____ shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash and cash equivalents, working capital, total assets and total stockholders' (deficit) equity by \$ _____ million, assuming no change in the assumed initial public offering price per share and after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before you decide to invest in our common stock, you should carefully consider the risks described below, together with the other information contained in this prospectus, including our consolidated financial statements and the related notes included elsewhere in this prospectus. If any of the following risks actually occurs, our business, financial condition, results of operations and future growth prospects could be harmed. 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, expect to incur significant and increasing losses for at least the next several years, and may never achieve or maintain profitability.

We have incurred significant annual net operating losses in every year since our inception. We expect to continue to incur significant and increasing net operating losses for at least the next several years. Our net losses were \$8.7 million and \$13.4 million for the years ended December 31, 2013 and 2014, respectively, and \$19.1 million for the nine months ended September 30, 2015. As of September 30, 2015, we had an accumulated deficit of \$42.8 million. We have not generated any revenues from product sales, have not completed the development of any product candidate and may never have a product candidate approved for commercialization. We have financed our operations to date primarily through private placements of our preferred stock. We have devoted substantially all of our financial resources and efforts to research and development and general and administrative expense to support such research and development. Our net losses may fluctuate significantly from quarter to quarter and year to year. Net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' (deficit) equity and working capital.

We anticipate that our expenses will increase substantially if and as we:

- continue to develop and begin clinical trials with respect to our lead product candidate, SY-1425, including a Phase 2 clinical trial we expect to initiate in mid-2016;
- continue research, preclinical and clinical development efforts for our cyclin-dependent kinase 7, or CDK7, inhibitor program, for which we plan to submit an investigational new drug application, or IND, in the second half of 2016 and to initiate a Phase 1/2 clinical trial in the first half of 2017;
- initiate and continue research, preclinical and clinical development efforts for our preclinical programs;
- further develop our gene control platform;
- seek to identify and develop additional product candidates;
- acquire or in-license other product candidates or technologies;
- seek regulatory and marketing approvals for our product candidates that successfully complete clinical trials, if any;
- establish sales, marketing, distribution and other commercial infrastructure in the future to commercialize various products for which we may obtain marketing approval, if any;
- require the manufacture of larger quantities of product candidates for clinical development and, potentially, commercialization;
- maintain, expand and protect our intellectual property portfolio;
- hire and retain additional personnel, such as clinical, quality control and scientific personnel;

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- add operational, financial and management information systems and personnel, including personnel to support our product development and help us comply with our obligations as a public company; and
- add equipment and physical infrastructure to support our research and development programs.

Our ability to become and remain profitable depends on our ability to generate revenue. We do not expect to generate significant revenue unless and until we are, or any future collaborator is, able to obtain marketing approval for, and successfully commercialize, one or more of our product candidates. Successful commercialization will require achievement of key milestones, including initiating and successfully completing clinical trials of our product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those products for which we, or any of our future collaborators, may obtain marketing approval, satisfying any post-marketing requirements and obtaining reimbursement for our products from private insurance or government payors. Because of the uncertainties and risks associated with these activities, we are unable to accurately predict the timing and amount of revenues, and if or when we might achieve profitability. We and any future collaborators may never succeed in these activities and, even if we do, or any future collaborators do, we may never generate revenues that are large enough for us to achieve profitability. Even 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, expand our business, maintain our research and development efforts, diversify our pipeline of product candidates or continue our operations and cause a decline in the value of our common stock.

We have a limited operating history, no products approved for sale and no history of commercializing pharmaceutical products, which may make it difficult to evaluate the prospects for our future viability.

We commenced operations in 2011. Our operations to date have been limited to financing and staffing our company, developing our gene control platform and conducting preclinical research. We have not yet demonstrated an ability to successfully conduct clinical trials, obtain marketing approvals, manufacture a commercial-scale product or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Accordingly, you should consider our prospects in light of the costs, uncertainties, delays and difficulties frequently encountered by companies in the early stages of development, especially clinical stage biopharmaceutical companies such as ours. 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 or a history of successfully developing and commercializing pharmaceutical products.

We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. We will eventually need to transition from a company with a development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We expect our financial condition and operating results to continue to 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 quarterly or annual periods as indications of future operating performance.

We will need substantial additional funding, and if we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or 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 initiate clinical trials of SY-1425, advance the development of our CDK7 inhibitor program, initiate new research and

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preclinical development efforts and seek marketing approval for any product candidates that we successfully develop. Moreover, under license agreements with various licensors, we are obligated to make milestone payments upon the successful completion of specified development and commercialization activities. In addition, if we obtain marketing approval for any product candidate that we may successfully develop, we may incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of a future collaborator. Furthermore, following the closing of this offering, we expect to incur significant 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 or eliminate our research and development programs or any future commercialization efforts.

We plan to use the net proceeds of this offering primarily to fund our ongoing research and development efforts. We will be required to expend significant funds in order to advance the development of SY-1425 and our CDK7 inhibitor program, as well as our other preclinical programs. In addition, while we may seek one or more collaborators for future development of our current product candidate or any future product candidates that we may develop 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 of this offering and our existing cash and cash equivalents will not be sufficient to fund all of the efforts that we plan to undertake or to fund the completion of development of our product candidate or our other preclinical programs. 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 and cash equivalents as of September 30, 2015 and the \$40 million of aggregate proceeds from our Series B preferred stock financing that we completed in January 2016, will enable us to fund our operating expenses and capital expenditure requirements at least through . Our estimate as to how long we expect the net proceeds from this offering, together with our existing cash and cash equivalents, 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 funding requirements, both short-term and long-term, will depend on many factors, including:

- the scope, progress, timing, costs and results of clinical trials of SY-1425 and any CDK7 inhibitors we successfully advance into clinical development;
- research and preclinical development efforts for any future product candidates that we may develop;
- our ability to enter into and the terms and timing of any collaborations, licensing agreements or other arrangements;
- the number of future product candidates that we pursue and their development requirements;
- the outcome, timing and costs of seeking regulatory approvals;
- the costs of commercialization activities for any of our product candidates that receive marketing approval to the extent such costs are not the responsibility of any future collaborators, including

- the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- the costs of acquiring potential new product candidates or technology;
- the costs of any physician education programs relating to selecting and treating genomically defined patient populations;
- the timing and amount of milestone and other payments due to licensors for patent and technology rights used in our development platform;
- revenue received from commercial sales, if any, of our current and future product candidates;
- our headcount growth and associated costs as we expand our research and development and establish a commercial infrastructure;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against intellectual property related claims; and
- the costs of operating as a public company.

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 technologies or product candidates.

We expect our expenses to increase in connection with our planned operations. To the extent that we raise additional capital through the sale of common stock, convertible securities or other equity 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 or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, 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, limit, reduce or terminate 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 Product Candidates

Our approach to the discovery and development of product candidates based on our gene control platform is novel and unproven, and we do not know whether we will be able to develop any products of commercial value.

We are focused on discovering and developing medicines for the treatment of cancer and other diseases based upon our gene control platform. We are leveraging our platform to create a pipeline of gene control drug candidates for genomically defined patients whose diseases have not been adequately addressed to date by other genomics approaches and to design and conduct efficient clinical trials with a higher likelihood of success. While we believe that applying our gene control platform to create medicines for genomically defined patient populations may potentially enable drug research and clinical development that is more efficient than conventional small molecule drug research and development, our approach is both novel and unproven. Because our approach is both novel and unproven, the cost

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and time needed to develop our product candidates is difficult to predict, and our efforts may not result in the discovery and development of commercially viable medicines. We may also be incorrect about the effects of our product candidates on the diseases of genomically defined patient populations, which may limit the utility of our approach or the perception of the utility of our approach. Furthermore, our estimates of genomically defined patient populations available for study and treatment may be lower than expected, which could adversely affect our ability to conduct clinical trials and may also adversely affect the size of any market for medicines we may successfully commercialize.

We have not yet succeeded and may never succeed in demonstrating efficacy and safety for our current or any future product candidates in clinical trials or in obtaining marketing approval thereafter. For example, although we have discovered and evaluated compounds using our novel gene control platform, we have not yet advanced a compound into any phase of clinical development.

Our gene control platform may fail to help us discover and develop additional potential product candidates.

A significant portion of the research that we are conducting involves identifying novel targets and points of intervention and developing new compounds using our gene control platform. The drug discovery that we are conducting using our gene control platform may not be successful in identifying compounds that have commercial value or therapeutic utility. Our gene control platform may initially show promise in identifying potential product candidates, yet fail to yield viable product candidates for clinical development or commercialization for a number of reasons, including:

- compounds created through our gene control platform may not demonstrate efficacy, safety or tolerability;
- potential product candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to receive marketing approval and achieve market acceptance;
- competitors may develop alternative therapies that render our potential product candidates non-competitive or less attractive; or
- a potential product candidate may not be capable of being produced at an acceptable cost.

Our research programs to identify new product candidates will require substantial technical, financial and human resources, and we may be unsuccessful in our efforts to identify new product candidates. If we are unable to identify suitable additional compounds for preclinical and clinical development, our ability to develop product candidates and obtain product revenues in future periods could be compromised, which could result in significant harm to our financial position and adversely impact our stock price.

In the near term, we are dependent on the success of SY-1425 and our CDK7 inhibitor program. If we are unable to initiate or complete the clinical development of, obtain marketing approval for or successfully commercialize SY-1425 or a product candidate in our CDK7 inhibitor program, either alone or with a collaborator, or if we experience significant delays in doing so, our business could be substantially harmed.

We currently have no products approved for sale and are investing a significant portion of our efforts and financial resources in the development of SY-1425 and our CDK7 inhibitor program. Our prospects are substantially dependent on our ability, or that of any future collaborator, to develop, obtain marketing approval for and successfully commercialize product candidates in one or more disease indications.

The success of SY-1425 and our CDK7 inhibitor program will depend on several factors, including the following:

- initiation and successful enrollment and completion of clinical trials;

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- a safety, tolerability and efficacy profile that is satisfactory to the U.S. Food and Drug Administration, or FDA, or any comparable foreign regulatory authority for marketing approval;
- timely receipt of marketing approvals 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 suppliers and manufacturers including with respect to the supply of active pharmaceutical ingredient for SY-1425, for which we and TMRC Co. Ltd., or TMRC, are currently negotiating an agreement;
- establishment of arrangements with third-party manufacturers to obtain finished drug product that is appropriately packaged for sale;
- adequate ongoing availability of raw materials and drug product for clinical development and any commercial sales;
- obtaining and maintaining patent, trade secret protection and regulatory exclusivity, both in the United States and internationally, including our ability to maintain our license agreement with TMRC, which we refer to as the TMRC license agreement;
- protection of our rights in our intellectual property portfolio;
- 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;
- successful identification of biomarkers for patient selection;
- continued availability of appropriate tissue samples to enable the identification of novel targets in genomically defined subsets of patients; and
- our ability to compete with other therapies.

Many of these factors are beyond our control, including clinical development, the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing and sales efforts of any future collaborator. If we are unable to develop, receive marketing approval for and successfully commercialize SY-1425 or any product candidates under our CDK7 inhibitor program, on our own or with any future collaborator, or experience delays as a result of any of these factors or otherwise, our business could be substantially harmed.

If clinical trials of any future product candidates that we, or any future collaborators, may develop fail to satisfactorily demonstrate safety and efficacy to the FDA and other regulators, we, or any future collaborators, may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of these product candidates.

We, and any future collaborators, are not permitted to commercialize, market, promote or sell any product candidate in the United States without obtaining marketing approval from the FDA. Foreign regulatory authorities, such as the European Medicines Agency, or the EMA, impose similar requirements. We, and any future collaborators, must complete extensive preclinical development and clinical trials to demonstrate the safety and efficacy of our product candidates in humans before we will be able to obtain these approvals.

Clinical testing is expensive, is difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. The clinical development of our product

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candidates is susceptible to the risk of failure inherent at any stage of product development, including failure to demonstrate efficacy in a clinical trial or across a broad population of patients, the occurrence of adverse events that are severe or medically or commercially unacceptable, failure to comply with protocols or applicable regulatory requirements and determination by the FDA or any comparable foreign regulatory authority that a product candidate may not continue development or is not approvable. For example, a Phase 2 clinical trial of tamibarotene (SY-1425) for the treatment of late-stage non-small cell lung cancer, or NSCLC, under a previous license between TMRC and a third party was terminated when interim data suggested that the primary endpoint of progression-free survival for 18 months after starting therapy would not be reached. Although we have no current plans to conduct studies of SY-1425 in NSCLC, we face a similar risk of failure in our planned clinical trials of SY-1425. It is possible that even if one or more of our product candidates has a beneficial effect, that effect will not be detected during clinical evaluation as a result of one or more of a variety of factors, including the size, duration, design, measurements, conduct or analysis of our clinical trials. Conversely, as a result of the same factors, our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any. Similarly, in our clinical trials we may fail to detect toxicity or intolerability caused by our product candidates, or mistakenly believe that our product candidates are toxic or not well tolerated when that is not in fact the case.

Any inability to successfully complete preclinical and clinical development could result in additional costs to us, or any future collaborators, and impair our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties. Moreover, if we, or any future collaborators, are required to conduct additional clinical trials or other testing of our product candidates beyond the trials and testing that we or they contemplate, if we, or they, are unable to successfully complete clinical trials of our product candidates or other testing, or the results of these trials or tests are unfavorable, uncertain or are only modestly favorable, or there are unacceptable safety concerns associated with our product candidates, we, or any future collaborators, may:

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

Our failure to successfully initiate and complete clinical trials of our product candidates and to demonstrate the efficacy and safety necessary to obtain regulatory approval to market any of our product candidates would significantly harm our business.

Adverse events or undesirable side effects caused by, or other unexpected properties of, product candidates that we develop may be identified during development and could delay or prevent their marketing approval or limit their use.

Adverse events or undesirable side effects caused by, or other unexpected properties of, SY-1425, any CDK7 inhibitors we may develop or any future product candidates that we may develop could cause us, any future collaborators, an institutional review board or regulatory authorities to interrupt, delay or halt clinical trials of one or more of our product candidates and could result in a more restrictive label or the delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities. Because gene control techniques are relatively new, side effects from gene

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control approaches may be unpredictable. Tamibarotene has been observed to be associated with adverse events, such as mild or moderate dry skin, skin rash, headache and bone pain, as well as retinoic acid syndrome and elevated levels of cholesterol, lipids, liver function enzymes and white blood cells, which were severe in certain cases. Furthermore, retinoids such as SY-1425 may cause birth defects and therefore may carry a warning on their label. Other examples of retinoids, a class of chemical compounds that are related to vitamin A, include all trans retinoic acid or ATRA, Retin-A, retinol (found in over-the-counter skin creams), isotretinoin and bexarotene. We have not yet tested any of our CDK7 inhibitors in humans so the safety profile that any such CDK7 inhibitors will demonstrate in human clinical trials is unknown. If any of our product candidates is associated with adverse events or undesirable side effects or has properties that are unexpected, we, or any future collaborators, may need to 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. Many compounds that initially showed promise in clinical or earlier stage testing have later been found to cause undesirable or unexpected side effects that prevented further development of the compound.

If we, or any future collaborators, experience any of a number of possible unforeseen events in connection with clinical trials of our current product candidate or any future product candidates that we, or any future collaborators, may develop, potential clinical development, marketing approval or commercialization of our product candidates could be delayed or prevented.

We, or any future collaborators, may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent clinical development, marketing approval or commercialization of our current product candidate or any future product candidates that we, or any future collaborators, may develop, including:

- regulators or institutional review boards may not authorize us, any future collaborators or our or their investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we, or any future collaborators, may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- clinical trials of our product candidates may produce unfavorable or inconclusive results;
- we, or any future collaborators, may decide, or regulators may require us or them, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we, or any future collaborators, anticipate, patient enrollment in these clinical trials may be slower than we, or any future collaborators, anticipate or participants may drop out of these clinical trials at a higher rate than we, or any future collaborators, anticipate;
- our estimates of the genomically defined patient populations available for study may be higher than actual patient numbers and result in our inability to sufficiently enroll our trials;
- the cost of planned clinical trials of our product candidates may be greater than we anticipate;
- our third-party contractors or those of any future collaborators, including those manufacturing our product candidates or components or ingredients thereof or conducting clinical trials on our behalf or on behalf of any future collaborators, may fail to comply with regulatory requirements or meet their contractual obligations to us or any future collaborators in a timely manner or at all;
- patients that enroll in a clinical trial may misrepresent their eligibility to do so or may otherwise not comply with the clinical trial protocol, resulting in the need to drop the patients from the clinical trial, increase the needed enrollment size for the clinical trial or extend the clinical trial's duration;

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- we, or any future collaborators, may have to delay, suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate;
- regulators or institutional review boards may require that we, or any future collaborators, or our or their investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or their standards of conduct, a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate or findings of undesirable effects caused by a chemically or mechanistically similar product or product candidate;
- the FDA or comparable foreign regulatory authorities may disagree with our, or any future collaborators', clinical trial designs or our or their interpretation of data from preclinical studies and clinical trials;
- the FDA or comparable foreign regulatory authorities may fail to approve or subsequently find fault with the manufacturing processes or facilities of third-party manufacturers with which we, or any future collaborators, enter into agreements for clinical and commercial supplies;
- the supply or quality of raw materials or manufactured product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient, inadequate or not available at an acceptable cost, or we may experience interruptions in supply; 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 to obtain marketing approval.

Product development costs for us, or any future collaborators, will increase if we, or they, experience delays in testing or pursuing marketing approvals and we, or they, may be required to obtain additional funds to complete clinical trials and prepare for possible commercialization of our product candidates. We do not know whether any preclinical tests or clinical trials will begin as planned, will need to be restructured, or will be completed on schedule or at all. Significant preclinical study or clinical trial delays also could shorten any periods during which we, or any future collaborators, may have the exclusive right to commercialize our product candidates or allow our competitors, or the competitors of any future collaborators, to bring products to market before we, or any future collaborators, do and impair our ability, or the ability of any future collaborators, to successfully commercialize our product candidates and may harm our business and results of operations. In addition, many of the factors that lead to clinical trial delays may ultimately lead to the denial of marketing approval of any of our product candidates.

Failure to successfully validate, develop and obtain regulatory approval for companion diagnostics could harm our drug development strategy.

As one of the key elements of our development strategy, we seek to identify genomically defined subsets of patients within a disease category who may derive benefit from the product candidates we are developing. In collaboration with partners, we plan to develop companion diagnostics to help us to more accurately identify patients within a particular subset, both during our clinical trials and in connection with the commercialization of our product candidates that we are developing or may in the future develop. Companion diagnostics are subject to regulation by the FDA and comparable foreign regulatory authorities as medical devices and require separate regulatory approval prior to commercialization. We do not develop companion diagnostics internally and thus we will be dependent on the sustained cooperation and effort of our third-party collaborators in developing and obtaining approval for these companion diagnostics. We and our collaborators may encounter difficulties in developing and obtaining approval for the companion diagnostics, including issues relating to selectivity/specificity, analytical validation, reproducibility, or clinical validation. Any delay or failure by our

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collaborators to develop or obtain regulatory approval of the companion diagnostics could delay or prevent approval of our product candidates. In addition, our collaborators may encounter production difficulties that could constrain the supply of the companion diagnostics, and both they and we may have difficulties gaining acceptance of the use of the companion diagnostics in the clinical community. If such companion diagnostics fail to gain market acceptance, it would have an adverse effect on our ability to derive revenues from sales, if any, of our products. In addition, the diagnostic company with whom we contract may decide to discontinue selling or manufacturing the companion diagnostic that we anticipate using in connection with development and commercialization of our product candidates or our relationship with such diagnostic company may otherwise terminate. We may not be able to enter into arrangements with another diagnostic company to obtain supplies of an alternative diagnostic test for use in connection with the development and commercialization of our product candidates or do so on commercially reasonable terms, which could adversely affect and/or delay the development or commercialization of our product candidates.

If we, or any future collaborators, experience delays or difficulties in the enrollment of patients in clinical trials, our or their receipt of necessary regulatory approvals could be delayed or prevented.

We, or any future collaborators, may not be able to initiate or continue clinical trials for our current product candidate or any future product candidates that we, or any future collaborators, may develop if we, or they, are unable to locate and enroll a sufficient number of eligible patients to participate in clinical trials. Patient enrollment is a significant factor in the timing of clinical trials, and is affected by many factors, including:

- the size and nature of the patient population;
- the severity of the disease under investigation;
- the availability of approved therapeutics for the relevant disease;
- the proximity of patients to clinical sites;
- the eligibility criteria for the trial;
- the design of the clinical trial;
- efforts to facilitate timely enrollment;
- competing clinical trials; and
- clinicians' and patients' perceptions as to the potential advantages and risks of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating.

In particular, we intend to enrich our clinical trials with patients most likely to respond to our gene control therapies. However, genomically defined diseases may have relatively low prevalence and it may be difficult for us or third parties with whom we collaborate to identify patients for our trials, which may lead to delays in enrollment for our trials. We intend to develop, or engage third parties to develop, companion diagnostics for use in our clinical trials, but we or such third parties may not be successful in developing such companion diagnostics, furthering the difficulty in identifying genomically defined subsets of patients for our clinical trials. Our inability to enroll a sufficient number of genomically defined patients for our clinical trials would result in significant delays and could 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. Further, if we are unable to include a sufficient number of genomically defined patients in our trials, this could compromise our ability to seek participation in FDA's expedited review and approval programs, including Breakthrough Therapy designation and Fast Track designation, or otherwise to seek to accelerate clinical development and regulatory timelines.

Our inability, or the inability of any future collaborators, to enroll a sufficient number of patients for our, or their, clinical trials could result in significant delays or may require us or them to abandon one or more clinical trials altogether. Enrollment delays in our, or their, clinical trials may result in increased development costs for our product candidates, delay or halt the development of and approval processes for our product candidates and jeopardize our, or any future collaborators', ability to commence sales of and generate revenues from our product candidates, which could cause the value of our company to decline and limit our ability to obtain additional financing, if needed.

Results of preclinical studies and early clinical trials may not be predictive of results of future late-stage clinical trials.

We have not conducted any clinical trials, and all our data results from preclinical studies. We cannot assure you that we will be able to replicate in human clinical trials the results we observed in animal models. Moreover, the outcome of preclinical studies and early clinical trials may not be predictive of the success of later clinical trials, and interim results of clinical trials do not necessarily predict success in future clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in earlier development, and we could face similar setbacks. The design of a clinical trial can determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval. In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for the product candidates. Even if we, or any future collaborators, believe that the results of clinical trials for our product candidates warrant marketing approval, the FDA or comparable foreign regulatory authorities may disagree and may not grant marketing approval of our product candidates.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. If we fail to receive positive results in clinical trials of our product candidates, the development timeline and regulatory approval and commercialization prospects for our most advanced product candidates, and, correspondingly, our business and financial prospects would be negatively impacted.

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 our current product candidate or any future product candidates that we, or any future collaborators, may develop.

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 any of our product candidates, it may require that we conduct additional clinical trials, preclinical studies 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 trials or 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 trials or studies, if performed and completed, may not be considered sufficient by the FDA to approve our NDAs. In addition, our development programs contemplate the development of companion diagnostics by our third-party collaborators. Companion diagnostics are subject to regulation as medical devices and must themselves

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be approved for marketing by the FDA or certain other foreign regulatory agencies before we may commercialize our product candidates.

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

Even if any product candidates that we, or any future collaborators, may develop receive marketing approval, we or others may later discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, which could compromise our ability, or that of any future collaborators, to market the product.

Clinical trials of SY-1425, any product candidates we may develop under our CDK7 inhibitor program or any future product candidates that we, or any future collaborators, may develop will 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, following approval of a product candidate, we, or others, discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, any of the following adverse events could occur:

- regulatory authorities may withdraw their approval of the product or seize the product;
- we, or any future collaborators, may be required to recall the product, change the way the product is administered or conduct additional clinical trials;
- additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the particular product;
- 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 product may become less competitive; and
- our reputation may suffer.

Any of these events could harm our business and operations, and could negatively impact our stock price.

Even if our current product candidate, or any future product candidate that we, or any future collaborators, may develop receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success, in which case we may not generate significant revenues or become profitable.

We have never commercialized a product, and even if one of our product candidates is approved by the appropriate regulatory authorities for marketing and sale, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. Physicians are often reluctant to switch their patients from existing therapies even when new and potentially more effective or convenient treatments enter the market. Further, patients often acclimate to the therapy that they are currently taking and do not want to switch unless their physicians recommend switching products or they are required to switch therapies due to lack of reimbursement for existing therapies.

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Efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may not be successful. If any of our product candidates is approved but does not achieve an adequate level of market acceptance, we may not generate significant revenues 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.

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 intend to focus on developing product candidates for specific indications that we identify as most likely to succeed, in terms of both their potential for marketing approval and commercialization. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that may prove to have greater commercial potential.

Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable product candidates. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to the product candidate.

If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution arrangements with third parties, we may not be successful in commercializing any product candidates if approved.

We do not have a sales, marketing or distribution infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved product, we must either develop a sales and marketing organization or outsource these functions to third parties. We plan to build focused capabilities to commercialize development programs for certain indications where we believe that the medical specialists for the indications are sufficiently concentrated to allow us to effectively promote the product with a targeted sales team. The

development of sales, marketing and distribution capabilities will require substantial resources, will be time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing and distribution capabilities is delayed or does not occur for any reason, we could have prematurely or unnecessarily incurred these commercialization costs. This may be costly, and our investment could be lost if we cannot retain or reposition our sales and marketing personnel. In addition, we may not be able to hire or retain a sales force in the United States that is sufficient in size or has adequate expertise in the medical markets that we plan to target. If we are unable to establish or retain a sales force and marketing and distribution capabilities, our operating results may be adversely affected. If a potential partner has development or commercialization expertise that we believe is particularly relevant to one of our products, then we may seek to collaborate with that potential partner even if we believe we could otherwise develop and commercialize the product independently.

In certain indications, we plan to seek to enter into collaborations that we believe may contribute to our ability to advance development and ultimately commercialize our product candidates. We also intend to seek to enter into collaborations where we believe that realizing the full commercial value of our development programs will require access to broader geographic markets or the pursuit of broader patient populations or indications. As a result of entering into arrangements with third parties to perform sales, marketing and distribution services, our product revenues or the profitability of these product revenues may be lower, perhaps substantially lower, than if we were to directly market and sell products in those markets. Furthermore, we may be unsuccessful in entering into the necessary arrangements with third parties or may be unable to do so on terms that are favorable to us. In addition, we may have little or no control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively.

If we do not establish sales, marketing and distribution capabilities, either on our own or in collaboration with third parties, we will not be successful in commercializing any of our product candidates that receive marketing approval.

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

The development and commercialization of new products is highly competitive. We expect that we, and any future collaborators, will face significant competition from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide with respect to any of our product candidates that we, or any future collaborators, may seek to develop or commercialize in the future. Specifically, there are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of product candidates for the treatment of the key indications of our most advanced programs, such as the use of chemotherapy followed by stem cell transplantation in the case of AML, MDS and ALL. SY-1425 may also face competition from other drug candidates currently in clinical development for relapsed or refractory AML and MDS, including drug candidates in development from Daiichi Sankyo Company, Limited, Boehringer Ingelheim GmbH, Agios Pharmaceuticals, Inc., Novartis AG, Astellas Pharma Inc. and Karyopharm Therapeutics Inc. We are aware of only one other selective RARa program, which is being undertaken by IO Therapeutics, Inc. and which appears to be in early preclinical development. Our CDK7 inhibitors may face competition from other drug candidates currently in clinical development for relapsed or refractory AML and MDS or from other drug candidates currently in development for relapsed and refractory ALL, including drug candidates in development from Amgen Inc., Novartis AG, F. Hoffman-La Roche AG and Juno Therapeutics, Inc. We are aware of only one other CDK7 inhibitor program being undertaken by a German academic group, Lead Discovery Center, which appears to be in early preclinical development.

Our competitors may succeed in developing, acquiring or licensing technologies and products that are more effective, have fewer side effects or more tolerable side effects or are less costly than any

product candidates that we are currently developing or that we may develop, which could render our product candidates obsolete and noncompetitive.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer or more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we, or any future collaborators, may develop. Our competitors also may obtain FDA or other marketing approval for their products before we, or any future collaborators, are able to obtain approval for ours, which could result in our competitors establishing a strong market position before we, or any future collaborators, are able to enter the market.

Many of our existing and potential future competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining marketing approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller 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 necessary for, the development of our product candidates.

Even if we, or any future collaborators, are able to commercialize any product candidate that we, or they, develop, the product may become subject to unfavorable pricing regulations, third-party payor reimbursement practices or healthcare reform initiatives, any of which could harm our business.

The commercial success of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by third-party payors, including government health care programs and private health insurers. If coverage is not available, or reimbursement is limited, we, or any future collaborators, may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us, or any future collaborators, to establish or maintain pricing sufficient to realize a sufficient return on our or their investments. In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors and coverage and reimbursement levels for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time consuming and costly process that may require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved drugs. Marketing approvals, pricing and reimbursement for new drug products 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 or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we, or any future collaborators, might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy time periods, which may 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 or the ability of any future collaborators to recoup our or their investment in one or more product candidates, even if our product candidates obtain marketing approval.

Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Therefore, our ability, and the ability of any future collaborators, to commercialize successfully any of our product candidates will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from third-party payors. Third-party payors decide which medications they will cover and establish reimbursement levels. The healthcare industry is acutely focused on cost containment, both in the United States and elsewhere. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect our ability or that of any future collaborators to sell our product candidates profitably. These payors may not view our products, if any, as cost-effective, and coverage and reimbursement may not be available to our customers, or those of any future collaborators, or may not be sufficient to allow our products, if any, to be marketed on a competitive basis. Cost-control initiatives could cause us, or any future collaborators, to decrease the price we, or they, might establish for products, which could result in lower than anticipated product revenues. If the prices for our products, if any, decrease or if governmental and other third-party payors do not provide coverage or adequate reimbursement, our prospects for revenue and profitability will suffer.

There may also be delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the indications 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 paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Reimbursement rates may vary, by way of example, according to the use of the product and the clinical setting in which it is used. Reimbursement rates may also be based on reimbursement levels already set for lower cost drugs or may be incorporated into existing payments for other services.

In addition, increasingly, third-party payors are requiring higher levels of evidence of the benefits and clinical outcomes of new technologies and are challenging the prices charged. Further, the net reimbursement for drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. An inability to promptly obtain coverage and adequate payment rates from both government-funded and private payors for any of our product candidates for which we, or any future collaborator, obtain marketing approval could significantly harm our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

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

We will face an inherent risk of product liability claims as a result of the clinical testing of our product candidates despite obtaining appropriate informed consents from our clinical trial participants. We will face an even greater risk if we or any future collaborators commercially sell any product that we may or they may develop. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Regardless of the merits or eventual outcome, liability claims may result in:

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

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- withdrawal of clinical trial participants;
- significant costs to defend resulting 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 products that we may develop.

Although we intend to maintain clinical trial liability insurance coverage in the amount of up to \$5.0 million in the aggregate, this insurance may not fully cover potential liabilities that we may incur. The cost of any product liability litigation or other proceeding, even if resolved in our favor, could be substantial. We will need to increase our insurance coverage if and when we commercialize any product that receives marketing approval. In addition, insurance coverage is becoming increasingly expensive. If we are unable to obtain or maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims, it could prevent or inhibit the development and commercial production and sale of our product candidates, which could harm our business, financial condition, results of operations and prospects.

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

Once an NDA is approved, the product covered thereby becomes a "reference-listed drug" in the FDA's publication, "Approved Drug Products with Therapeutic Equivalence Evaluations," or the Orange Book. 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. Rather, the applicant generally must show that its product 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 products may be significantly less costly to bring to market than the reference-listed drug and companies that produce generic products 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 may be typically lost to the generic product.

The FDA may not approve an ANDA for a generic product 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 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 product, in which case the applicant may submit its application four years following approval of the reference-listed drug. Because the composition of matter patent for SY-1425 has expired, it is possible that another applicant could obtain approval of tamibarotene from the FDA before us, in which case our NDA would not be eligible for NCE exclusivity. See "**Risks Related to Our Intellectual Property—We do not have composition of matter patent protection with respect to SY-1425.**" If any product we develop does not receive five years of NCE exclusivity, the FDA may approve generic versions of such product three years after its date of approval, subject to the requirement that the ANDA applicant certifies to any patents listed for our products in the Orange Book. Manufacturers may seek to launch these generic products following the expiration of the applicable marketing exclusivity period, even if we still have patent protection for our product.

Competition that our products may face from generic versions of our products could negatively impact our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on our investments in those product candidates.

Risks Related to Our Dependence on Third Parties

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

We expect to rely on third parties, such as contract research organizations, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials. We currently rely and expect to continue to rely on third parties to conduct certain aspects of our research and preclinical testing. 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 product 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 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 practices, 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. We also are required to register ongoing clinical trials and post the results of 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 medicines.

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 our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our medicines, producing additional losses and depriving us of potential product revenue.

We will be required to obtain all the active pharmaceutical ingredients for our lead product candidate, SY-1425, from TMRC, a sole source supplier, and we have not yet entered into a supply agreement with TMRC.

Under the TMRC license agreement pursuant to which we obtained an exclusive license under patent rights, data, regulatory filings and other intellectual property for the development and commercialization of SY-1425 in North America and Europe for the treatment of human cancer indications, we agreed to enter into negotiations for a supply agreement obligating us to purchase all of our clinical and commercial requirements for active pharmaceutical ingredients for SY-1425 from TMRC. However, we may not be able to enter into a supply agreement on commercially reasonable terms, or at all, in time for the commencement of such clinical trial. We anticipate entering into this supply agreement prior to the commencement of our Phase 2 clinical trial of SY-1425.

Under the TMRC license agreement, we and TMRC agreed to negotiate a reasonable risk mitigation strategy and plan, which would likely include the selection and oversight of back-up suppliers to avoid potential interruptions in the supply of active pharmaceutical ingredients for SY-1425. Until any such strategy and plan is implemented, we will need to rely entirely on TMRC and its suppliers for our clinical and any commercial supplies of the active pharmaceutical ingredients in SY-1425. Toko Pharmaceuticals Ind. Co. Ltd., or Toko, is the owner of patent rights currently licensed to TMRC, from which our license agreement with TMRC derives its rights, and manufactures the active pharmaceutical ingredients of SY-1425, which it then provides to TMRC. We and TMRC have agreed to use commercially reasonable efforts to enable us to enter into a standby license with Toko, which we refer to as the standby license, whereby Toko would agree to cooperate with us to establish alternative supply arrangements if TMRC fails to supply active pharmaceutical ingredients for SY-1425. However, Toko is under no obligation to enter into the standby license with us. If TMRC is unable to supply the active pharmaceutical ingredients for SY-1425, or if we are unable to procure the active pharmaceutical ingredients for SY-1425 from TMRC on commercially favorable terms, we will need to identify, qualify, and obtain FDA approval of an alternative supplier of the active pharmaceutical ingredients for SY-1425. If we are not able to secure Toko's consent to do so, or we are otherwise unable or delayed, the supply of SY-1425 may be interrupted, which could result in delays in the clinical development and any future commercialization of SY-1425.

We currently depend on third-party manufacturers to produce our preclinical and clinical drug supplies and we intend to rely upon third-party manufacturers to produce commercial supplies of any approved product candidates.

We do not have any manufacturing facilities. We currently rely, and expect to continue to rely, on third-party manufacturers for the manufacture of our product candidates for preclinical and clinical testing and for commercial supply of any of these product candidates for which we or our collaborators obtain marketing approval.

We do not currently have a long term supply agreement with any third-party manufacturers. For a discussion of additional risks relating to the supply of active pharmaceutical ingredients for SY-1425, see "—We will be required to obtain all the active pharmaceutical ingredients for our lead product candidate, SY-1425, from TMRC, a sole source supplier, and we have not yet entered into a supply agreement with TMRC." 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:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us; and
- reliance on the third party for regulatory compliance, quality assurance, and safety and pharmacovigilance reporting.

Third-party manufacturers may not be able to comply with current good manufacturing practices, or cGMP, regulations or similar regulatory requirements outside the United States. 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 medicines, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our medicines and harm our business and results of operations.

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Any medicines that we may develop may compete with other product candidates and products 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 for bulk drug substances. If any one of our current contract manufacturers cannot perform as agreed, we may be required to replace that manufacturer. 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 medicines may adversely affect our future profit margins and our ability to commercialize any medicines that receive marketing approval on a timely and competitive basis.

We expect to seek to establish collaborations and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans.

We expect to seek one or more collaborators for the development and commercialization of one or more of our product candidates. Likely collaborators may include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. In addition, if we are able to obtain marketing approval for product candidates from foreign regulatory authorities, we intend to enter into strategic relationships with international biotechnology or pharmaceutical companies for the commercialization of such product candidates outside of the United States.

We 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 potential differentiation of our product candidate from competing product candidates, design or results of clinical trials, the likelihood of approval by the FDA or comparable foreign regulatory authorities and the regulatory pathway for any such approval, the potential market for the product candidate, the costs and complexities of manufacturing and delivering the product to patients and the potential of competing products. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available for collaboration and whether such a collaboration could be more attractive than the one with us for our product candidate. 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 product revenue.

Collaborations are complex and time consuming to negotiate and document.

Any collaboration agreements that we enter into in the future may contain, restrictions on our ability to enter into potential collaborations or to otherwise develop specified product candidates. Further, 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 we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, 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 enter into collaborations with third parties for the development and commercialization of any product candidates, our prospects with respect to those product candidates will depend in significant part on the success of those collaborations.

We expect to enter into collaborations for the development and commercialization of one or more product candidates we may develop. We have not entered into any collaborations to date. If we enter into such collaborations, we will have limited control over the amount and timing of resources that our collaborators will dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on any future collaborators' abilities to successfully perform the functions assigned to them in these arrangements. In addition, any future collaborators may have the right to abandon research or development projects and terminate applicable agreements, including funding obligations, prior to or upon the expiration of the agreed upon terms.

Collaborations involving our product candidates pose a number of risks, including the following:

- 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 and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs, based on clinical trial results, changes in the collaborators' strategic focus or available funding or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- 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 intellectual property or 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; and
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If any future collaborator of ours is involved in a business combination, it could decide to delay, diminish or terminate the development or commercialization of any product candidate licensed to it by us.

Risks Related to Our Intellectual Property

If we fail to comply with our obligations under our existing and any future intellectual property licenses with third parties, we could lose license rights that are important to our business.

We are party to several license agreements under which we license patent rights and other intellectual property related to or business, including: a license agreement with Dana-Farber under which we were granted an exclusive worldwide license under specified patents relating to CDK7 inhibitors and JNK inhibitors; a license agreement with the Whitehead Institute for Biomedical Research, or Whitehead, and the Dana-Farber Cancer Institute, or Dana-Farber, pursuant to which we were granted a predominantly exclusive, with certain non-exclusive exceptions (see corresponding agreement summary in "Business—License Agreements—Whitehead Institute for Biomedical Research and Dana-Farber Cancer Institute, Inc.") worldwide license under specified patents relating to modulators of Myc/Max Screen and relating to Chem-Seq; a license agreement with Whitehead pursuant to which we were granted an exclusive worldwide license under specified patents relating to super-enhancers until April 2016, which license can remain exclusive thereafter, on a field-by-field basis, as long as we can demonstrate that we are using commercially reasonable efforts in the applicable field; and the TMRC license agreement, pursuant to which we were granted a license under specified patent rights, data, regulatory filings and other intellectual property for the North American and European development and commercialization of SY-1425 for the treatment of human cancer indications. We may enter into additional license agreements in the future. Our license agreements impose, and we expect that future license agreements will impose, various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with our obligations under these licenses, our licensors may have the right to terminate these license agreements, in which event we might not be able to market any product that is covered by these agreements, or our licensors may convert the license to a non-exclusive license, which could adversely affect the value of the product candidate being developed under the license agreement. Termination of these license agreements or reduction or elimination of our licensed rights may also result in our having to negotiate new or reinstated licenses with less favorable terms.

We do not have composition of matter patent protection with respect to SY-1425.

We own certain patents and patent applications with claims directed to specific methods of using SY-1425 and we expect to have marketing exclusivity from the FDA and EMA for a period of seven and ten years, respectively because SY-1425 has not been approved in these markets. However, composition of matter protection in the United States and elsewhere covering SY-1425 has expired. We may be limited in our ability to list our patents in the FDA's Orange Book if the use of our product, consistent with its FDA-approved label, would not fall within the scope of our patent claims. Also, our competitors may be able to offer and sell products so long as these competitors do not infringe any other patents that we (or third parties) hold, including patents with claims directed to the manufacture of SY-1425 and/or method of use patents. In general, method of use patents are more difficult to enforce than composition of matter patents because, for example, of the risks that the FDA may approve alternative uses of the subject compounds not covered by the method of use patents, and others may engage in off-label sale or use of the subject compounds. Physicians are permitted to prescribe an approved product for uses that are not described in the product's labeling. Although off-label prescriptions may infringe our method of use patents, the practice is common across medical specialties and such infringement is difficult to prevent or prosecute. FDA approval of uses that are not covered by our patents would limit our ability to generate revenue from the sale of SY-1425, if approved for commercial sale. Off-label sales would limit our ability to generate revenue from the sale of SY-1425, if approved for commercial sale.

Our intellectual property licenses with third parties may be subject to disagreements over contract interpretations, which could narrow the scope of our rights to the relevant intellectual property or technology or increase our financial or other obligations to our licensors.

The agreements under which we currently license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could harm our business, financial condition, results of operations and prospects.

We may not be successful in obtaining or maintaining necessary rights to current or future product candidates through acquisitions and in-licenses.

We currently have rights to certain intellectual property, through licenses from third parties, to develop SY-1425 and product candidates under our CDK7 inhibitor program. Because our programs may require the use of proprietary rights by third parties, the growth of our business likely will depend, in part, on our ability to acquire, in-license or use these proprietary rights. We may be unable to acquire or in-license any compositions, methods of use, processes or other intellectual property rights from third parties that we identify as necessary for any product candidates. The licensing or acquisition of third-party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment.

We sometimes collaborate with non-profit and academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, 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 or we may decide not to execute such option if we believe such license is not necessary to pursue our program. If we are unable or opt not to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program.

If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may be required to expend significant time and resources to redesign our product candidates or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected product candidate, which could harm our business significantly.

We depend upon our license with TMRC, and we may not be able to maintain that license.

We and TMRC have agreed to use commercially reasonable efforts to enter into a standby license with Toko such that if at any time the license agreement between Toko and TMRC relating to the SY-1425 rights, which we refer to as the Toko license agreement, that TMRC has licensed to us terminates or otherwise ceases to be in effect for any reason, Toko would agree to grant directly to us such rights and licenses with respect to SY-1425 as are necessary for us to continue to develop SY-1425. However, we have not yet entered into the standby license with Toko, and there is no assurance that we will do so on terms that are acceptable to us, or at all. In the absence of the standby

license, if the TMRC license agreement terminates then we may lose rights to SY-1425 that may be necessary to the development and commercialization of SY-1425, which could have a material adverse impact on our business.

If we are unable to obtain and maintain sufficient patent protection for any product candidates, or if the scope of the patent protection is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize our product candidates may be adversely affected.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary product candidates. If we do not adequately protect our intellectual property, our competitors may be able to erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability. To protect our proprietary position, we file patent applications in the United States and abroad related to our novel product candidates that are important to our business. We also license or purchase patent applications filed by others. The patent application and approval process is expensive and time consuming. We may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner.

Agreements through which we license patent rights may not give us control over patent prosecution or maintenance, so that we may not be able to control which claims or arguments are presented and may not be able to secure, maintain, or successfully enforce necessary or desirable patent protection from those patent rights. We have not had and do not have primary control over patent prosecution and maintenance for certain of the patents and patent applications we license, and therefore cannot guarantee that these patents and applications will be prosecuted in a manner consistent with the best interests of our business. We cannot be certain that patent prosecution and maintenance activities by our licensors have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents.

We, or any future partners, collaborators or licensees, may fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection for them. Therefore, we may miss potential opportunities to strengthen our patent position.

It is possible that defects of form in the preparation or filing of our patents or patent applications may exist, or may arise in the future, for example with respect to proper priority claims, inventorship, claim scope or patent term adjustments. If we or our partners, collaborators, licensees, or licensors, whether current or future, fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our partners, collaborators, licensees or licensors, are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised. If there are material defects in the form, preparation, prosecution, or enforcement of our patents or patent applications, such patents may be invalid and/or unenforceable, and such applications may never result in valid, enforceable patents. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain. No consistent policy regarding the breadth of claims allowed in biotechnology and pharmaceutical patents has emerged to date in the United States or in many foreign jurisdictions. In addition, the determination of patent rights with respect to pharmaceutical compounds commonly involves complex legal and factual questions, which has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain.

Pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications. Assuming the other requirements for patentability are met, currently, the first to file a patent application is generally entitled to the patent. However, prior to March 16, 2013, in the United States, the first to invent was entitled to the patent. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases, not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. Similarly, we cannot be certain that parties from whom we do or may license or purchase patent rights were the first to make relevant claimed inventions, or were the first to file for patent protection for them. If third parties have filed patent applications on inventions claimed in our patents or applications on or before March 15, 2013, an interference proceeding in the United States can be initiated by such third parties to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. If third parties have filed such applications after March 15, 2013, a derivation proceeding in the United States can be initiated by such third parties to determine whether our invention was derived from theirs.

Moreover, because the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, our patents or pending patent applications may be challenged in the courts or patent offices in the United States and abroad. There is no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found. If such prior art exists, it may be used to invalidate a patent, or may prevent a patent from issuing from a pending patent application. For example, such patent filings may be subject to a third-party preissuance submission of prior art to the U.S. Patent and Trademark Office, or USPTO, to other patent offices around the world. Alternately or additionally, we may become involved in post-grant review procedures, oppositions, derivations, proceedings, reexaminations, *inter partes* review or interference proceedings, in the United States or elsewhere, challenging patents or patent applications in which we have rights, including patents on which we rely to protect our business. An adverse determination in any such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. In addition, 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.

Pending and future patent applications may not result in patents being issued which protect our business, in whole or in part, or which effectively prevent others from commercializing competitive 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 or in the same manner as the laws of the United States.

Issued patents that we have or may obtain or license may not 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 patents by developing similar or alternative technologies or products in a non-infringing manner. Our competitors may also seek approval to market their own products similar to or otherwise competitive with our products. Alternatively, our competitors may seek to market generic versions of any approved products by submitting ANDAs to the FDA in which they claim that patents owned or licensed by us are invalid, unenforceable or not infringed. In these circumstances, we may need to defend or assert our patents, or both, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other

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agency with jurisdiction may find our patents invalid or unenforceable, or that our competitors are competing in a non-infringing manner. Thus, even if we have valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives. We are aware of a third party that is offering super-enhancer identification and analysis services, which we believe infringe our recently issued in-licensed United States patent relating to this subject matter. We are in communication with that third party and are seeking to have them cease offering those services in light of our issued patent. If we are unsuccessful we may be required to file infringement claims against that party with all of the associated risks of patent infringement litigation set forth herein. If that party continues to offer these services, it may affect our ability to attract corporate partners who are interested in super-enhancer identification and analysis and may negatively affect the value of our technology platform and therefore harm our business.

Pursuant to the terms of some of our license agreements with third parties, some of our third party licensors have the right, but not the obligation in certain circumstances to control enforcement of our licensed patents or defense of any claims asserting the invalidity of these patents. Even if we are permitted to pursue such enforcement or defense, we will require the cooperation of our licensors, and cannot guarantee that we would receive it and on what terms. We cannot be certain that our licensors will allocate sufficient resources or prioritize their or our enforcement of such patents or defense of such claims to protect our interests in the licensed patents. If we cannot obtain patent protection, or enforce existing or future patents against third parties, our competitive position and our financial condition could suffer.

If we are unable to protect the confidentiality of our trade secrets, the value of our technology could be materially adversely affected and our business would be harmed.

In addition to the protection afforded by patents, we also rely on trade secret protection for certain aspects of our technology platform, including certain aspects of our gene control platform. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, consultants, independent contractors, advisors, contract manufacturers, suppliers and other third parties. We also enter into confidentiality and invention or patent assignment agreements with employees and certain consultants. Any party with whom we have executed such an agreement may breach that agreement and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time consuming, and the outcome is unpredictable. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret. Further, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such third party, or those to whom they communicate such technology or information, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our business and competitive position could be harmed.

We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our patents, trademarks, copyrights or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming and divert the time and attention of our management and scientific personnel. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents, in addition to counterclaims asserting that our patents are invalid or unenforceable, or both. In any patent infringement proceeding, there is

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a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patent claims do not cover the invention. An adverse outcome in a litigation or proceeding involving one or more of our patents could limit our ability to assert those patents against those parties or other competitors, and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

Even if we establish infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could adversely affect the price of shares of our common stock. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings.

If we are sued for infringing intellectual property rights of third parties, such litigation could be costly and time consuming and could prevent or delay us from developing or commercializing our product candidates.

Our commercial success depends, in part, on our ability to develop, manufacture, market and sell our product candidates and use our gene control technology without infringing the intellectual property and other proprietary rights of third parties. Third parties may have U.S. and non-U.S. issued patents and pending patent applications relating to compounds and methods of use for the treatment of the disease indications for which we are developing our product candidates. If any third-party patents or patent applications are found to cover our product candidates or their methods of use, we may not be free to manufacture or market our product candidates as planned without obtaining a license, which may not be available on commercially reasonable terms, or at all.

There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, litigation or other adversarial proceedings regarding intellectual property rights with respect to our product candidates, including interference proceedings before the USPTO. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may be accused of infringing. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Accordingly, third parties may assert infringement claims against us based on existing or future intellectual property rights. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. The pharmaceutical and biotechnology industries have produced a significant number of patents, and it may not always be clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to

interpretation by the courts, and the interpretation is not always uniform. If we were sued for patent infringement, we would need to demonstrate that our product candidates, products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do this. Proving invalidity is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could significantly harm our business and operating results. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

If we are found to infringe a third party's intellectual property rights, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing product candidate or product. Alternatively, we may be required to obtain a license from such third party in order to use the infringing technology and continue developing, manufacturing or marketing the infringing product candidate or product. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. Alternatively or additionally, it could include terms that impede or destroy our ability to compete successfully in the commercial marketplace. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

Changes to the patent law in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Recent patent reform legislation in the United States, including the Leahy-Smith America Invents Act, or the America Invents Act, could increase those uncertainties and costs. The America Invents Act was signed into law on September 16, 2011, and many of the substantive changes became effective on March 16, 2013. The America Invents Act reforms United States patent law in part by changing the U.S. patent system from a "first to invent" system to a "first inventor to file" system, expanding the definition of prior art, and developing a post-grant review system. This legislation changes United States patent law in a way that may weaken our ability to obtain patent protection in the United States for those applications filed after March 16, 2013.

Further, the America Invents Act created new procedures to challenge the validity of issued patents in the United States, including post-grant review and *inter partes* review proceedings, which some third parties have been using to cause the cancellation of selected or all claims of issued patents of competitors. For a patent with an effective filing date of March 16, 2013 or later, a petition for post-grant review can be filed by a third party in a nine month window from issuance of the patent. A petition for *inter partes* review can be filed immediately following the issuance of a patent if the patent has an effective filing date prior to March 16, 2013. A petition for *inter partes* review can be filed after the nine month period for filing a post-grant review petition has expired for a patent with an effective filing date of March 16, 2013 or later. Post-grant review proceedings can be brought on any ground of invalidity, whereas *inter partes* review proceedings can only raise an invalidity challenge based on published prior art and patents. These adversarial actions at the USPTO review patent claims without the presumption of validity afforded to U.S. patents in lawsuits in U.S. federal courts, and use a lower

burden of proof than used in litigation in U.S. federal courts. Therefore, it is generally considered easier for a competitor or third party to have a U.S. patent invalidated in a USPTO post-grant review or *inter partes* review proceeding than invalidated in a litigation in a U.S. federal court. If any of our patents are challenged by a third party in such a USPTO proceeding, there is no guarantee that we or our licensors or collaborators will be successful in defending the patent, which would result in a loss of the challenged patent right to us.

In addition, recent court rulings in cases such as *Association for Molecular Pathology v. Myriad Genetics, Inc.*; *BRCA1- & BRCA2- Based Hereditary Cancer Test Patent Litigation*; and *Promega Corp. v. Life Technologies Corp.* have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents once obtained. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

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

Filing, prosecuting and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. The requirements for patentability may differ in certain countries, particularly in developing countries; thus, even in countries where we do pursue patent protection, there can be no assurance that any patents will issue with claims that cover our products.

Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws. Additionally, laws of some countries outside of the United States and Europe do not afford intellectual property protection to the same extent as the laws of the United States and Europe. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, including India, China and other developing countries, do not favor the enforcement of patents and other intellectual property rights. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. Consequently, we may not be able to prevent third parties from practicing our inventions in certain countries outside the United States and Europe. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop and market their own products and, further, may export otherwise infringing products to territories where we have patent protection, if our ability to enforce our patents to stop infringing activities is inadequate. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Agreements through which we license patent rights may not give us sufficient rights to permit us to pursue enforcement of our licensed patents or defense of any claims asserting the invalidity of these patents (or control of enforcement or defense) of such patent rights in all relevant jurisdictions as requirements may vary.

Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, could result in substantial costs and divert our efforts and resources from other aspects of our business. Moreover, such proceedings could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims

against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Furthermore, while we intend to protect our intellectual property rights in major markets for our products, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our products. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate.

Patent terms may be inadequate to protect our competitive position on our products for an adequate amount of time.

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. We expect to seek extensions of patent terms in the United States and, if available, in other countries where we are prosecuting patents. In the United States, the Drug Price Competition and Patent Term Restoration Act of 1984 permits a patent term extension of up to five years beyond the normal expiration of the patent, which is limited to the approved indication (or any additional indications approved during the period of extension). However, the applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case.

We may be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees and our licensors' employees, including our senior management, were previously employed at universities or at other biotechnology or pharmaceutical companies, some of which may be competitors or potential competitors. Some of these employees, including each member of our senior management, executed proprietary rights, non-disclosure and non-competition agreements, or similar agreements, in connection with such previous employment. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such third party. Litigation may be necessary to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel or sustain damages. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms or at all. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while we typically require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own, which may result in claims by or against us related to the ownership of such intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our senior management and scientific personnel.

Obtaining and maintaining patent protection depends on 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.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and applications are required to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and applications. The USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process and after a patent has issued. There are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction.

Risks Related to Regulatory Approval and Marketing of Our Product Candidates 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 products are subject to extensive regulation by the FDA and comparable foreign regulatory authorities. 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 applicable regulatory authorities outside the United States. Our product candidates are in various 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 lengthy, expensive and uncertain. 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 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. Moreover, the FDA or other regulatory authorities may fail to approve the companion diagnostics we contemplate developing with partners. 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.

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 product 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, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we, or any future collaborators, ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

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

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

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

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

Regulatory authorities in some jurisdictions, including the United States and Europe, 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. We, or any future collaborators, may seek orphan drug designations for product candidates and may be unable to obtain such designations.

Even if we, or any future collaborators, obtain orphan drug designation for a product candidate, we, or they, may not be able to obtain orphan drug exclusivity for that product candidate. Generally, a product with orphan drug designation only becomes entitled to orphan drug exclusivity if it receives the first marketing approval for the indication for which it has such designation, in which case the FDA or the EMA will be precluded from approving another marketing application for the same drug for that indication for the applicable exclusivity period. The applicable exclusivity period is seven years in the United States and 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. Orphan drug exclusivity may be lost if the FDA or the EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

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 can be

approved for the same condition and the same drug can be approved for different conditions. Even after an orphan drug is approved, the FDA can subsequently approve the same drug 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.

Even if we, or any future collaborators, obtain marketing approvals for our product candidates, the terms of approvals and ongoing regulation of our products may limit how we manufacture and market our products, which could impair our ability to generate revenue.

Once marketing approval has been granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation. We, and any future collaborators, must therefore 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 product's approved labeling. Thus, we and any future collaborators will not be able to promote any products we develop for indications or uses for which they are not approved.

In addition, manufacturers of approved products and those manufacturers' facilities are 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, any 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 any future collaborators, receive marketing approval for one or more of our product candidates, we, and any 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 any future collaborators, are not able to comply with post-approval regulatory requirements, we, and any future collaborators, could have the marketing approvals for our products withdrawn by regulatory authorities and our, or any future collaborators', ability to market any future products 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.

Any of our product candidates for which we, or any future collaborators, obtain marketing approval in the future could be subject to post-marketing restrictions or withdrawal from the market and we, or any future collaborators, may 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 products following approval.

Any of our product candidates for which we, or any future collaborators, obtain marketing approval, as well as the manufacturing processes, post-approval studies and measures, labeling, advertising and promotional activities for such product, among other things, will be subject to ongoing requirements of and review by the FDA and other regulatory authorities. 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. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including the requirement to implement a Risk Evaluation and Mitigation Strategy.

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The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a product. The FDA and other agencies, including the Department of Justice, closely regulate and monitor the post-approval marketing and promotion of products 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 any 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 health care fraud and abuse laws and state consumer protection laws.

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

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- restrictions on coverage by third-party payors;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of products;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

We may seek a Breakthrough Therapy designation for one or more of our 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.

We may seek a Breakthrough Therapy designation for one or more of our product candidates. A Breakthrough Therapy is defined as a product that is intended, alone or in combination with one or more other products, to treat a serious 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. For 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. Products 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 FDA.

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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 products 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 one or more of our 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 product 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 product 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.

Current and future legislation may increase the difficulty and cost for us and any 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 a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability, or the ability of any future collaborators, to profitably sell any products for which we, or they, obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any future collaborators, may receive for any approved products.

In March 2010 for example, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the PPACA. Among the provisions of the PPACA of potential importance to our business and 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 rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of healthcare fraud and abuse laws, including the civil False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;

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- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices to eligible beneficiaries during their coverage gap period, as a condition for a manufacturer's outpatient drugs 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 teaching hospitals;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted since the PPACA 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 will stay in effect through 2024 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.

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 product labeling and post-marketing testing and other requirements.

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

In some countries, such as the countries 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. To obtain reimbursement or pricing approval in some countries, we, or any future collaborators, may be required to conduct a clinical trial that compares the cost-effectiveness of our product to 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 business could be harmed.

We may be subject to certain healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, fines, disgorgement, exclusion from participation in government healthcare programs, curtailment or restricting of our operations, and diminished profits and future earnings.

Healthcare providers, third-party payors and others will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our future arrangements with healthcare providers and third-party payors will 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 any products for which we obtain marketing approval. Potentially applicable U.S. federal and state healthcare laws and regulations include the following:

Anti-Kickback Statute. The federal Anti-Kickback Statute prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, 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 under federal healthcare programs such as Medicare and Medicaid;

False Claims Laws. The federal false claims laws, including the civil False Claims Act, impose criminal and civil penalties, including those from civil whistleblower or *qui tam* actions against individuals or entities for knowingly presenting, or causing to be presented to the federal government claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;

HIPAA. The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing or attempting to execute a scheme to defraud any healthcare benefit program;

HIPAA and HITECH. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or the HITECH Act, also imposes obligations on certain types of individuals and entities, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

False Statements Statute. The federal false statements statute prohibits 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;

Transparency Requirements. The federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to report annually to the U.S. Department of Health and Human Services information related to physician payments and other transfers of value and physician ownership and investment interests; and

Analogous State and Foreign Laws. Analogous state laws and regulations, such as state anti-kickback and false claims laws, and transparency laws, may apply to sales or marketing arrangements, and claims involving healthcare items or services reimbursed by non-governmental third party payors, including private insurers, and 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. Many state 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

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by HIPAA, thus complicating compliance efforts. Foreign laws also govern the privacy and security of health information in many circumstances.

Efforts to ensure that our business arrangements with third parties, and our business generally, 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 products from government funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, and reputational harm, any of which could substantially disrupt our operations. If any of the physicians or other providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

We are subject to U.S. and foreign anti-corruption and anti-money laundering laws with respect to our operations and non-compliance with such laws can subject us to criminal and/or civil liability and harm our business.

We are subject to the U.S. Foreign Corrupt Practices Act of 1977, as amended, or the FCPA, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and possibly other state and national anti-bribery and anti-money laundering laws in countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, third-party intermediaries, joint venture partners and collaborators from authorizing, promising, offering, or providing, directly or indirectly, improper payments or benefits to recipients in the public or private sector. We may have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. In addition, we may engage third party intermediaries to promote our clinical research activities abroad and/or to obtain necessary permits, licenses, and other regulatory approvals. We can be held liable for the corrupt or other illegal activities of these third-party intermediaries, our employees, representatives, contractors, partners, and agents, even if we do not explicitly authorize or have actual knowledge of such activities.

Prior to the completion of this offering, we will adopt a Code of Business Conduct and Ethics, which will be effective upon the completion of this offering, and expect to prepare and implement policies and procedures to ensure compliance with such code. The Code of Business Conduct and Ethics mandates compliance with the FCPA and other anti-corruption laws applicable to our business throughout the world. However, we cannot assure you that our employees and third party intermediaries will comply with this code or such anti-corruption laws. Noncompliance with anti-corruption and anti-money laundering laws could subject us to whistleblower complaints, investigations, sanctions, settlements, prosecution, other enforcement actions, disgorgement of profits, significant fines, damages, other civil and criminal penalties or injunctions, suspension and/or debarment from contracting with certain persons, the loss of export privileges, reputational harm, adverse media coverage, and other collateral consequences. If any subpoenas, investigations, or other enforcement actions are launched, or governmental or other sanctions are imposed, or if we do not prevail in any possible civil or criminal litigation, our business, results of operations and financial condition could be materially harmed. In addition, responding to any action will likely result in a materially significant diversion of management's attention and resources and significant defense and compliance costs and other professional fees. In certain cases, enforcement authorities may even cause us to appoint an independent compliance monitor which can result in added costs and administrative burdens.

We are subject to governmental export and import controls that could impair our ability to compete in international markets due to licensing requirements and subject us to liability if we are not in compliance with applicable laws.

Our products and solutions are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, and various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls. Exports of our products and solutions outside of the United States must be made in compliance with these laws and regulations. If we fail to comply with these laws and regulations, we and certain of our employees could be subject to substantial civil or criminal penalties, including the possible loss of export or import privileges; fines, which may be imposed on us and responsible employees or managers; and, in extreme cases, the incarceration of responsible employees or managers.

In addition, changes in our products or solutions or changes in applicable export or import laws and regulations may create delays in the introduction, provision, or sale of our products and solutions in international markets, prevent customers from using our products and solutions or, in some cases, prevent the export or import of our products and solutions to certain countries, governments or persons altogether. Any limitation on our ability to export, provide, or sell our products and solutions could adversely affect our business, financial condition and results of operations.

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 harm 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. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our 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 for failure to comply with such laws and regulations.

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, but this insurance may not provide adequate coverage against potential liabilities. However, we do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us.

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

Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. The most recent global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as the most recent global financial crisis, could result in a variety of risks to our business, including weakened demand for our product candidate and our ability to raise additional capital when needed on acceptable terms, if at all. This is particularly true in the European Union, which is undergoing a continued severe economic crisis. A weak or declining economy could strain our suppliers, possibly

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resulting in supply disruption, or cause delays in payments for our services by third-party payors or our collaborators. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

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

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

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 have established, 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. 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.

Risks Related to Employee Matters and Managing Growth

Our future success depends on our ability to retain our executive officers and to attract, retain and motivate qualified personnel.

We are highly dependent on the pharmaceutical research and development and business development expertise of Nancy Simonian, M.D., our president and chief executive officer; Kyle D. Kovalanka, our chief operating officer; Eric R. Olson, Ph.D., our chief scientific officer; David A. Roth, M.D., our chief medical officer; Jorge Conde, our chief financial officer; and Jonathan Garen, our chief business officer. Each of these executive officers is employed "at will," meaning any of them may terminate his or her employment with us at any time with or without notice and for any reason or no reason. In the future, we may be dependent on other members of our management, scientific and development team.

Our ability to compete in the biotechnology and pharmaceuticals industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. Our industry has experienced a high rate of turnover of management personnel in recent years. If we lose one or more of our executive officers or other key employees, our ability to implement our business strategy successfully could be seriously harmed. Furthermore, replacing executive officers or other key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain marketing approval of and commercialize products successfully. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key employees 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.

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 other entities and may have commitments under consulting or advisory contracts with those entities that may limit their availability to us. If we are unable to continue to attract and retain highly qualified personnel, our ability to develop and commercialize our product candidates will be limited.

We expect to expand our organization, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

As of January 28, 2016, we had 48 full-time employees. We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug manufacturing, regulatory affairs and sales, marketing and distribution. To manage these growth activities, 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. Our management may need to devote a significant amount of its attention to managing these growth activities. 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 or relocation of our operations, retain key employees, or identify, recruit and train additional qualified personnel. Our inability to manage the expansion or relocation of our operations effectively may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could also require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If we are unable to effectively manage our expected growth, our expenses may increase more than expected, our ability to generate revenues could be reduced and we may not be able to implement our business strategy, including the successful commercialization of our product candidates.

We may engage in acquisitions that could disrupt our business, cause dilution to our stockholders or reduce our financial resources.

In the future, we may enter into transactions to acquire other businesses, products or technologies. Because we have not made any acquisitions to date, our ability to do so successfully is unproven. If we do identify suitable candidates, we may not be able to make such acquisitions on favorable terms, or at all. Any acquisitions we make may not strengthen our competitive position, and these transactions may be viewed negatively by customers or investors. We may decide to incur debt in connection with an acquisition or issue our common stock or other equity securities to the stockholders of the acquired company, which would reduce the percentage ownership of our existing stockholders. We could incur losses resulting from undiscovered liabilities of the acquired business that are not covered by the

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indemnification we may obtain from the seller. In addition, we may not be able to successfully integrate the acquired personnel, technologies and operations into our existing business in an effective, timely and non-disruptive manner. Acquisitions may also divert management attention from day-to-day responsibilities, increase our expenses and reduce our cash available for operations and other uses. We cannot predict the number, timing or size of future acquisitions or the effect that any such transactions might have on our operating results.

Risks Related to Our Common Stock and This Offering

No public market for our common stock currently exists, and 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. This price will not necessarily reflect the price at which investors in the market will be willing to buy and sell our shares following this offering. 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, if developed, be maintained following this offering. If an active market for our common stock does not develop or is not maintained, 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. An inactive trading market may also impair our ability to raise capital to continue to fund operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

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

The initial public offering price of our common stock is substantially higher than the 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 net tangible book value per share after this offering. Based on 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, you will experience immediate dilution of \$ per share, representing the difference between our pro forma net tangible book value per share after giving effect to this offering and the assumed initial public offering price. Purchasers of common stock in this offering will have contributed approximately % of the aggregate price paid by all purchasers of our stock and will own approximately % of our common stock outstanding after this offering, excluding any shares of our common stock that they may have acquired prior to this offering. Furthermore, if the underwriters exercise their over-allotment option or our previously issued options to acquire common stock at prices below the assumed initial public offering price are exercised, you will experience further dilution. For additional information on the dilution that you will experience immediately after this offering, see the section titled "Dilution."

The price of our common stock is likely to be highly volatile, which could result in substantial losses for purchasers of our common stock in this offering.

Our stock price is likely to be highly volatile. The stock market in general and the market for smaller 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 and you may lose some or all of your investment. The market price for our common stock may be influenced by many factors, including:

- the timing and results of clinical trials of SY-1425 and any product candidates that we may advance into clinical development under our CDK7 inhibitor program;
- the success of existing or new competitive products or technologies;

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- regulatory actions with respect to our product candidates or our competitors' products and product candidates;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- commencement or termination of collaborations for our 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 clinical development programs;
- the results of our efforts to develop additional product candidates or products;
- actual or anticipated changes in estimates as to financial results or development timelines or recommendations by securities analysts;
- 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.

Additionally, our stock price is likely to be volatile, and in the past companies that have experienced volatility in the market price of their stock have been subject to an increased incidence of securities class action litigation. 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 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 or in ways with which you agree.

Although we currently intend to use the net proceeds from this offering in the manner described in the section titled "Use of Proceeds" in this prospectus, 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. You will not have the opportunity to influence our decisions on how to use our net proceeds from this offering. The failure by our management to apply these funds effectively could result in financial losses that could harm 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, and may remain an emerging growth company for up to five years. For so long as we remain an emerging growth company, we are permitted and plan 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 SOX Section 404, not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, reduced disclosure obligations regarding executive compensation and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. In this prospectus, we have provided only two years of audited financial statements and 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 and corporate governance practices.

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. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The NASDAQ Global Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. We expect that we will need to hire additional accounting, finance and other personnel in connection with our becoming, and our efforts to comply with the requirements of being, a public company and our management and other personnel will need to devote a substantial amount of time towards maintaining compliance with these requirements. These requirements will increase our legal and financial compliance costs and will make some activities more time consuming and costly. For example, we expect that the rules and regulations applicable to us as a public company may make it more difficult and more expensive for us to obtain director and officer liability insurance, which could make it more difficult for us to attract and retain qualified members of our board of directors. We are currently evaluating these rules and regulations, and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

We have identified material weaknesses in our internal control over financial reporting. If we are unable to remedy our material weaknesses, or if we fail to establish and maintain effective internal controls, we may be unable to produce timely and accurate financial statements, and we may conclude that our internal control over financial reporting is not effective, which could adversely impact our investors' confidence and our stock price.

Prior to this offering, we were a private company and had limited accounting and financial reporting personnel and other resources with which to address our internal controls and related procedures. In connection with the audit of our consolidated financial statements for the years ended December 31, 2013 and 2014, we and our independent registered public accounting firm identified material weaknesses in our internal control over financial reporting. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis. The material weaknesses related to our controls over the classification of certain indirect and other expenses between general and administrative and research and development, and to the accounting for stock-based compensation. We also identified deficiencies related to our controls over our accounting for income taxes. The material weaknesses that we identified were due to the lack of appropriate oversight and review procedures by accounting personnel to properly identify and evaluate certain accounting matters that resulted in errors in our financial statements.

We are implementing measures designed to improve our internal control over financial reporting to remediate these material weaknesses, including the following:

- we are formalizing our processes and internal control documentation and strengthening supervisory reviews by our management;
- we have hired additional qualified accounting personnel and engaged financial consultants, both of whom have significant accounting and financial reporting experience, which will enable the implementation of internal controls over financial reporting and segregating duties amongst accounting personnel;
- we expect to hire additional senior accounting and finance staff to complete this remediation; and
- we intend to implement certain accounting systems to automate manual processes, such as tracking and accounting for stock-based awards.

We expect to incur additional costs to remediate these weaknesses, primarily personnel costs and external consulting fees. We cannot assure you that the measures we have taken to date, together with any measures we may take in the future, will be sufficient to remediate the control deficiencies that led to the material weaknesses in our internal control over financial reporting or to avoid potential future material weaknesses. In addition, neither our management nor an independent registered public accounting firm has ever performed an evaluation of our internal control over financial reporting in accordance with the provisions of the Sarbanes-Oxley Act because no such evaluation has been required. Had we or our independent registered public accounting firm performed an evaluation of our internal control over financial reporting in accordance with the provisions of the Sarbanes-Oxley Act, additional material weaknesses may have been identified. If we are unable to successfully remediate our existing or any future material weaknesses in our internal control over financial reporting, or if we identify any additional material weaknesses, the accuracy and timing of our financial reporting may be adversely affected, we may be unable to maintain compliance with securities law requirements regarding timely filing of periodic reports in addition to applicable stock exchange listing requirements, investors may lose confidence in our financial reporting, and our stock price may decline as a result.

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We also could become subject to investigations by NASDAQ, the Securities and Exchange Commission, or SEC, or other regulatory authorities.

As a result of becoming a public company, we will be obligated to develop and maintain proper and effective internal controls over financial reporting. Any failure to maintain the adequacy of these internal controls may adversely affect investor confidence in our company and, as a result, the value of our common shares.

Pursuant to SOX Section 404 we will be required to furnish a report by our management on our internal control over financial reporting beginning with our second filing of an Annual Report on Form 10-K with the Securities and Exchange Commission, or SEC, after we become a public company. 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. This assessment will need to include disclosure of any material weaknesses identified by our management in our internal control over financial reporting. Our independent registered public accounting firm will not be required to attest to the effectiveness of our internal control over financial reporting until our first annual report required to be filed with the SEC following the date we are no longer an "emerging growth company," as defined in the JOBS Act. At such time as we are required to obtain auditor attestation, if we then have a material weakness, we would receive an adverse opinion regarding our internal control over financial reporting from our independent registered accounting firm.

To achieve compliance with SOX 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. During our evaluation of our internal control, if we identify one or more material weaknesses in our internal control over financial reporting, we will be unable to assert that our internal control over financial reporting is effective. We cannot assure you that there will not be material weaknesses or significant deficiencies in our internal control over financial reporting in the future. Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition or results of operations. If we are unable to conclude that our internal control over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness or significant deficiency in our internal control over financial reporting, we could lose investor confidence in the accuracy and completeness of our financial reports, the market price of our ordinary shares could decline, and we could be subject to sanctions or investigations by NASDAQ, the SEC or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets.

A significant portion of our total outstanding shares is 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 decline 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 of common stock intend to sell shares, could reduce the market price of our common stock. Following this offering, we will have _____ shares of common stock outstanding based on the 69,507,802 shares of our common stock outstanding as of January 28, 2016 after giving effect to the conversion of all outstanding shares of our preferred stock into 59,958,081 shares of our common stock upon the closing

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of this offering. Of these shares, the _____ shares sold by us in this offering may be resold in the public market immediately, unless purchased by our affiliates. The remaining 69,507,802 shares are currently restricted under securities laws or as a result of lock-up or other agreements, but will be able to be sold after this offering as described in the "Shares Eligible for Future Sale" section of this prospectus. The representatives of the underwriters may release these stockholders from their lock-up agreements with the underwriters at any time and without notice, which would allow for earlier sales of shares in the public market.

Moreover, after this offering, holders of an aggregate of 62,122,135 shares of our common stock will have rights, subject to conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We also plan to register all 22,635,367 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 and once vested, subject to volume limitations applicable to affiliates and the lock-up agreements described in the "Underwriting" section of this prospectus. If additional shares are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

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

As of December 31, 2014, we had federal and state net operating loss carryforwards of \$20.3 million and \$20.2 million, respectively, and federal research and development tax credit carryforwards of \$0.8 million, each of which if not utilized will expire at various dates through 2034. These net operating loss and tax credit carryforwards could expire unused and be unavailable to offset future income tax liabilities. In addition, under Section 382 of the Internal Revenue Code of 1986, as amended, and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50% change, by value, in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income may be limited. We have not determined if we have experienced Section 382 ownership changes in the past and if a portion of our net operating loss and tax credit carryforwards are subject to an annual limitation under Section 382. In addition, we may experience ownership changes in the future as a result of subsequent shifts in our stock ownership, including this offering, some of which may be outside of our control. We have not conducted a detailed study to document whether our historical activities qualify to support the research and development credit carryforwards. A detailed study could result in adjustment to our research and development credit carryforwards. If we determine that an ownership change has occurred and our ability to use our historical net operating loss and tax credit carryforwards is materially limited, or if our research and development carryforwards are adjusted, it would harm our future operating results by effectively increasing our future tax obligations.

We do not anticipate paying any cash dividends on our capital stock in the foreseeable future. Accordingly, stockholders must rely on capital appreciation, if any, for any return on their investment.

We have never declared nor paid cash dividends on our capital stock. We currently plan to retain all of our future earnings, if any, to finance the operation, development and growth of our business. In addition, the terms of any future debt or credit 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.

Concentration of ownership of our common stock among our existing executive officers, directors and principal stockholders may prevent new investors from influencing significant corporate decisions.

Based upon shares outstanding as of January 28, 2016, upon the closing of this offering, our executive officers and directors, combined with our stockholders who owned more than 5% of our outstanding common stock before this offering and their affiliates, 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 ownership control may:

- delay, defer or prevent a change in control;
- entrench our management or the board of directors; or
- impede a merger, consolidation, takeover or other business combination involving us that other stockholders may desire.

Some of these persons or entities may have interests different than yours. For example, because many of these stockholders purchased their shares at prices substantially below the price at which shares are being sold in this offering and have held their shares for a longer period, they may be more interested in selling our company to an acquirer than other investors or they may want us to pursue strategies that deviate from the interests of other stockholders.

Provisions in our certificate of incorporation and bylaws and under Delaware law may prevent or frustrate attempts by our stockholders to change our management or hinder efforts to acquire a controlling interest in us.

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 all members of the board are not 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 nominations for election to the board of directors or for proposing matters that can be acted on at stockholder meetings;
- 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 a special meeting of stockholders;
- 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 certificate of incorporation or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, 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. This could discourage, delay or prevent someone from acquiring us or merging with us, whether or not it is desired by, or beneficial to, our stockholders. This could also have the effect of discouraging others from making tender offers for our common stock, including transactions that may be in your best interests. These provisions may also prevent changes in our management or limit the price that investors are willing to pay for our stock.

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

The trading market for our common stock will likely depend in part on the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. We do not currently have research coverage, and there can be no assurance that analysts will cover us, or provide favorable coverage. Securities or industry analysts may elect not to provide research coverage of our common stock after this offering, and such lack of research coverage may negatively impact the market price of our common stock. In the event we do have analyst coverage, if one or more analysts downgrade our stock or change their opinion of our stock, our share price would likely decline. In addition, if one or more analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our share price or trading volume to decline.

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 our company and our directors and officers.

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 or officers, which may discourage such lawsuits against us and our directors and officers.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This prospectus contains forward-looking statements that involve substantial risks and uncertainties. The forward-looking statements are contained principally in the sections of this prospectus entitled "Prospectus Summary," "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Business," but are also contained elsewhere in this prospectus. 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. In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. The forward-looking statements and opinions contained in this prospectus are based upon information available to us as of the date of this prospectus and, while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information.

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

- our plans to initiate clinical trials for SY-1425 and product candidates we may advance under our CDK7 inhibitor program;
- planned clinical trials for our product candidates, whether conducted by us or by any future collaborators, including the timing of these trials and of the anticipated results;
- our plans to research, develop and commercialize our current and future product candidates;
- our expectations regarding the potential benefits of our gene control platform and our approach;
- our plans to seek to enter into collaborations for the development and commercialization of certain product candidates;
- the potential benefits of any future collaboration;
- the timing of and our ability to obtain and maintain regulatory 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 products or product candidates with significant commercial potential;
- our expectations related to the use of proceeds from this offering;
- our estimates regarding expenses, future revenue, capital requirements and need 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

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or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. New risks and uncertainties emerge from time to time, and it is not possible for us to predict all risks and uncertainties that could have an impact on the forward-looking statements contained in this prospectus. 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. The Private Securities Litigation Reform Act of 1995 and Section 27A of the Securities Act of 1933, as amended, do not protect any forward-looking statements that we make in connection with this offering.

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. All of the market data used in this prospectus involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. We believe that the information from these industry publications, surveys and studies is reliable. The industry in which we operate is subject to a high degree of uncertainty and risk due to a variety of important factors, including those described in the section titled "Risk Factors." These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us.

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 \$ _____ million, or \$ _____ million if the underwriters exercise their over-allotment option 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, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

Each \$1.00 increase (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 (decrease) our net proceeds from this offering 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 underwriting discounts and commissions and estimated offering expenses payable by us. Each increase (decrease) of _____ shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase (decrease) our net proceeds from this offering by \$ _____ million, assuming no change in the assumed initial public offering price per share and after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

As of September 30, 2015, we had cash and cash equivalents of \$45.0 million. In January 2016, we received an additional \$40 million of aggregate proceeds from our preferred stock financing. We currently estimate that we will use the net proceeds from this offering as follows:

- approximately \$ _____ million to fund our proof-of-concept Phase 2 clinical trial of SY-1425 in AML and MDS, including clinical research outsourcing, drug manufacturing, companion diagnostic development and internal personnel costs, with costs to be approximately allocated based on the number of AML and MDS patients enrolled in this trial, respectively;
- approximately \$ _____ million to fund our IND-enabling activities and Phase 1/2 clinical trial for our CDK7 inhibitor program, including clinical research outsourcing, drug manufacturing and internal personnel costs;
- approximately \$ _____ million to begin development of SY-1425 for additional indications;
- approximately \$ _____ million for new and ongoing research activities, including for our preclinical programs and our platform with a goal of systematically delivering additional INDs; and
- the remainder for working capital and other general corporate purposes.

To the extent our actual net proceeds from this offering are insufficient to fund this allocation, we expect to use some of our existing cash and cash equivalents to fund any difference.

This expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions. 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. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering. We have no current agreements, commitments or understandings for any material acquisitions or licenses of any products, businesses or technologies.

Based on our planned use of the net proceeds from this offering, we estimate that such funds will be sufficient to enable us to reach proof-of-concept data readouts for SY-1425 in AML and MDS and our CDK7 inhibitor program in acute leukemias and 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 do not expect that the net proceeds from this offering and our existing cash and cash equivalents will be sufficient to enable us to fund the completion of development of any of our product candidates.

Pending our use of the net proceeds from this offering, we intend to invest the net proceeds in 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. Any future determination to pay cash dividends will be made at the discretion of our board of directors and will depend on restrictions and other factors our board of directors may deem relevant. Investors should not purchase our common stock with the expectation of receiving cash dividends.

CAPITALIZATION

The following table sets forth our cash and cash equivalents and our capitalization as of September 30, 2015 on:

- an actual basis excluding 1,243,296 shares of our common stock that are subject to repurchase by us;
- a pro forma basis to give effect to (i) the completion of our Series B preferred stock financing in January 2016, in which we issued and sold an aggregate of 12,714,150 shares of our Series B preferred stock for an aggregate purchase price of \$40 million, (ii) the conversion of all outstanding shares of our preferred stock, including the Series B preferred stock sold in January 2016, into an aggregate of 59,958,081 shares of common stock, (iii) the change in our total stockholders' (deficit) equity resulting from the stock-based compensation expense associated with the vesting of 200,000 shares of restricted common stock, and the vesting of performance-based option awards to purchase up to 222,706 shares of our common stock and (iv) the filing and effectiveness of our restated certificate of incorporation, each upon the closing of this offering; and
- a pro forma as adjusted basis to give further effect to the 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 underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this table together with our consolidated financial statements and the related notes included elsewhere in this prospectus and the sections of this prospectus titled "Selected

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Consolidated Financial Data," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Description of Capital Stock."

	September 30, 2015		
	Actual	Pro Forma	Pro Forma As Adjusted
	(unaudited) (in thousands, except share and per share data)		
Cash and cash equivalents	\$ 44,985	\$ 84,817	\$
Series A convertible preferred stock, \$0.001 par value; 30,350,000 shares authorized, issued and outstanding, actual; no shares authorized, issued and outstanding, pro forma and pro forma as adjusted	\$ 29,015	\$ —	\$
Series B convertible preferred stock, \$0.001 par value; 16,893,931 shares authorized, issued and outstanding, actual; no shares authorized, issued and outstanding pro forma and pro forma as adjusted	52,998	—	
Stockholders' (deficit) equity:			
Preferred stock, \$0.001 par value: no shares authorized, issued and outstanding actual; 10,000,000 shares authorized, no shares issued and outstanding pro forma and pro forma as adjusted	—	—	
Common stock, \$0.001 par value; 78,886,062 shares authorized, 8,384,486 shares issued and outstanding, actual; 200,000,000 shares authorized, 68,542,567 shares issued and outstanding, pro forma; 200,000,000 shares authorized, shares issued and outstanding, pro forma as adjusted	8	69	
Additional paid-in capital	4,636	127,068	
Accumulated deficit	(42,824)	(43,472)	
Total stockholders' (deficit) equity	(38,180)	83,665	
Total capitalization	\$ 43,833	\$ 83,665	\$

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. Each \$1.00 increase (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 (decrease) the pro forma as adjusted amount of each additional paid-in-capital, total stockholders' (deficit) 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 underwriting discounts and commissions and estimated expenses payable by us. Each increase (decrease) of shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of additional paid-in-capital, total stockholders' (deficit) equity and total capitalization by \$ million, assuming no change in the assumed initial public offering price per share and after deducting underwriting discounts and commissions and estimated expenses payable by us.

The number of shares of our common stock shown as outstanding on an actual, pro forma and pro forma as adjusted basis in the table above does not include:

- 7,088,929 shares of our common stock issuable upon the exercise of stock options outstanding as of September 30, 2015, at a weighted-average exercise price of \$0.74 per share;

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- 384,752 shares of our common stock available for future issuance as of September 30, 2015 under our 2012 equity incentive plan; and
- 11,700,000 and 2,200,000 additional shares of our common stock that will become available for future issuance under our 2016 stock incentive plan and our 2016 employee stock purchase plan, respectively, each of which will become effective immediately prior to the closing of this offering, as well as any automatic increases in the number of shares of common stock reserved for future issuance under these plans.

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 deficit as of September 30, 2015 was \$38.2 million, or \$3.97 per share of our common stock. Our historical net tangible book deficit is the amount of our total tangible assets less our total liabilities. Historical net tangible book deficit per share represents historical net tangible book deficit, including our convertible preferred stock divided by the 9,627,782 shares of our common stock outstanding as of September 30, 2015, including 1,243,296 shares of unvested restricted stock subject to repurchase by us.

Our pro forma net tangible book value as of September 30, 2015 was \$83.7 million, or \$1.20 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 completion of our Series B preferred stock financing in January 2016 in which we issued and sold an aggregate of 12,714,150 shares of our Series B preferred stock for an aggregate purchase price of \$40 million and the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 59,958,081 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 69,585,863 shares of our common stock outstanding as of September 30, 2015.

After giving 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 underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of September 30, 2015 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 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 September 30, 2015	\$ (3.97)
Increase per share attributable to pro forma adjustments	5.17
Pro forma net tangible book value per share as of September 30, 2015	1.20
Increase in net tangible book value per share attributable to new investors	_____
Pro forma as adjusted net tangible book value per share after this offering	_____
Dilution per share to new investors	\$ _____

The dilution information discussed above is illustrative only and will change based on the actual initial public offering price and other terms of this offering determined at pricing. Each \$1.00 increase (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 (decrease) the pro forma as adjusted net tangible book value per share 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 underwriting discounts and commissions and estimated offering expenses payable by us. An increase (decrease)

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

If the underwriters exercise their over-allotment option in full, the pro forma as adjusted net tangible book value will increase to \$ _____ per share, representing an immediate increase to existing stockholders of \$ _____ per share and an immediate dilution of \$ _____ per share to new investors. If any shares are issued upon exercise of outstanding options, you will experience further dilution.

The following table summarizes, on a pro forma as adjusted basis as of September 30, 2015, 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 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%	100%	100%	

Each \$1.00 increase (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 (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 (decrease) of _____ shares in the number of shares offered by us, as set forth on the cover page of this prospectus, would increase (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 number of shares purchased from us by existing stockholders is based on 69,585,863 shares of our common stock outstanding as of September 30, 2015, after giving effect to the completion of our Series B preferred stock financing in January 2016 in which we issued and sold an aggregate of 12,714,150 shares of our Series B preferred stock and the automatic conversion of all of our outstanding shares of preferred stock into 59,958,081 shares of common stock upon the closing of this offering, and excludes:

- 7,088,929 shares of our common stock issuable upon the exercise of stock options outstanding as of September 30, 2015, at a weighted-average exercise price of \$0.74 per share;
- 384,752 additional shares of our common stock available for future issuance as of September 30, 2015 under our 2012 equity incentive plan; and

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- 11,700,000 and 2,200,000 additional shares of our common stock that will become available for future issuance under our 2016 stock incentive plan and our 2016 employee stock purchase plan, respectively, each of which will become effective immediately prior to the closing of this offering, as well as any automatic increases in the number of shares of common stock reserved for future issuance under these plans.

To the extent that stock options are exercised, new stock options are issued under our equity incentive plans, or we issue additional shares of common stock in the future, there will be further dilution to investors participating in this offering. In addition, we may choose to raise additional capital because of market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans. If we raise additional capital through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

If the underwriters exercise their overallotment option in full, the following will occur:

- the percentage of shares of our common stock held by existing stockholders will decrease to _____ % of the total number of shares of our common stock outstanding after this offering; and
- the number of shares of our common stock held by new investors will increase to _____, or _____ % of the total number of shares of our common stock outstanding after this offering.

SELECTED CONSOLIDATED FINANCIAL DATA

You should read the following selected consolidated financial data together with our consolidated financial statements and the related notes included elsewhere in 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, 2013 and 2014 and the balance sheet data as of December 31, 2013 and 2014 from our audited consolidated financial statements included elsewhere in this prospectus. We have derived the statement of operations data for the nine months ended September 30, 2014 and 2015 and the balance sheet data as of September 30, 2015 from our unaudited consolidated financial statements included elsewhere in this prospectus, which have been prepared on the same basis as the audited consolidated financial statements. In the opinion of management, the unaudited consolidated financial data reflects all adjustments, consisting only of normal recurring adjustments, necessary for a fair presentation of the financial information as of and for the periods presented. 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,		Nine Months Ended September 30,	
	2013	2014	2014	2015
	(unaudited)			
	(in thousands, except share and per share data)			
Statements of Operations Data:				
Revenue	\$ —	\$ —	\$ —	\$ 317
Operating expenses:				
Research and development	6,266	10,923	7,901	16,030
General and administrative	2,367	2,512	1,843	3,418
Total operating expenses	8,633	13,435	9,744	19,448
Loss from operations	(8,633)	(13,435)	(9,744)	(19,131)
Other income (expense), net	(32)	4	2	2
Net loss and comprehensive loss	\$ (8,665)	\$ (13,431)	\$ (9,742)	\$ (19,129)
Net loss per share applicable to common stockholders—basic and diluted(1)	\$ (2.25)	\$ (2.74)	\$ (1.93)	\$ (3.26)
Weighted-average number of common shares used in net loss per share applicable to common stockholders—basic and diluted(1)	4,110,716	5,718,844	5,599,543	6,997,532
Pro forma net loss per share—basic and diluted (unaudited)(1)		\$ (0.37)		\$ (0.36)
Weighted-average number of common shares used in pro forma net loss per share—basic and diluted (unaudited)(1)		35,901,743		54,250,987

- (1) See Note 2 to our consolidated financial statements included elsewhere in this prospectus for a description of the method used to calculate basic and diluted net loss per share and unaudited pro forma basic and diluted net loss per share as well as the weighted-average number of common shares used in the calculation of the per share amounts.

	<u>December 31,</u>		<u>September 30,</u>
	<u>2013</u>	<u>2014</u>	<u>2015</u>
	<u>(unaudited)</u>		
	<u>(in thousands)</u>		
Balance Sheet Data:			
Cash and cash equivalents	\$ 3,801	\$ 60,393	\$ 44,985
Working capital(1)	3,003	59,291	40,821
Total assets	4,921	61,494	50,042
Convertible preferred stock	13,266	82,013	82,013
Total stockholders' deficit	(9,293)	(21,772)	(38,180)

- (1) We define working capital as current assets less current liabilities. See our consolidated financial statements for further details regarding our current assets and 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 section of this prospectus titled "Selected Consolidated Financial Data" and our consolidated financial statements and related notes included elsewhere in this prospectus. This discussion and other parts of this prospectus contain forward-looking statements that involve risk 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 biopharmaceutical company applying a pioneering approach to discover and develop medicines that control the expression of genes with the aim of treating cancer and other serious diseases. We have built a proprietary platform that provides a unique lens to systematically and efficiently identify crucial genes that become dysregulated in diseased cells and create medicines that return cells to a non-diseased state. We believe that our platform will allow us to create a pipeline of gene control medicines that will provide a profound and durable benefit for currently underserved patients. By focusing on genomically defined subsets of patients, we believe we can conduct efficient clinical trials with a higher likelihood of success. We intend to submit an investigational new drug application, or IND, to the Food and Drug Administration, or FDA, and advance our lead product candidate, SY-1425 (tamibarotene), into a Phase 2 clinical trial, in mid-2016. This trial is expected to initially enroll genomically defined subsets of patients with acute myelogenous leukemia, or AML, and myelodysplastic syndromes, or MDS, identified by our gene control platform. We plan to submit an IND for our second program targeting cyclin-dependent kinase 7, or CDK7, which is an important gene control target in several cancers, initially for the treatment of acute leukemias, in the second half of 2016. Leveraging our platform, we are also generating a pipeline of novel preclinical drug candidates for genomically defined subsets of patients. Our goal is to build a fully integrated biopharmaceutical company based on our leadership position in gene control.

Since our inception in November 2011, we have devoted substantially all of our resources to organizing and staffing our company, business planning, raising capital, developing our technology platform and conducting preclinical research for our product candidates. We do not have any products approved for sale and have not generated any revenue from product sales. We have financed our operations to date primarily through private placements of preferred stock. From inception through September 30, 2015, we have raised an aggregate of \$82.0 million of gross proceeds from sales of our preferred stock and the issuance of convertible notes that subsequently converted to preferred stock to fund operations. In January 2016, we completed the sale of shares of our Series B preferred stock for aggregate proceeds of \$40 million.

Since inception, we have incurred significant operating losses. Our net losses were \$8.7 million and \$13.4 million for the years ended December 31, 2013 and 2014, respectively, and \$19.1 million for the nine months ended September 30, 2015. As of September 30, 2015, we had an accumulated deficit of \$42.8 million. We expect to continue to incur significant expenses and operating losses for the foreseeable future. We anticipate that our expenses will increase significantly in connection with our ongoing activities, as we:

- pursue clinical development of our lead product candidate, SY-1425, including a Phase 2 clinical trial we expect to initiate in the middle of 2016;
- continue development efforts for our CDK7 inhibitor program, for which we plan to submit an IND in the second half of 2016 and initiate a Phase 1/2 clinical trial in the first half of 2017;

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- continue our disease mapping efforts;
- initiate and continue research, preclinical and clinical development efforts for other gene control programs;
- seek regulatory and marketing approvals for our product candidates that successfully complete clinical trials, if any;
- continue investment in our proprietary gene control platform;
- develop and scale up our manufacturing processes and capabilities to support our ongoing preclinical activities and clinical trials of our product candidates;
- maintain, expand and protect our intellectual property portfolio;
- hire and retain key scientific personnel; and
- expand our operational, financial and management systems and increase personnel, including personnel to support our clinical development and manufacturing efforts and our operations as a public company upon closing of this offering.

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 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 September 30, 2015, we had cash and cash equivalents of \$45.0 million. We believe that the anticipated net proceeds from this offering, together with our existing cash and cash equivalents as of September 30, 2015 and the \$40 million of aggregate proceeds from our Series B preferred stock financing that we completed in January 2016, will enable us to fund our operating expenses and capital expenditure requirements through at least the next months. See "—Liquidity and Capital Resources."

Financial Operations Overview

Revenue

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from product sales for the foreseeable future. For additional information about our revenue recognition policy, see the section titled "—Critical Accounting Policies and Estimates—Revenue."

Expenses

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including development of our gene control platform and gene control product candidates, which initially focus on cancer indications, and which include:

- employee-related expenses including salaries and benefits;
- stock-based compensation expense;
- external costs of funding research performed by third parties that conduct research and development and preclinical activities on our behalf and of purchasing lab supplies used in designing, developing and manufacturing preclinical study materials;
- consulting, licensing and professional fees related to research and development activities; and

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- facilities costs, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities and insurance.

Research and development costs are expensed as incurred. Nonrefundable advance payments made to vendors for goods or services that will be received in the future for use in research and development activities are deferred and capitalized, even when there is no alternative future use for the research and development, until related goods or services are provided.

The following summarizes our most advanced current research and development programs:

- Our lead product candidate, SY-1425, is an oral, potent and selective RARa agonist. We plan to initiate a Phase 2 clinical trial in genomically defined patients with AML and MDS in mid-2016.
- Our CDK7 inhibitor program is focused on the treatment of subsets of cancers that are dependent on certain transcription factors for their growth and survival. We have generated potent and highly selective small molecule CDK7 inhibitors. We expect to select our development candidate in the first half of 2016, submit an IND in the second half of 2016 and initiate a Phase 1/2 clinical trial in patients with acute leukemias in the first half of 2017.

We typically use our employee, consultant and infrastructure resources across our development programs. We track outsourced development costs by product candidate or development program, but we do not allocate personnel costs, other internal costs or external consultant costs to specific product candidates or development programs.

We have not provided program costs for the years ended December 31, 2013 and 2014 because prior to 2015, we did not track or record our research and development expenses on a program-by-program basis. The following table summarizes our research and development expenses by program (in thousands) for the nine months ended September 30, 2015:

CDK7 external costs	\$ 4,799
SY-1425 external costs	824
Other research and platform programs external costs	3,813
Employee-related expenses, including stock-based compensation	5,539
Facilities and other expenses	1,055
Total research and development expenses	<u>\$ 16,030</u>

We expect our research and development expenses will increase for the foreseeable future as we seek to advance our programs. At this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the development of our product candidates. We are also unable to predict when, if ever, material net cash inflows will commence from sales of our product candidates. This is due to the numerous risks and uncertainties associated with developing such product candidates, including the uncertainty of:

- successful completion of preclinical studies, including IND-enabling activities and minimally efficacious dose studies in animals, where applicable and requested under the FDA's good laboratory practice, or GLP, requirements;
- approval of INDs for our product candidates to commence planned or future clinical trials;
- successful enrollment in, and completion of preclinical studies and clinical trials;
- successful data from our clinical program that supports an acceptable benefit-risk profile of our product candidates in the intended populations;
- successful development, and subsequent clearance or approval, of companion diagnostics for use as screening criteria for potential patients;
- receipt of regulatory approvals from applicable regulatory authorities;

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- establishment of arrangements with third-party manufacturers for clinical supply and commercial manufacturing and, where applicable, commercial manufacturing capabilities;
- establishment and maintenance of patent and trade secret protection or regulatory exclusivity for our product candidates;
- commercial launch of our product candidates, if and when approved, whether alone or in collaboration with others;
- enforcement and defense of intellectual property rights and claims;
- maintenance of a continued acceptable safety profile of the product candidates following approval; and
- retention of key research and development personnel.

Any changes in the outcome of any of these variables with respect to the development of our product candidates in preclinical and clinical development could mean a significant change in the costs and timing associated with the development of these product candidates. For example, if the FDA or another regulatory authority were to delay our planned start of clinical trials or require us to conduct clinical trials or other testing beyond those that we currently expect or if we experience significant delays in enrollment in any of our planned clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development of our product candidates.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in executive, finance and administrative functions. Other significant costs include corporate facility costs not otherwise included in research and development expenses, legal fees related to patent and corporate matters and fees for accounting and consulting services.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support our continued research activities and development of our product candidates and remediate our material weakness in our internal control over financial reporting. We also anticipate that we will incur increased accounting, audit, legal, regulatory, compliance and director and officer insurance costs as well as investor and public relations expenses associated with being a public company.

Other Income (Expense), Net

Other income (expense), net consists of interest income on our cash and cash equivalents and interest expense related to our convertible promissory notes and equipment financing arrangements.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles, or U.S. GAAP. The preparation of these financial statements requires us to make judgments and estimates that affect the reported amounts of assets, liabilities, revenues 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 are believed to be reasonable under the circumstances. Actual results may differ from these estimates under different assumptions or conditions. On an ongoing basis, we evaluate our judgments and estimates in light of changes in circumstances, facts and experience. The effects of material revisions in estimates, if any, will be reflected in the financial statements prospectively from the date of the change in estimates.

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While our significant accounting policies are described in more detail in the notes to our financial statements appearing elsewhere in this prospectus, we believe the following accounting policies used in the preparation of our financial statements require the most significant judgments and estimates.

Revenue

As of September 30, 2015, all of our revenue was generated exclusively from our research agreement with a multinational pharmaceutical company. We recognize revenue in accordance with Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 605 *Revenue Recognition*, or ASC 605. Accordingly, revenue is recognized for each unit of accounting when all of the following criteria are met:

- persuasive evidence of an arrangement exists;
- delivery has occurred or services have been rendered;
- the seller's price to the buyer is fixed or determinable; and
- collectability is reasonably assured.

We analyze multiple element arrangements based on the guidance in ASC Topic 605-25, *Revenue Recognition—Multiple Element Arrangements*, or ASC 605-25. Pursuant to the guidance in ASC 605-25, we evaluate multiple element arrangements to determine (1) the deliverables included in the arrangement and (2) whether the individual deliverables represent separate units of accounting or whether they must be accounted for as a combined unit of accounting. This evaluation involves subjective determinations and we are required to make judgements about the individual deliverables and whether such deliverables are separate from other aspects of the contractual relationship. Deliverables are considered separate units of accounting provided that: (i) the delivered item(s) has value to the customer on a standalone basis and (ii) the arrangement includes a general right of return relative to the delivered item(s), delivery or performance of the undelivered item(s) is considered probable and substantially within our control.

We recognize arrangement consideration allocated to each unit of accounting when all of the revenue recognition criteria in ASC 605 are satisfied for that particular unit of accounting. In the event that a deliverable does not represent a separate unit of accounting, we recognize revenue from the combined unit of accounting over the contractual or estimated performance period for the undelivered items, which is typically the term of our research and development obligations. If there is no discernible pattern of performance or objectively measurable performance measures do not exist, then we recognize revenue under the arrangement on a straight-line basis over the period we are expected to complete our performance obligations or upon completion when the final act is of such significance to the overall arrangement that performance has not substantively occurred until the completion of that act. Conversely, if the pattern of performance over which the service is provided to the customer can be determined and objectively measurable performance measures exist, then we recognize revenue under the arrangement using the proportional performance method.

Our research agreement contains a single unit of accounting and we recognize service revenue based upon the completed performance method of revenue recognition as we are unable to reasonably estimate the period of performance of the services and the delivery of the final study report is significant to the arrangement.

Research and Development Expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued expenses as of each balance sheet date. This process involves reviewing open contracts 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 cost incurred for the

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service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. The significant estimates in our accrued research and development expenses include the costs incurred for services performed by our service providers in connection with research and development activities for which we have not yet been invoiced.

We record our expenses related to research and development activities based on our estimates of the services received and efforts expended pursuant to quotes and contracts with vendors that conduct research and development 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 research and development expense. In accruing service fees, we estimate the time period over which services will be performed 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 prepaid accordingly. Non-refundable advance payments for goods and services that will be used in future research and development activities are deferred and capitalized, even when there is no alternative future use for the research and development, until related goods or services are provided.

Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts actually incurred.

We have and may in the future in-license the rights to develop and commercialize product candidates. For each in-license transaction we evaluate whether we have acquired processes or activities along with inputs that would be sufficient to constitute a "business" as defined under U.S. GAAP. A "business" as defined under U.S. GAAP consists of inputs and processes applied to those inputs that have the ability to create outputs. Although businesses usually have outputs, outputs are not required for an integrated set of activities to qualify as a business. When we determine that we have not acquired sufficient processes or activities to constitute a business, any up-front payments, as well as milestone payments, are immediately expensed as acquired research and development in the period in which they are incurred.

Stock-Based Compensation

We apply the fair value recognition provisions of ASC Topic 718, *Compensation—Stock Compensation*, or ASC 718. Determining the amount of stock-based compensation to be recorded requires us to develop estimates of the fair value of stock options as of their grant date. Calculating the fair value of stock-based awards requires that we make highly subjective assumptions.

We use the Black-Scholes option pricing model to value our stock option awards. Use of this valuation methodology requires that we make assumptions as to 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. Because we are a privately held company with a limited operating history, we utilize data from a representative group of public companies to estimate expected stock price volatility. For purposes of identifying representative companies, we considered characteristics such as number of product candidates in early stages of product development, area of therapeutic focus, length of trading history and similar vesting provisions. The expected volatility was determined using an average of the historical volatilities of the

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representative group of companies for a period equal to the expected term of the option grant. We intend to consistently apply this process using the same representative companies until a sufficient amount of historical information regarding the volatility of our own share price becomes available or until circumstances change, such that the identified entities are no longer representative companies. In the latter case, more suitable, similar entities whose share prices are publicly available would be utilized in the calculation.

We use the "simplified method" to estimate the expected term of stock option grants to employees. Under this approach, the weighted-average expected option term is presumed to be the average of the contractual term (ten years) and the vesting term (generally four years) of our stock options. We utilize this method due to lack of historical exercise data and the "plain-vanilla" nature of our stock-based awards. The risk-free rate is based on the yield curve of U.S. Treasury securities in effect at the time of grant with periods commensurate with the expected term of the options being valued. We have never paid, and do not anticipate paying, any cash dividends in the foreseeable future, and therefore use an expected dividend yield of zero in the option-pricing model.

We have computed the fair value of each stock option on the date of grant using the following weighted-average assumptions:

	December 31,		September 30,
	2013	2014	2015
Weighted-average risk-free interest rate	1.21%	2.00%	1.76%
Expected dividend yield	0%	0%	0%
Expected option term	6.11	7.03	6.09
Volatility	89.23%	85.51%	82.59%

We are also required to estimate forfeitures at the time of grant and revise those estimates in subsequent periods if actual forfeitures differ from our estimates. The term "forfeitures" is distinct from "cancellations" or "expirations" and represents only the unvested portion of the surrendered option. We use historical data to estimate pre-vesting option forfeitures and record stock-based compensation expense only for those awards that are expected to vest. To the extent that actual forfeitures differ from our estimates, the difference is recorded as a cumulative adjustment in the period in which the estimates are revised. Stock-based compensation expense recognized in the financial statements is based on awards that are ultimately expected to vest. Through September 30, 2015, actual forfeitures have not been material.

We expense the fair value of our stock-based awards to employees on a straight-line basis over the associated service period, which is generally the vesting period. For stock-based awards granted to consultants and non-employees, we recognize compensation expense over the period during which the services are rendered by such consultants and non-employees. At the end of each financial reporting period prior to completion of the service, the fair value of these awards is remeasured using the then-current fair value of our common stock for restricted stock and updated assumptions in the Black-Scholes option-pricing model for stock options.

We record the expense for stock-based awards that contain performance-based milestones in accordance with the accelerated attribution model. Management evaluates when the achievement of a performance-based milestone is probable based on the expected satisfaction of the performance conditions as of the reporting date. For certain of our performance-based awards, notwithstanding any vesting in accordance with the achievement of performance-based milestones, such awards vest in full on the sixth anniversary of the vesting commencement date. Compensation expense for such awards is recognized over the six-year vesting period unless management determines that the achievement of any performance-based milestones are probable, in which case expense is accelerated.

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The following table presents the grant dates, number of underlying shares of common stock and the per share exercise prices of stock options granted between January 1, 2014 and January 28, 2016, along with the fair value per share utilized to calculate stock-based compensation expense:

<u>Date of Issuance</u>	<u>Type of Award</u>	<u>Number of Shares</u>	<u>Exercise Price of Award per Share(1)</u>	<u>Fair Value of Common Stock per Share at Grant</u>	<u>Per Share Estimated Fair Value of Award(2)</u>
1/29/2014	Options	5,000	\$ 0.27	\$ 0.26	\$ 0.19
6/3/2014	Options	677,922	\$ 0.37	\$ 0.37	\$ 0.27
9/4/2014	Options	66,373	\$ 0.37	\$ 0.37	\$ 0.27
10/22/2014	Options	344,190	\$ 0.81	\$ 0.81	\$ 0.58
2/5/2015	Options	841,990	\$ 0.81	\$ 1.10(3)	\$ 0.83
6/9/2015	Options	1,447,904	\$ 0.81	\$ 1.59(3)	\$ 1.27
9/17/2015	Options	241,250	\$ 1.85	\$ 1.85	\$ 1.33
9/21/2015	Options	967,769	\$ 1.85	\$ 1.85	\$ 1.30
10/11/2015	Options	204,400	\$ 1.85	\$ 1.98(4)	\$ 1.42
10/21/2015	Options	177,500	\$ 1.85	\$ 1.98(4)	\$ 1.42
12/23/2015	Options	1,076,432	\$ 2.42	\$ 2.41	\$ 1.71

- (1) The Exercise Price of Award per Share represents the fair value of our common stock on the date of grant, as determined by our board of directors, taking into account our most recently available independent third-party valuation of our common stock as well as additional factors that may have changed since the date of such valuation.
- (2) The Per Share Estimated Fair Value of Award reflects the fair value of options as estimated at the date of grant using the Black-Scholes option-pricing model.
- (3) At the time of the option grants on February 5, 2015 and June 9, 2015, our board of directors determined the fair value of our common stock was \$0.81 per share, based on an independent third-party valuation report dated as of October 9, 2014. However, as described below, in connection with a retrospective fair value assessment for financial reporting purposes we adjusted the fair value of common stock at the date of these grants.
- (4) At the time of the option grants on October 11, 2015 and October 21, 2015, our board of directors determined the fair value of our common stock was \$1.85 per share, based on an independent third-party valuation report dated as of September 9, 2015. In connection with a retrospective fair value assessment for financial reporting purposes performed as of October 21, 2015, we adjusted the fair value of common stock at the date of these grants.

Stock-based compensation expense totaled approximately \$0.9 million for the year ended December 31, 2014 and \$2.4 million for the nine months ended September 30, 2015. As of September 30, 2015, we had \$6.4 million of unrecognized compensation expense related to unvested stock options and unvested restricted stock which we expect to recognize over a weighted-average period of 2.7 years. We expect the impact of our stock-based compensation expense for restricted stock and stock options granted to employees, directors and other service providers to increase in future periods due to potential increases in the value of our common stock and headcount.

Determination of Fair Value of Common Stock on Grant Dates

We are required to estimate the fair value of our common stock underlying our stock-based awards when performing the fair value calculations using the Black-Scholes option pricing model. The fair value of our common stock underlying our stock-based awards was determined on each grant date by our board of directors, with input from management, considering our most recently available independent third-party valuations of common stock and our board of directors' assessment of

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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 grant. These independent third-party valuations of our common stock were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants *Audit and Accounting Practice Aid Series: Valuation of Privately Held Company Equity Securities Issued as Compensation*, or the Practice Aid. 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 us to estimate the fair value of our common stock in connection with our accounting for stock options and restricted stock, as the fair value of our common stock will be its trading price on The NASDAQ Global Market.

For financial reporting purposes, we performed common stock valuations, with the assistance of an independent third-party valuation specialist, as of April 1, 2014, October 9, 2014 and September 9, 2015 which resulted in valuations of our common stock of \$0.37, \$0.81 and \$1.85, respectively, as of those dates. In September 2015, with the assistance of an independent third-party valuation specialist, we performed retrospective common stock valuations for financial reporting purposes as of March 31, 2015 and June 30, 2015, which resulted in valuations of our common stock of \$1.23 and \$1.59 per share, respectively, as of those dates. In conducting these independent third-party valuations, we considered all objective and subjective factors that we believed to be relevant for each valuation conducted, including our best estimate of our business condition, prospects and operating performance at each valuation date. Within the valuations performed, a range of factors, assumptions and methodologies were used. The significant factors included:

- the lack of an active public market for our common and preferred stock;
- prices of shares of our preferred stock that we had sold to outside investors in arm's length transactions, and the rights, preferences and privileges of that convertible stock relative to our common stock;
- our results of operations and financial position and the status of our research and preclinical development efforts;
- the material risks related to our business;
- our business strategy;
- the market performance of publicly traded companies in the life sciences and biotechnology sectors;
- the likelihood of achieving a liquidity event for the holders of our common stock, such as an initial public offering, or IPO, given prevailing market conditions; and
- recent independent third-party valuations of our common stock prepared in accordance with methodologies outlined in the Practice Aid.

There are significant judgments and estimates inherent in the determination of the fair value of our common stock. These judgments and estimates include assumptions regarding our future operating performance, the time to completing an IPO or other liquidity event, the related company valuations associated with such events and the determinations of the appropriate valuation methods. If we had made different assumptions, our stock-based compensation expense, net loss and net loss per share applicable to common stockholders could have been significantly different.

Common Stock Valuations Methodologies

Common stock valuation methodologies. The valuations of our common stock were prepared in accordance with the guidelines in the Practice Aid, which prescribes several valuation approaches for determining the value of an enterprise, such as the cost, market and income approaches, and various methodologies for allocating the value of an enterprise to its capital structure and specifically the common stock.

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The market approach estimates the fair value of a company by applying market multiples of comparable companies in a similar line of business and considers the price that investors have paid for the equity of publicly traded companies or venture investments in a private firm. Through the creation of multiples of revenue, operating income, net income and other key metrics for comparable assets, a method of obtaining a relative valuation of an asset can be made.

Generally, our enterprise value was determined using the market approach valuation method.

Methods used to allocate our enterprise value to classes of securities. In accordance with the Practice Aid, we considered the following methods for allocating the enterprise value across our classes and series of capital stock to determine the fair value of our common stock at each valuation date:

OPM. The option pricing method, or 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 exceed the value of the liquidation preferences at the time of a liquidity event, such as a strategic sale or merger. The common stock is modeled as a call option on the underlying equity value at a predetermined exercise price. In the model, the exercise price is based on a comparison with the total equity value rather than, as in the case of a regular call option, a comparison with a per share stock price. Thus, common stock is considered to be a call option with a claim on the enterprise at an exercise price equal to the remaining value immediately after the preferred stock liquidation preference is paid.

The OPM uses the Black-Scholes option-pricing model to price the call options. This model defines the securities' fair values as functions of the current fair value of a company and uses assumptions, such as the anticipated timing of a potential liquidity event and the estimated volatility of the equity securities.

The OPM backsolve approach was used to estimate enterprise value under the OPM. The OPM backsolve approach uses the OPM to derive the implied equity value for one type of equity security from a contemporaneous sale transaction involving another type of the company's equity securities. In the OPM, the assumed volatility factor was based on the historical trading volatility of our publicly traded peer companies. At each valuation date, a determination was made by us as to the appropriate volatility to be used, considering such factors as the expected time to a liquidity event and our stage of development.

To derive the fair value of the common stock using the OPM, the proceeds to the common stockholders were calculated based on the preferences and priorities of the preferred stock and common stock. We then applied a discount for lack of marketability to the common stock to account for the lack of access to an active public market.

PWERM. Under a probability-weighted expected return method, or PWERM, the value of the various equity securities are estimated based upon an analysis of future values for the enterprise, 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.

Hybrid Method. The hybrid method is a PWERM where the equity value in one of the scenarios is calculated using an OPM. In the hybrid method used by us, two types of future-event scenarios were considered: an IPO and an unspecified liquidity event. The enterprise value for the IPO scenario was determined using a market approach. The enterprise value for the unspecified liquidity event scenario was determined using the OPM backsolve approach. The relative probability of each type of future-event scenario was determined based on an analysis of market conditions at the time, including

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then-current IPO valuations of similarly situated companies, and expectations as to the timing and likely prospects of the future-event scenarios.

To determine the enterprise value for the IPO scenario, we used the guideline public company method, which includes comparisons to publicly traded companies in the biopharmaceutical industry that recently completed IPOs. That enterprise value was then discounted back to the valuation date at an appropriate risk-adjusted discount rate.

To derive the fair value of the common stock for each scenario under the hybrid method, the proceeds to the common stockholders were calculated based on the conversion rights and preferences of the preferred stock. We then applied a discount for lack of marketability to the common stock to account for the lack of access to an active public market.

Prior to January 1, 2015, our common stock valuations were prepared utilizing OPM. Our common stock valuations in 2015 were prepared utilizing the hybrid method.

Results of Operations

Comparison of Nine Months Ended September 30, 2014 and 2015

The following table summarizes our results of operations for the nine months ended September 30, 2014 and 2015, together with the changes in those items in dollars (in thousands):

	Nine Months Ended September 30,		Dollar Change	Percentage Change
	2014	2015 (unaudited)		
Revenue	\$ —	\$ 317	\$ 317	n/a
Operating expenses:				
Research and development	7,901	16,030	8,129	103%
General and administrative	1,843	3,418	1,575	85%
Total operating expenses	9,744	19,448	9,704	100%
Other income (expense), net	2	2	—	0
Net loss and comprehensive loss	<u>\$ (9,742)</u>	<u>\$ (19,129)</u>	<u>\$ (9,387)</u>	<u>96%</u>

Revenue

Revenue was \$0.3 million for the nine months ended September 30, 2015 and related to the completion of a research project under our research agreement with a multinational pharmaceutical company. We did not earn any revenue for the nine months ended September 30, 2014.

Research and Development Expense

Research and development expense increased by \$8.1 million from \$7.9 million for the nine months ended September 30, 2014 to \$16.0 million for the nine months ended September 30, 2015. The

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following table summarizes our research and development expenses for the nine months ended September 30, 2014 and September 30, 2015 (in thousands):

	Nine Months Ended		Dollar Change
	September 30,		
	2014	2015	
		(unaudited)	
External research and preclinical development	\$ 4,037	\$ 8,079	\$ 4,042
Employee-related expenses, excluding stock-based compensation	2,170	3,466	1,296
Stock-based compensation	514	2,073	1,559
Consulting, licensing and professional fees	517	1,357	840
Facilities and other expenses	663	1,055	392
Total research and development expenses	<u>\$ 7,901</u>	<u>\$ 16,030</u>	<u>\$ 8,129</u>

The increase in research and development expense was primarily attributable to research and develop activities associated with advancing our lead preclinical programs and enhancing our internal capabilities and included the following:

- approximately \$4.0 million for costs from third parties that conduct research and development and preclinical activities on our behalf, including approximately \$2.1 million in chemistry expenses for contract chemistry personnel and increased chemistry analysis and \$0.8 million for in vivo study costs;
- approximately \$1.6 million for increased stock-based compensation expense;
- approximately \$1.3 million for increased personnel related expenses, including increased salary and benefits primarily due to the hire of research and development personnel;
- approximately \$0.8 million in consulting, licensing and professional fees including the \$0.5 million upfront payment made under the TMRC license agreement; and
- approximately \$0.4 million for increases in facilities costs including rent, depreciation and maintenance expenses.

General and Administrative Expense

General and administrative expense increased by \$1.6 million from \$1.8 million for the nine months ended September 30, 2014 to \$3.4 million for nine months ended September 30, 2015. The increase in general and administrative expense was primarily attributable to the following:

- approximately \$0.8 million for employee-related costs, including salary and benefits as a result of the increase in administrative function headcount;
- approximately \$0.4 million primarily for consulting and professional fees, including increased corporate legal fees in support of the negotiations of the TMRC license agreement and the negotiations of our operating lease agreement for office space and increased public relations expenses; and
- approximately \$0.2 million for increased stock-based compensation expense.

Other Income (Expense), Net

Other income (expense), net for the nine months ended September 30, 2014 and September 30, 2015 was \$2,000 and was comprised of interest income on our invested cash and cash equivalents, offset by interest expense related to our equipment financing arrangements.

Comparison of Years Ended December 31, 2013 and 2014

The following table summarizes our results of operations for the years ended December 31, 2013 and December 31, 2014, respectively, together with the changes in those items in dollars (in thousands):

	Year Ended December 31,		Dollar Change	Percentage Change
	2013	2014		
Revenue	\$ —	\$ —	\$ —	0%
Operating expenses:				
Research and development	6,266	10,923	4,657	74%
General and administrative	2,367	2,512	145	6%
Total operating expenses	8,633	13,435	4,802	56%
Other income (expense), net	(32)	4	36	(113)%
Net loss and comprehensive loss	\$ (8,665)	\$ (13,431)	\$ (4,766)	55%

Revenue

During the years ended December 31, 2013 and 2014, respectively, we did not earn any revenue.

Research and Development Expense

Research and development expense increased by \$4.7 million from \$6.3 million for the year ended December 31, 2013 to \$10.9 million for the year ended December 31, 2014. The following table summarizes our research and development expenses for the years ended December 31, 2014 and December 31, 2013, respectively (in thousands):

	Year Ended December 31,		Dollar Change
	2013	2014	
External research and preclinical development	\$ 2,499	\$ 5,520	\$ 3,021
Employee-related expenses, excluding stock-based compensation	1,864	2,984	1,120
Stock-based compensation	673	830	157
Consulting, licensing and professional fees	466	682	216
Facilities and other expenses	764	907	143
Total research and development expenses	\$ 6,266	\$ 10,923	\$ 4,657

The increase in research and development expense was primarily attributable to research and development associated with advancing our preclinical programs and enhancing our internal capabilities, and included the following:

- approximately \$3.0 million for costs from third parties that conduct research and development and preclinical activities on our behalf, including approximately \$2.0 million in chemistry expenses for contract chemistry personnel and increased chemistry analysis and \$0.5 million for high-throughput sequencing; and
- approximately \$1.1 million for increased personnel related expenses, including salary and benefits primarily due to the hire of research personnel.

[Table of Contents](#)*General and Administrative Expense*

General and administrative expense increased by \$0.1 million from \$2.4 million for the year ended December 31, 2013 to \$2.5 million for the year ended December 31, 2014. The increase in general and administrative expense was primarily attributable to the following:

- approximately \$0.3 million for employee compensation costs, including salary and benefits as a result of the increase in administrative function headcount; offset by
- approximately \$0.2 million decrease in consulting and professional fees.

Other Income (Expense), Net

Other income (expense), net for the years ended December 31, 2013 and 2014 was (\$32,000) and \$4,000, respectively. Interest expense in 2013 was related to the interest accrued on our convertible promissory notes, which were converted into shares of preferred stock in April 2013, and interest income in 2014 was related to the interest on our invested cash and cash equivalents.

Liquidity and Capital Resources*Sources of Liquidity*

We have funded our operations from inception through September 30, 2015 primarily through gross proceeds of \$82.0 million from sales of our preferred stock and the issuance of convertible notes that subsequently converted into preferred stock. As of September 30, 2015, we had cash and cash equivalents of \$45.0 million. In January 2016, we completed the sale of shares of our Series B preferred stock for aggregate proceeds of \$40 million.

Cash Flows

The following table provides information regarding our cash flows for the years ended December 31, 2013 and 2014 and the nine months ended September 30, 2014 and September 30, 2015 (in thousands):

	Year Ended December 31,		Nine Months Ended September 30,	
	2013	2014	2014	2015
Net cash provided by (used in):				(unaudited)
Operating activities	\$ (7,194)	\$ (11,969)	\$ (8,466)	\$ (14,829)
Investing activities	(878)	(201)	(187)	(883)
Financing activities	10,045	68,762	15,764	304
Net increase (decrease) in cash and cash equivalents	<u>\$ 1,973</u>	<u>\$ 56,592</u>	<u>\$ 7,111</u>	<u>\$ (15,408)</u>

Net Cash Used in Operating Activities

The use of cash in all periods resulted primarily from our net losses adjusted for non-cash charges and changes in components of working capital.

Net cash used in operating activities was \$12.0 million during the year ended December 31, 2014 compared to \$7.2 million during the year ended December 31, 2013. The increase in cash used in operating activities was primarily due to an increase in net loss of \$4.8 million for the year ended December 31, 2014 as compared to the year ended December 31, 2013.

Net cash used in operating activities was \$14.8 million during the nine months ended September 30, 2015 compared to \$8.5 million during the nine months ended September 30, 2014. The increase in cash used in operating activities was primarily due to an increase in our net loss of \$9.4 million for the nine months ended September 30, 2015 as compared to the nine months ended September 30, 2014.

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Net Cash Used in Investing Activities

Net cash used in investing activities was \$0.2 million during the year ended December 31, 2014 compared to \$0.9 million during the year ended December 31, 2013. The decrease in cash used in investing activities was due to decreased purchases of property and equipment.

Net cash used in investing activities was \$0.9 million during the nine months ended September 30, 2015 compared to \$0.2 million during the nine months ended September 30, 2014. The increase in cash used in investing activities was due to increased purchases of property and equipment.

Net Cash Provided by Financing Activities

Net cash provided by financing activities was \$68.8 million during the year ended December 31, 2014 compared to \$10.1 million during the year ended December 31, 2013. The increase in cash provided by financing activities was primarily due to the issuance of \$15.8 million of Series A-3 preferred stock and \$53.1 million of Series B preferred stock during the year ended December 31, 2014. In the year ended December 31, 2013, \$10.0 million of Series A-2 preferred stock was issued.

Net cash provided by financing activities was \$0.3 million during the nine months ended September 30, 2015 compared to \$15.8 million during the nine months ended September 30, 2014. The decrease in cash provided by financing activities was primarily due to the issuance of \$15.8 million of Series A-3 preferred stock during the nine months ended September 30, 2014, with no preferred stock issuance occurring during the nine months ended September 30, 2015.

Funding Requirements

We expect our expenses to increase in connection with our ongoing activities, particularly as we initiate clinical trials of SY-1425, advance the development of our CDK7 inhibitor program, initiate new research and preclinical development efforts and seek marketing approval for any product candidates that we successfully develop. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to establishing sales, marketing, distribution and other commercial infrastructure to commercialize such products. Furthermore, 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 would be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts.

We believe that the anticipated net proceeds from this offering, together with our existing cash and cash equivalents as of September 30, 2015 and the \$40 million in aggregate proceeds from our Series B preferred stock financing that we completed in January 2016, will enable us to fund our operating expenses and capital expenditure requirements through at least the next months. Our future capital requirements will depend on many factors, including:

- the scope, progress, timing, costs and results of clinical trials of SY-1425 and any CDK7 inhibitors we successfully advance into clinical development;
- research and preclinical development efforts for any future product candidates that we may develop;
- our ability to enter into and the terms and timing of any collaborations, licensing agreements or other arrangements;
- the number of future product candidates that we pursue and their development requirements;
- the outcome, timing and costs of seeking regulatory approvals;
- the costs of commercialization activities for any of our product candidates that receive marketing approval to the extent such costs are not the responsibility of any future collaborators, including

- the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- the costs of acquiring potential new product candidates or technology;
- the costs of any physician education programs relating to selecting and treating genomically defined patient populations;
- the timing and amount of milestone and other payments due to licensors for patent and technology rights used in our development platform;
- revenue received from commercial sales, if any, of our current and future product candidates;
- our headcount growth and associated costs as we expand our research and development and establish a commercial infrastructure;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against intellectual property related claims; and
- the costs of operating as a public company.

Identifying potential product candidates and conducting preclinical studies and clinical trials is a time-consuming, expensive and uncertain process that takes many years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise funds through additional collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate 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.

Contractual Obligations

As of December 31, 2014, we had no significant contractual obligations. The remaining lease commitment under our operating lease for our previous office space at 480 Arsenal Street in Watertown, Massachusetts, which expired in August 2015, was \$206,000 as of December 31, 2014.

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The following table summarizes our significant contractual obligations as of payment due date by period at September 30, 2015 (in thousands):

	Total	Less Than 1 Year	1 to 3 Years	3 to 5 Years	More than 5 Years
Operating lease commitments(1)	\$ 6,452	\$ 1,148	\$ 2,523	\$ 2,668	\$ 113
Capital lease(2)	\$ 390	\$ 131	\$ 259	—	—

- (1) We lease office space at 620 Memorial Drive in Cambridge, Massachusetts under a non-cancelable operating lease that expires in October 2020.
- (2) We have a capital lease for laboratory equipment that expires in March 2018.

We enter into agreements in the normal course of business with our contract research organizations and institutions to license intellectual property. We have not included these future payments in the table of contractual obligations above since the contracts are cancelable at any time by us, generally upon 30 to 90 days prior written notice.

Our license agreements include potential milestone payments that are contingent upon the successful development and commercialization of products using the intellectual property licensed under such agreements. Under our agreements with Dana-Farber and Whitehead, the maximum aggregate potential milestone payments payable by us total approximately \$6.9 million. Under the applicable agreement, we are also required to pay annual maintenance fees, as well as tiered, single-digit percentage royalties, on a country-by-country, product-by-product basis, on net product sales.

Under the TMRC license agreement, we may make additional payments upon the successful achievement of pre-specified clinical and regulatory milestones in an aggregate amount of approximately \$13.0 million per indication. We are obligated to pay the balance of the upfront license fee under this agreement upon the execution of a supply agreement with TMRC for the supply of the active pharmaceutical agreement in SY-1425, which we expect to occur by the end of 2015. Upon the successful dosing of the first patient in our Phase 2 clinical trial of SY-1425, which we expect to occur in mid-2016, we are obligated to make a \$1.0 million milestone payment.

These future obligations are not reflected in the table above as these payments are contingent upon achievement of developmental and commercial milestones, the likelihood of which cannot be reasonably estimated at this time.

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 under applicable Securities and Exchange Commission rules.

Quantitative and Qualitative Disclosures About Market Risk

We are exposed to market risk related to changes in interest rates. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments, including cash equivalents, are in the form of a money market fund and marketable securities and are invested in U.S. Treasury obligations.

We are also exposed to market risk related to changes in foreign currency exchange rates. We contract with vendors that are located in Asia and Europe and certain invoices are denominated in foreign currencies. We are subject to fluctuations in foreign currency rates in connection with these arrangements. We do not currently hedge our foreign currency exchange rate risk. As of September 30, 2015, we had minimal or no liabilities denominated in foreign currencies.

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation had a material effect on our business, financial condition or results of operations

during the years ended December 31, 2013 and 2014 and the nine months ended September 30, 2014 and September 30, 2015, respectively.

Internal Control over Financial Reporting

In connection with the audit of our financial statements as of and for the years ended December 31, 2014 and 2013, we identified material weaknesses in our internal control over financial reporting. The material weaknesses related to our controls over the classification of certain indirect and other expenses between general and administrative and research and development, and to the accounting for stock-based compensation. We also identified deficiencies related to our controls over our accounting for income taxes. The material weaknesses were due to the lack of appropriate oversight and review procedures by accounting personnel to properly identify and evaluate certain accounting matters that resulted in errors in our financial statements.

We are implementing measures designed to improve our internal control over financial reporting to remediate these material weaknesses, including the following:

- we are formalizing our processes and internal control documentation and strengthening supervisory reviews by our management;
- we have hired additional qualified accounting personnel and engaged financial consultants, all of whom have significant accounting and financial reporting experience, which will enable the implementation of internal controls over financial reporting and segregating duties among accounting personnel;
- we expect to hire additional senior accounting and finance staff to complete this remediation; and
- we intend to implement certain accounting systems to automate manual processes, such as tracking and accounting for stock-based awards.

These additional resources and procedures are designed to enable us to broaden the scope and quality of our internal review of underlying information related to financial reporting and to formalize and enhance our internal control procedures. With the oversight of senior management, we have begun taking steps and plan to take additional measures to remediate the underlying causes of the material weaknesses.

We, and our independent registered public accounting firm, were not required to perform an evaluation of our internal control over financial reporting as of December 31, 2014 in accordance with the provisions of the Sarbanes-Oxley Act. Accordingly, we cannot provide assurance that we have identified all, or that we will not in the future have additional, material weaknesses. Material weaknesses may still exist when we report on the effectiveness of our internal control over financial reporting as required by reporting requirements under Section 404 of the Sarbanes-Oxley Act after the closing of this offering.

JOBS Act

In April 2012, the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, was enacted. Section 107 of the JOBS Act provides that an emerging growth company, or EGC, can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act of 1933, as amended, or the Securities Act, for complying with new or revised accounting standards. Thus, an EGC can 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 extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

We are in the process of evaluating the benefits of relying on other exemptions and reduced reporting requirements under the JOBS Act. Subject to certain conditions, as an EGC, we intend to

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rely on certain of these exemptions, including the exemption from the requirement to provide an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act and with the exemption from any requirement that may be adopted by the Public Company Accounting Oversight Board, or PCAOB, regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, known as the auditor discussion and analysis. We will remain an EGC until the earlier of (i) the last day of the fiscal year in which we have total annual gross revenues of \$1.0 billion or more; (ii) the last day of the fiscal year following the fifth anniversary of the date of the closing of this offering; (iii) the date on which we have issued more than \$1.0 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission.

BUSINESS

Overview

We are a biopharmaceutical company applying a pioneering approach to discover and develop medicines that control the expression of genes with the aim of treating cancer and other serious diseases. We have built a proprietary platform that provides a unique lens to systematically and efficiently identify crucial genes that become dysregulated in diseased cells and create medicines that return cells to a non-diseased state. We believe that our platform will allow us to create a pipeline of gene control medicines that will provide a profound and durable benefit for currently underserved patients. By focusing on genomically defined subsets of patients, we believe we can conduct efficient clinical trials with a higher likelihood of success. We intend to submit an investigational new drug application, or IND, to the U.S. Food and Drug Administration, or FDA, and advance our lead product candidate, SY-1425 (tamibarotene), into a Phase 2 clinical trial, in mid-2016. This trial is expected to initially enroll genomically defined subsets of patients with acute myelogenous leukemia, or AML, and myelodysplastic syndromes, or MDS, identified by our gene control platform. We plan to submit an IND for our second program targeting cyclin-dependent kinase 7, or CDK7, which is an important gene control target in several cancers, initially for the treatment of acute leukemias, in the second half of 2016. Leveraging our platform, we are also generating a pipeline of novel preclinical drug candidates for genomically defined subsets of patients. Our goal is to build a fully integrated biopharmaceutical company based on our leadership position in gene control.

There are approximately 200 different cell types in a given individual. Despite having identical genomes, each of these cell types has a different function. For example, a skin cell functions differently from a muscle cell despite sharing the exact same DNA. A small number of genes are crucial for determining cell type and function. The coordinated activity, or expression, of these genes is referred to as the gene control program. By understanding gene control programs, we believe we have the ability to uncover the drivers of cell type and function in healthy and diseased cells. To understand the cell's gene control program, we use genomic tools to locate enhancers, which are specialized regions of DNA that are associated with specialized proteins that are involved in the expression of genes. We are focused on super-enhancers, a very small subset of enhancers where large amounts of specialized proteins congregate to control the expression of crucial genes responsible for cell type and function.

In disease, gene control programs are altered. Analysis of super-enhancers within diseased and healthy cells in specific patient segments enables us to systematically and efficiently identify disease-causing alterations in a cell's gene control program and pinpoint targets for therapeutic intervention.

The discovery and development of targeted therapies, in which the right drug is matched to the right patient, has dramatically improved the ability to treat certain cancers and other serious diseases. The success of targeted therapies relies in large part on the identification of patients with a specific genetic alteration who are more likely to benefit from a particular treatment. Many targeted therapies in oncology focus on targeting one abnormal protein resulting from a genetic alteration found in regions of the genome that encode for proteins, which represent less than 2% of the entire genome. The identification of viable targets by sequencing the encoded regions of DNA has been largely exhausted, and inhibiting abnormal proteins resulting from genetic alterations can often lead to drug resistance and limited durable clinical benefit, underscoring the need for new approaches.

Researchers have long believed that genomic alterations in non-coding regions of DNA, which account for the other 98% of the genome, play a key role in driving disease. However, the scientific community has lacked the tools to study these regions of the genome, making these targets difficult to discover and drug. Gene control programs reside in these non-coding regions of the genome and, as a result, represent a largely untapped field for drug discovery and development. In contrast to therapies that target a single abnormal protein, gene control medicines target the underlying coordinated expression of genes that contribute to disease, opening up a wide array of potential new drug targets,

including transcription factors, transcriptional kinases and other transcriptional and regulatory proteins, that mediate the gene control program of a cell. Dysregulation of gene control programs is fundamental to many serious diseases, including cancer. We believe gene control medicines will allow us to influence multiple drivers of disease in a targeted fashion to achieve a profound and durable clinical benefit for patients.

The relatively few gene control medicines available are among the most important targeted therapies available today and are widely used for the treatment of cancer and inflammatory diseases. Drugs that target transcription factors, such as estrogen receptors in breast cancer, androgen receptors in prostate cancer and glucocorticoid receptors in inflammation, are important examples of gene control medicines that have produced transformative patient benefits. For example, tamoxifen, a gene control medicine targeting a transcription factor, revolutionized the treatment of certain breast cancers and is prescribed 1.9 million times annually in the United States, illustrating the significant therapeutic potential of gene control medicines. However, a lack of understanding of gene control programs has historically prevented a systematic approach to identifying these critical points of therapeutic intervention, making gene control a largely untapped field for drug discovery and development.

We believe that through our proprietary gene control platform, we have created a systematic and efficient approach to the discovery of novel disease targets and biomarkers. Our gene control platform consists of two fundamental pillars: mapping gene control programs and drugging gene control targets. The first pillar of our platform is our ability to map gene control programs. Starting from human tissue samples, we compare diseased cells to healthy cells and analyze the cells of different patient subsets within a disease to identify changes in gene control programs. We have invested significant resources in tissue processing, genomics and computational biology capabilities to industrialize the production of maps of gene control programs. We believe this approach allows us to systematically and efficiently pinpoint disease-driving genes and optimal points of therapeutic intervention. We have amassed one of the largest known datasets of these maps across a wide range of human diseases and cell types and have identified multiple novel disease targets. To date, we have mapped AML, breast cancer, renal cell carcinoma, polycystic kidney disease, spinal muscular atrophy and normal T-cells. Maps are either ongoing or planned in several cancers, including ovarian, pancreatic, hepatocellular carcinoma, colorectal, lung and melanoma, as well as several other diseases including Alzheimer's disease and inflammatory disorders. Our long-term goal is to map all serious diseases where we believe patients who are currently underserved can benefit from gene control medicines.

The second pillar of our platform is our ability to drug gene control targets. Because of the central role they play in gene control programs, the specialized proteins responsible for gene expression, such as transcription factors, transcriptional kinases and other transcriptional and regulatory proteins, are among the most promising and high potential gene control targets for therapeutic intervention. Transcription factors are proteins that bind directly to DNA sequences to control the transcription of genetic information from DNA. Transcription factors perform this function with other transcriptional and regulatory proteins, including transcriptional kinases. These gene control targets have historically been difficult to drug; however, through our significant investments in developing proprietary assays, which are internally developed tests that we use to measure the biochemical and cellular activity of known and novel compounds against gene control targets, and in our capabilities in biochemistry, structural biology and medicinal chemistry, we believe we will be able to overcome challenges that have prevented others from systematically and successfully developing gene control medicines. We are building a pipeline of product candidates to modulate gene control programs through two distinct approaches: internal efforts to discover novel drugs against these targets and externally focused efforts to link existing drugs to novel genomically defined patient populations identified through our platform. These externally focused efforts could enable us to identify drugs that we may seek to in-license or acquire or use as a starting point for our own drug discovery programs, to accelerate our development path. Our highly selective and potent inhibitors of CDK7 demonstrate our ability to create proprietary

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gene control product candidates. Our SY-1425 program demonstrates our ability to link existing drugs to novel genomically defined subsets of patients, which could allow us to accelerate our clinical development path.

We are leveraging our platform to develop a pipeline of gene control product candidates. Our most advanced drug programs are summarized in the table below:

<u>Program</u>	<u>Initial Indications</u>	<u>Planned Milestones</u>	<u>Potential Indications</u>	<u>Syros Commercial Rights</u>
SY-1425 (RARA agonist)	AML and MDS	Submit IND in 1H 2016 Initiate Phase 2 clinical trial in mid-2016 Expected data readout in mid-2017	Breast cancer, acute promyelocytic leukemia (APL)	North America, Europe
CDK7 inhibitor	Acute leukemias	Submit IND in 2H 2016 Initiate Phase 1/2 clinical trial in 1H 2017	Small cell lung cancer, triple negative breast cancer, <i>MYCN</i> -amplified neuroblastoma	Worldwide

Our lead product candidate, SY-1425, is an oral, potent and selective RARA agonist, or activator, that we are advancing based on our deep understanding of the role of transcription factors in certain cancers. We plan to initiate a Phase 2 clinical trial in a genomically defined group of AML and MDS patients in mid-2016. Using our platform, we have identified genomically defined subsets of AML and breast cancer patients that have a super-enhancer associated with the *RARA* gene, and we also identified a proprietary gene control biomarker, which we refer to as the *RARA* biomarker. In *in vivo* mouse models implanted with human AML tumors, SY-1425 was observed to be effective in stopping the growth of tumors that were positive for the *RARA* biomarker. Importantly, mice with *RARA* biomarker-positive tumors that were treated with SY-1425 experienced extended survival. We observed the *RARA* biomarker in approximately 25% of AML tissues we analyzed. We believe that a similar percentage of AML and MDS patients will have the *RARA* biomarker. This leads us to believe that approximately 16,000 patients diagnosed annually in the United States, Canada and the five largest European countries by population, Germany, the United Kingdom, France, Spain and Italy, have the form of AML or MDS that could be addressed by SY-1425. Similarly, we have observed the *RARA* biomarker in approximately 35% of breast cancer patient samples we analyzed, leading us to believe that approximately 55,000 metastatic breast cancer patients diagnosed annually in the countries listed above could benefit from SY-1425.

We have exclusive North American and European commercial rights for SY-1425 in human cancer under our license agreement with TMRC Co., Ltd., or TMRC. Tamibarotene is approved in Japan for the treatment of APL, a form of AML, for which tamibarotene has a well characterized efficacy and safety profile. Given the drug's demonstrated efficacy in APL and the significant unmet medical need, we also intend to explore SY-1425 for treatment of APL in North America and Europe. There are an

estimated 2,500 new APL cases diagnosed in the United States, Canada and the five largest European countries each year.

We are developing our CDK7 inhibitor program based on our deep understanding of transcriptional kinase biology and biochemistry. Our CDK7 inhibitor program is focused on the treatment of cancers that are dependent on a high and constant expression of certain transcription factors for their growth and survival, a phenomenon known as transcriptional addiction. Using our internal drug discovery capabilities, we have generated potent and highly selective small molecule CDK7 inhibitors. In preclinical studies, our selective CDK7 inhibitors were observed to have significant anti-tumor activity and to preferentially kill cancer cells over healthy cells in *in vivo* models of several aggressive and underserved cancers, including AML, acute lymphoblastic leukemia, or ALL, *MYCN*-amplified neuroblastoma, small cell lung cancer and triple negative breast cancer. We expect to select our development candidate and start IND-enabling activities in the first half of 2016, submit an IND in the second half of 2016 and initiate a Phase 1/2 clinical trial in patients with acute leukemias in the first half of 2017. We selected acute leukemias as our first clinical development indications due to high levels of observed efficacy in our preclinical models and because few treatment options exist for these patients. Subject to strong clinical results, there could be an opportunity for accelerated clinical development. We believe that all of the approximately 37,000 AML and 12,000 ALL patients diagnosed annually in the United States, Canada, the five largest European countries and Japan, which we refer to as the developed pharmaceutical markets, could benefit from an effective CDK7 inhibitor.

We were founded by leaders in the field of gene control from the Whitehead Institute for Biomedical Research at the Massachusetts Institute of Technology, or Whitehead, and the Dana-Farber Cancer Institute, or Dana-Farber, an affiliate of Harvard Medical School. Many of our employees have been members of teams that uncovered innovative scientific findings and delivered highly impactful drugs to the marketplace. Our management team consists of drug discovery, development and commercialization experts with experience in translating scientific discoveries into innovative treatments, including Avonex and Tysabri for multiple sclerosis, Velcade for hematological malignancies, Entyvio for ulcerative colitis, and Kalydeco and Orkambi for cystic fibrosis.

Our Principles

We maintain a culture that embodies the following core principles with the aim to provide long-term benefits to patients and to create significant value for our employees, investors and other stakeholders:

- We are committed to transforming the lives of patients.
- We are pioneering in our science.
- We challenge each other to achieve excellence.
- We work with passion, integrity and respect.
- We like rigorous work and serious fun.

Our Strategy

Our mission is to transform the lives of patients through the creation of novel gene control medicines by building a fully integrated, leading biopharmaceutical company. To achieve this mission, we are executing on the following strategy:

- **Rapidly and efficiently advance our lead programs through clinical development.** We intend to submit two INDs in 2016. We expect to submit an IND for SY-1425 and to enroll our first patient in a Phase 2 clinical trial in mid-2016. We expect to select a development candidate from our CDK7 inhibitor program in the first half of 2016, start IND-enabling activities in the first

half of 2016, submit an IND in the second half of 2016 and initiate a Phase 1/2 clinical trial in patients with acute leukemias in the first half of 2017. For both of these programs, we intend to enrich our clinical trials with patients most likely to respond, which we believe will enable us to rapidly establish clinical proof-of-concept. Because AML, MDS and ALL are diseases of significant unmet medical need, we could be eligible, subject to encouraging clinical results, to apply for Breakthrough Therapy designation and Fast Track designation which, if granted, could accelerate clinical development and regulatory review.

- **Develop a robust pipeline of gene control product candidates.** We plan to continue leveraging our gene control platform to systematically and efficiently pinpoint genes that cause disease and to identify optimal therapeutic points of intervention in genomically defined patient populations. Employing our unique drug discovery approach, we intend to continue to either internally discover selective small molecule inhibitors of these targets or link existing drugs to novel patient populations, enabling us to potentially accelerate our clinical development path. We aim to generate one IND submission every other year, on average.
- **Maintain our leadership position in the field of gene control.** We are pioneering a novel approach to discover and develop gene control medicines. To fortify our leadership position, we intend to enhance our mapping technologies to create the most extensive collection of maps of gene control programs. We also intend to expand our validation technologies to continue to identify and validate novel targets and biomarkers across many serious diseases. Our long-term goal is to map all serious diseases where gene control is a potential viable therapeutic strategy and to validate therapeutic targets from these maps. We plan to continue investing in building our drugging capabilities, including developing proprietary assays and enhancing our biochemistry, structural biology and medicinal chemistry expertise to create or acquire gene control medicines targeting disease drivers identified by our maps.
- **Continue to foster a culture of innovation.** We are committed to pioneering science and to leadership in gene control medicines. Our employees are critical to the successful achievement of our leadership vision. We will continue to foster an environment that encourages innovation, excellence and productivity and develops our team as leaders in the field of gene control.
- **Execute strategic collaborations to maximize value and extend the potential of our gene control platform across multiple disease areas.** We intend to engage in strategic collaborations around both our programs and our platform. With respect to our programs, we currently own the rights to develop and commercialize SY-1425 in North America and Europe for all cancer indications. We currently retain full commercial rights to our CDK7 inhibitor program and all our other preclinical programs. We intend to evaluate collaborations that could maximize value for our programs by allowing us to expand our geographic reach and expand into additional indications. With respect to our platform, we are seeking target and drug discovery collaborations that allow us to expand the potential of our platform in cancers and other serious diseases beyond those that we can address on our own.

Our Focus—Gene Control Medicines

There are approximately 200 different cell types in a given individual. Despite having identical genomes, each of these cell types has a different function. For example, a skin cell functions differently than a muscle cell despite sharing the exact same DNA. A small number of genes within a cell are crucial in determining cell type and function. The coordinated expression of these crucial genes, which we refer to as the cell's gene control program, is what ultimately determines the type and function of a cell. The gene control program in each cell is implemented by a number of cellular components, key to which are transcription factors, transcriptional kinases and other transcriptional and regulatory proteins.

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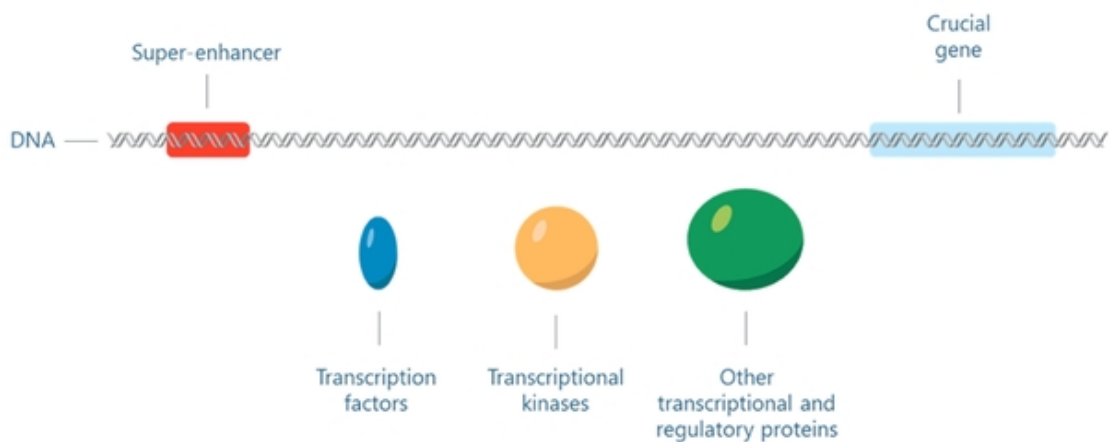
These proteins are associated with specific DNA regions, called enhancers, and control the rate of transcription of genetic information from DNA into the cell.

In disease, the gene control programs are altered, which changes the expression of the crucial genes determining cell type and function. This process is mediated by changes in transcription factors, transcriptional kinases and other transcriptional and regulatory proteins that regulate the coordinated expression of genes, which makes these proteins important points for therapeutic intervention.

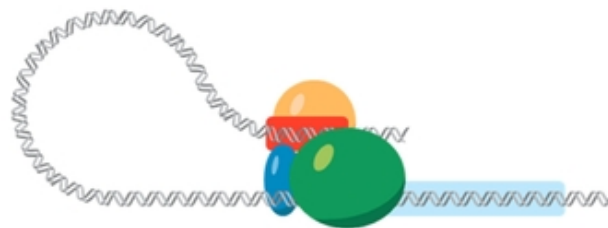
Richard A. Young, Ph.D., a Syros co-founder, a professor at Whitehead and the Department of Biology at the Massachusetts Institute of Technology, and a leader in gene control, has made recent and significant contributions to the understanding of gene control programs. Dr. Young's laboratory discovered that a very small number of enhancers, called super-enhancers, are central to orchestrating gene control programs by driving increased expression of crucial genes responsible for determining cell type and function. Analysis of the super-enhancers within a cell can rapidly and systematically enable an understanding of the gene control programs responsible for determining cell type and function and provide critical insights into important changes in disease, pinpointing targets for therapeutic intervention.

The graphics below illustrate how super-enhancers assemble the cellular components of the transcription process that drive the expression of genes that are crucial to cell type and function.

Multiple cellular components are associated with gene expression



Super-enhancers assemble these components to drive gene expression



Super-enhancers exist in both normal and diseased cells. In many different diseases, super-enhancers are associated with, and drive the expression of, disease-causing genes. For example, multiple well-known genes, such as *MYC*, are implicated in cancer and are associated with super-enhancers.

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Based on our identification and analysis of disease-specific super-enhancers, we can uncover new targets and patient populations for drug discovery and development.

The discovery and development of targeted therapies, in which the right drug is matched to the right patient, has dramatically improved the ability to treat cancer and other serious diseases. The success of targeted therapies relies in large part on identification of patients with a specific genetic alteration who are most likely to benefit from a particular treatment. Most targeted therapies in oncology focus on targeting one abnormal protein resulting from a genetic alteration. In contrast, gene control medicines target gene control programs that are implicated in disease at the level of gene expression, opening up a wide array of potential new drug targets, including transcription factors, transcriptional kinases and other transcriptional and regulatory proteins. Dysregulation of gene control programs is fundamental to many serious diseases, including cancer. We believe gene control medicines will allow us to influence multiple drivers of disease in a targeted fashion to achieve a profound and durable clinical benefit for patients.

The relatively few gene control medicines available are among the most important targeted therapies available today and are widely used for the treatment of cancer and inflammatory diseases. Drugs that target transcription factors, such as estrogen receptors in breast cancer, androgen receptors in prostate cancer and glucocorticoid receptors in inflammation, are important examples of gene control medicines that have produced transformative patient benefits. For example, tamoxifen, a gene control medicine targeting a transcription factor, revolutionized the treatment of certain breast cancers and is prescribed 1.9 million times annually in the United States, illustrating the significant therapeutic potential of gene control medicines. However, a lack of understanding of gene control programs has historically prevented a systematic approach to identifying these critical points of therapeutic intervention, making gene control a largely untapped field for drug discovery and development.

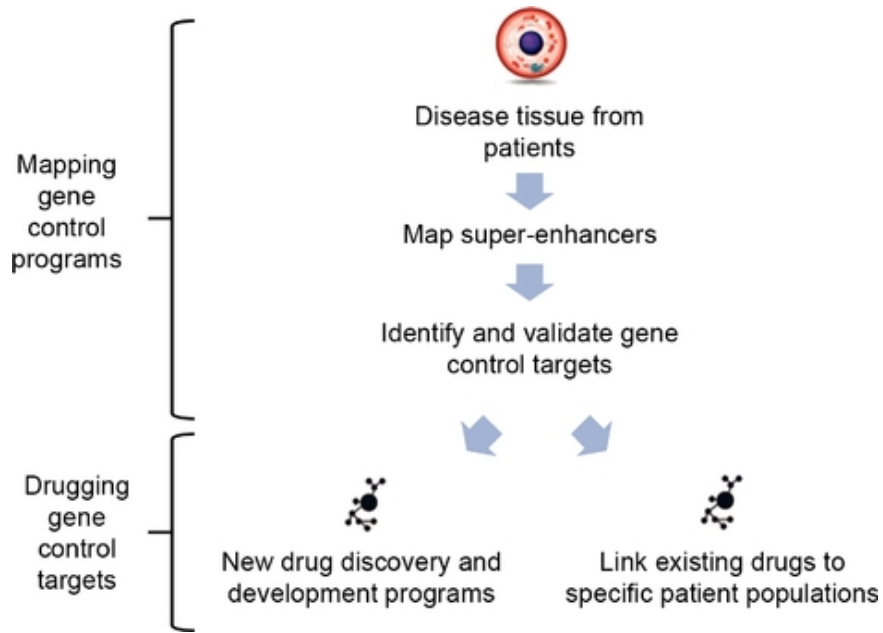
Until recently, understanding of gene control programs and opportunities to therapeutically intervene have been limited. Based on the work of Syros' scientific founders Dr. Young, James Bradner, M.D. and Nathanael Gray, Ph.D., and other scientists, there is now a growing scientific understanding of gene control. That understanding, combined with technological advancements, has enabled our pioneering approach to creating gene control medicines. We have built a platform that we believe enables us to systematically discover novel gene control targets and biomarkers in human disease and create gene control medicines for the treatment of cancer and other serious diseases.

Our Gene Control Platform

Our proprietary gene control platform consists of two fundamental pillars:

- *Mapping.* We map gene control programs to identify novel disease targets and biomarkers linked to specific patient populations.
- *Drugging.* We develop product candidates against gene control targets through:
 - internal drug discovery efforts focused on creating drugs targeting transcription factors, transcriptional kinases and other transcriptional and regulatory proteins; and
 - externally focused efforts to link existing drugs to specific patient populations identified through our platform. These externally focused efforts could enable us to identify drugs that

we may seek to in-license or acquire or use as a starting point for our own drug discovery programs to accelerate our development path.



Mapping Gene Control Programs

We have invested significant resources in building capabilities to discover novel gene control targets and biomarkers. Our approach is disease-focused. Our platform consists of technologies and capabilities to map and analyze gene control programs directly from patient tissue samples. We do this by employing our expertise and technologies in computational, gene control and cellular biologies. We have in-licensed intellectual property from the laboratories of our scientific founders at Whitehead and Dana-Farber. We have significantly improved this licensed technology, including computational algorithms and tissue processing systems, which have produced a highly efficient, scalable approach to analyze gene control programs using small amounts of patient tissue. In addition, we are developing our own intellectual property related to this technology. These advancements have enabled us to generate large sets of maps of gene control programs and identify novel targets across many diseases and cell types. We are in the process of mapping gene control programs in several other diseases, with the long-term goal of mapping gene control programs in all serious diseases where we believe currently underserved patients can benefit from gene control medicines.

Mapping Gene Control Programs in Disease

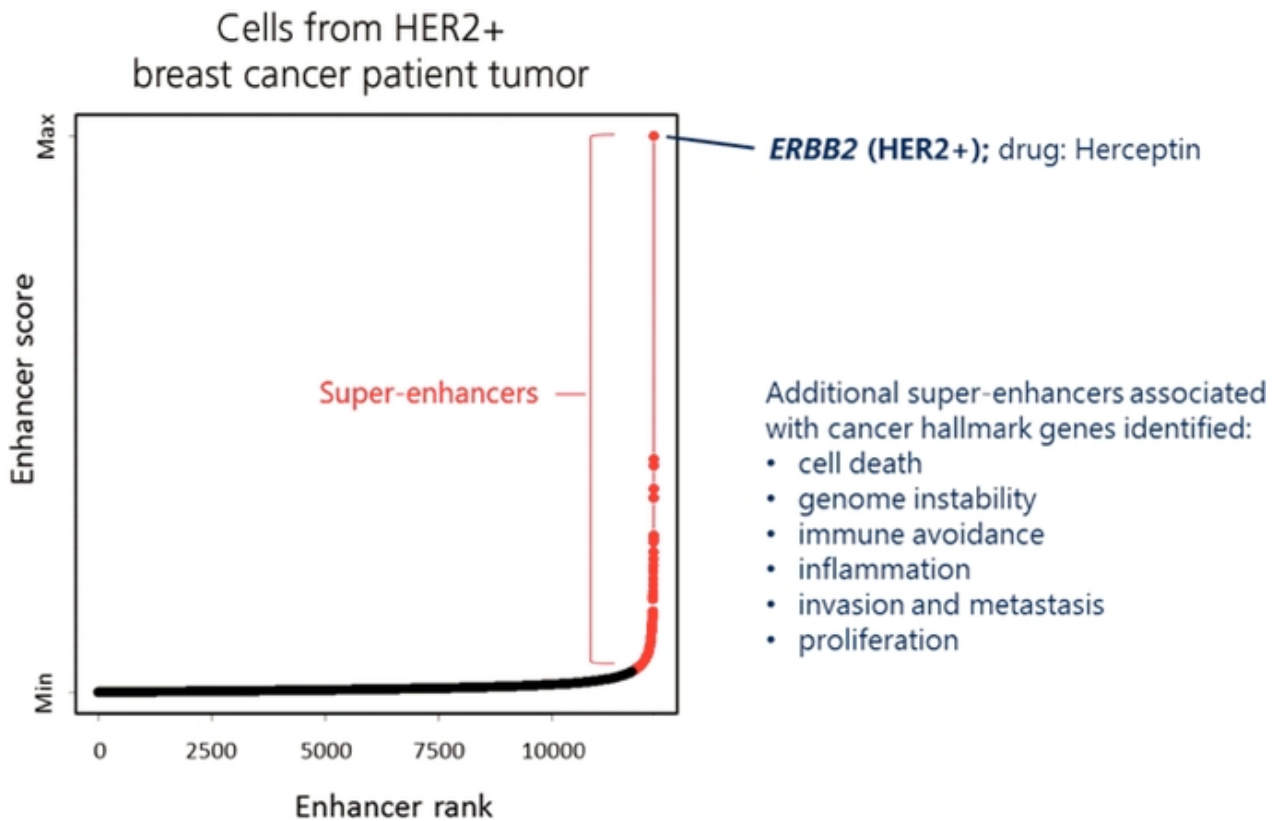
<u>Generated</u>	<u>Ongoing and Planned</u>
AML	Colorectal cancer
Breast cancer	Hepatocellular carcinoma
Polycystic kidney disease	Lung cancer
Renal cell carcinoma	Melanoma
Spinal muscular atrophy	Ovarian cancer
Normal T-cells	Pancreatic cancer
Macrophages	Additional cancers
	Alzheimer's disease
	Inflammatory disorders, including autoimmune diseases and fibrotic diseases
	Other rare genetic disorders

We use our platform to pinpoint crucial genes in disease. We compare diseased cells to healthy cells and analyze the cells of different patient subsets within a disease to identify novel targets in genomically defined subsets of patients. We obtain human disease tissue samples from our network of academic collaborators and commercial providers. We then analyze these samples using a variety of genomic tools, including chromatin immunoprecipitation followed by whole genome sequencing, or ChIP-seq, and proprietary computational methods. The combination of these tools allows us to identify the location of DNA elements, including super-enhancers and their associated genes, on the genome. We validate this potential pool of targets by using biological methods for knocking down or out the target gene in cell lines, or by testing existing drugs against a specific target, to determine if the target represents an attractive point of therapeutic intervention.

Validation of Our Approach

We have validated our approach by successfully linking known targets of successful, marketed drugs to super-enhancers in human tissue. For example, in breast cancer, we were able to recapitulate current knowledge of disease biology and identify clinically validated targets. In the graphic below, which represents a map of a tumor from a single breast cancer patient positive for overexpression of the *ERBB2* gene, which we refer to as HER2+ breast cancer, we illustrate how we use our maps of gene control programs to identify important targets in an individual's cancer. Based on the analysis, we generated a composite score for each enhancer in the sample based on its size and strength. This composite score allowed us to rank all of the enhancers found in the cancer cells and distinguish regular enhancers from super-enhancers. As shown below, the super-enhancers have significantly higher scores than other enhancers. Using this analysis, we identified 485 super-enhancers among the approximately 12,000 enhancers in this tumor. The unlabeled red dots in the graphic below represent super-enhancers associated with genes linked to hallmarks of cancer, including genes important in proliferation, invasion and metastasis and immune avoidance. Some of the products of these cancer

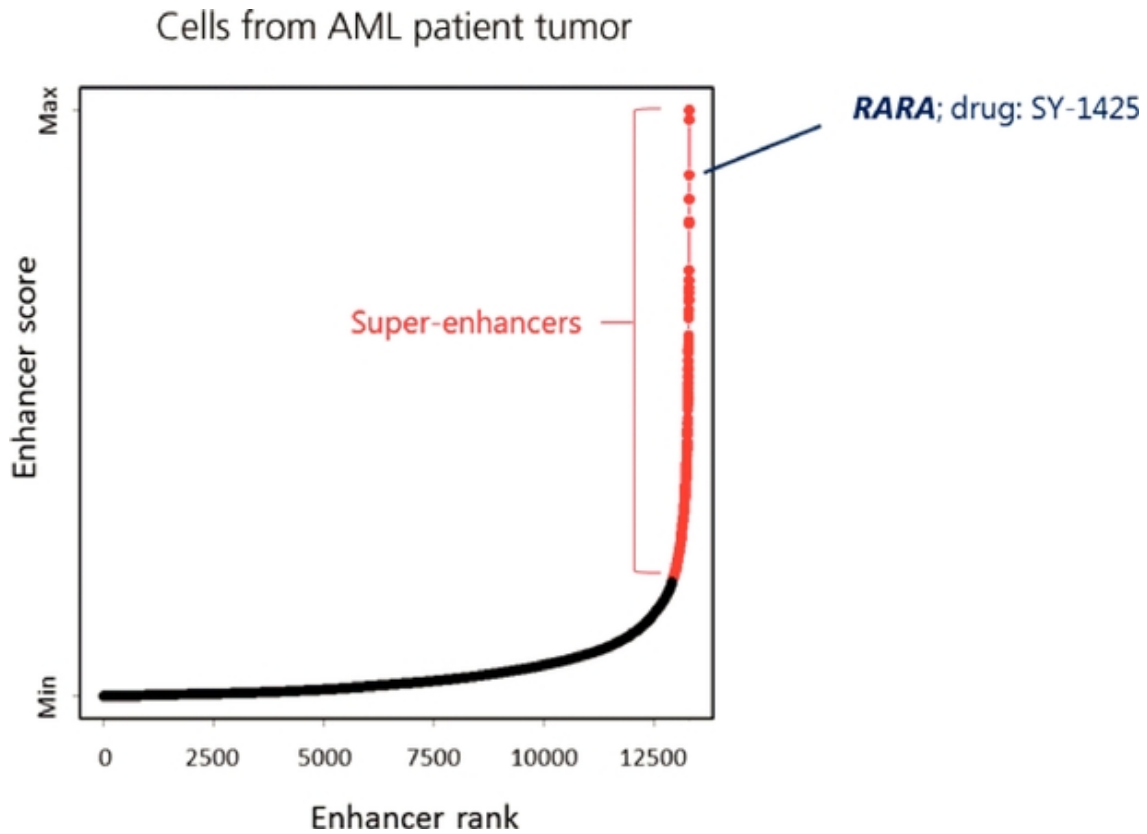
drivers are targeted by existing drugs. HER2+ patients, for example, are treated with Herceptin (trastuzumab).



Similarly, in ER+, or estrogen receptor-positive, breast cancer patient samples, super-enhancers were associated with *ESR1*, a gene that produces estrogen receptor. Through this approach, we have identified novel targets in multiple segments of breast cancer, including breast cancer that is HER2-negative, ER-negative and progesterone receptor-negative, or PR-, also known as triple negative breast cancer.

In addition to replicating known targets, we have been able to link super-enhancers to novel patient populations to identify several targets for therapeutic intervention. As an example, the graphic below shows the map of enhancers in a tumor from a single patient with AML. The super-enhancer associated with the *RARA* gene is among the largest super-enhancers in this tumor. Similar to the HER2+ example above, the unlabeled red dots in the graphic below represent other super-enhancers that could enable us to identify potential novel drug targets and biomarkers. We have mapped multiple

patients' tumor cells and have identified tissues from other AML patients with the same *RARA* super-enhancer.



Drugging Gene Control Targets

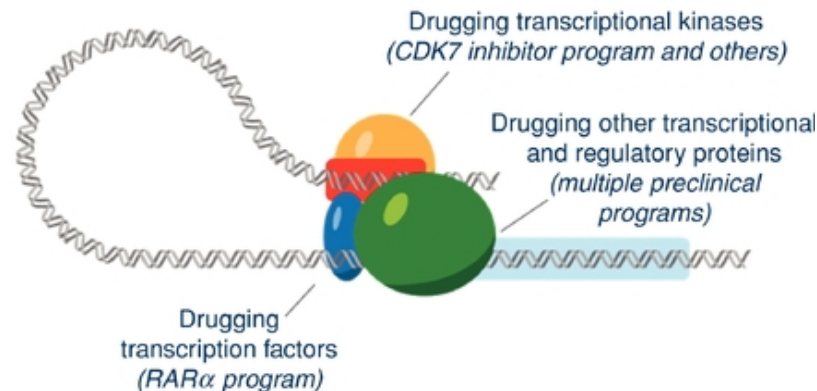
We develop product candidates against gene control targets through:

- internal drug discovery efforts focused on creating drugs targeting transcription factors, transcriptional kinases and other transcriptional and regulatory proteins; and
- linking existing drugs, which we could in-license, to specific patient populations identified through our platform—a strategy designed to accelerate our clinical development path.

We have developed core internal capabilities in computational biology, small molecule chemistry, biochemistry and structural biology to characterize the structure and function of transcription factors, transcriptional kinases and other transcriptional and regulatory proteins in order to generate novel chemical matter. Our capabilities enable us to pursue multiple drug discovery strategies to achieve

therapeutic gene control. The graphic below illustrates our areas of focus for development of product candidates.

Developing product candidates against gene control targets



Drugging Transcriptional Kinases

Our selective, potent and internally created inhibitors of CDK7 demonstrate our ability to identify tumors with transcriptional dependencies and to selectively drug transcriptional kinases. Using our core capabilities in gene control biology and biochemistry, we believe that we created the first selective, small molecule inhibitors of CDK7 with *in vivo* efficacy. We have generated a set of compounds from which we expect to select a development candidate for IND-enabling activities in the first half of 2016.

Drugging Transcription Factors

Leveraging our expertise in biology, biochemistry and chemistry, we have developed a suite of proprietary screens and assays to demonstrate direct binding of novel transcription factor inhibitors and to directly assess transcription factor inhibition in cells. Using our capabilities and expertise in X-ray crystallography and medicinal chemistry, we are developing proprietary atomic-level knowledge of the structural determinants of transcription factor inhibition by small molecules. We have generated novel molecules that are in early preclinical development and show biophysical evidence of potent direct transcription factor binding and robust cellular activity.

Linking Existing Drugs to Novel Patient Populations

SY-1425 demonstrates our ability to link existing drugs to novel genomically defined patient populations identified through our platform. We have established a process to systematically screen existing compounds for relationships between drug sensitivity and super-enhancers that we identified in human disease tissue. To date, we have identified multiple drug and enhancer relationships, the most advanced leading to our SY-1425 program. We expect this approach to enable us to more rapidly enter clinical development by accessing compounds that serve as accelerated starting points for our own programs.

Advantages of our Platform and Approach

We believe that there are significant advantages to systematically mapping, identifying and drugging gene control targets for specific patient populations. Among these advantages are:

- **Systematic, reproducible and unbiased approach to identifying core disease drivers in multiple serious diseases.** We take a disease-centric approach. We start with human tissue and, through our platform, systematically identify the core drivers of disease. We identify optimal points of

therapeutic intervention in a target- and pathway-agnostic manner, opening up a wide array of potential new drug targets.

- **Ability to discover and develop medicines that address significant patient need.** We are initially focused on difficult-to-treat cancers or cancer subtypes for which current therapies are inadequate. Because gene control medicines affect multiple disease-driving genes, we believe they will be less susceptible to the development of resistance than other types of genomic-based targeted medicines, potentially resulting in a more profound and durable benefit for patients. This is evidenced by the proven durable benefits of the gene control medicines available today.
- **Potential for efficient clinical development.** We intend to enrich our clinical trials with genomically defined subsets of patients who are most likely to respond to our treatment, which we believe will enable us to determine if there are strong signals of efficacy early in clinical development and well before investments are made in expensive late-stage clinical studies. Subject to encouraging clinical results, we could be eligible to apply for Breakthrough Therapy designation and Fast Track designation which, if granted, could accelerate clinical development and regulatory review, allowing us to bring our therapies to patients expeditiously.

Our Clinical Programs

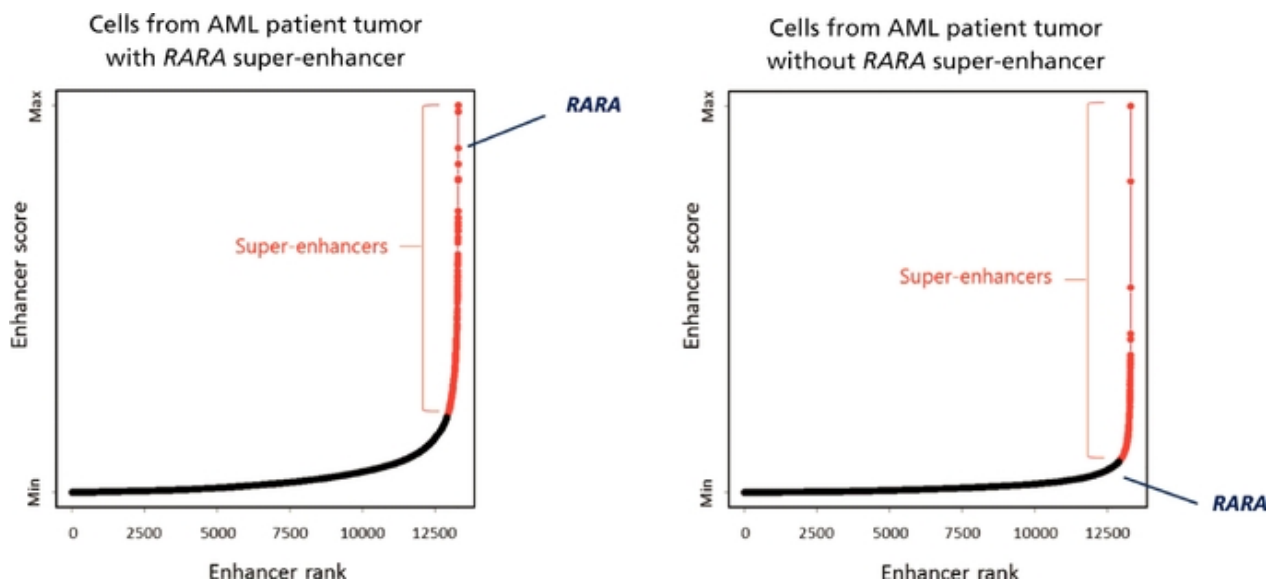
SY-1425

Overview

SY-1425 (tamibarotene) is an oral, potent and selective agonist of the transcription factor RAR a. In September 2015, we in-licensed rights to develop and commercialize SY-1425 for oncology indications in North America and Europe. In mid-2016, we plan to initiate a Phase 2 clinical trial that will enroll genomically defined patients with AML and MDS. We plan to select patients for this trial using the *RARA* biomarker we identified. We believe patients whose tumors have this biomarker will be more likely to experience a profound and durable clinical benefit from treatment with SY-1425.

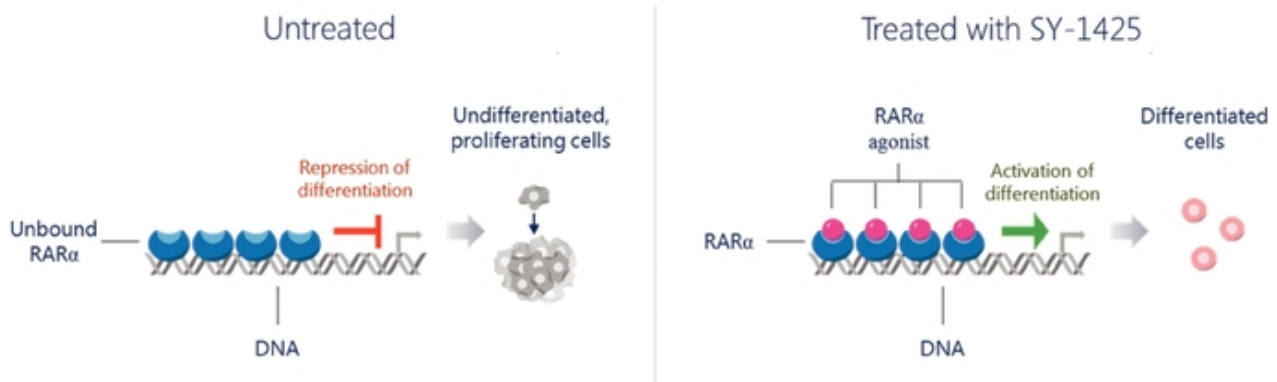
Linking SY-1425 to Novel Patient Populations

We leveraged our platform to map gene control programs in primary AML and breast cancer patient tissue samples. We discovered that *RARA*, the gene that produces RARa, was associated with a super-enhancer in some patients' tumors but not in others, as illustrated in the graphic below.



The function of RAR α differs depending on whether it is bound to its ligand. In the absence of a ligand, RAR α represses differentiation. We believe that in tumors with the *RARA*-associated super-enhancer, there is an abundance of unliganded RAR α , resulting in the repression of differentiation, thereby locking the cell in an immature, proliferative state. Introducing an RAR α agonist, such as SY-1425, simulates the activity of a ligand, activating differentiation, as illustrated in the graphic below.

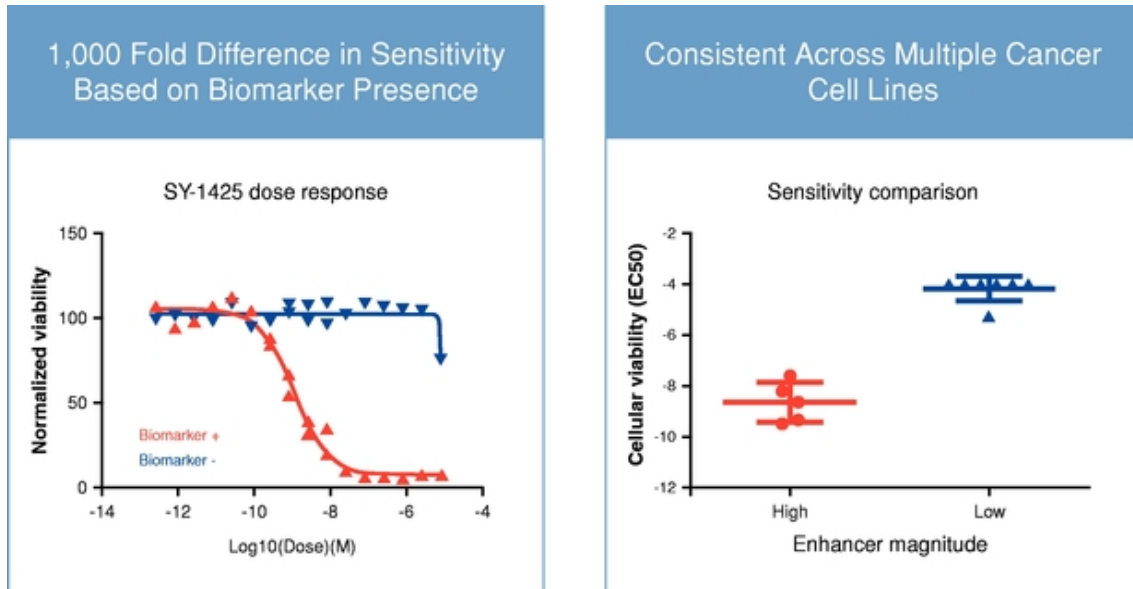
Patient with *RARA* super-enhancer



SY-1425 is an oral, selective RAR α agonist. Based on experiments we conducted, we have concluded that the mechanism of action of SY-1425 on non-APL AML cells with an *RARA*-associated super-enhancer is very similar to the mechanism of approved retinoic acid agonists in APL, a subset of AML with a genetic alteration of the *RARA* gene. This gives us increased confidence that SY-1425 may also work on this new subset of AML and MDS patients identified by our platform.

We selected SY-1425 based on its superior potency on RAR α , its selectivity for RAR α over related proteins RAR β and RAR γ and its superior pharmacokinetic profile compared to all trans retinoic acid, or ATRA, a pan-agonist of RAR α , RAR β , and RAR γ . SY-1425 is approved, as tamibarotene (marketed as Amnolake), in Japan for use in acute recurrent or intractable APL, in which it has demonstrated efficacy and a well-established safety profile.

Through our platform, we have identified a biomarker for the *RARA* super-enhancer that we will use for patient selection. Our *in vivo* studies demonstrated that cancer cells with the *RARA* biomarker showed reduced rates of proliferation and differentiated to more mature cells when treated with SY-1425, while cancer cells without the biomarker continued to proliferate. Our studies also demonstrated that cancer cells with the *RARA* biomarker were up to 1,000 times more sensitive to SY-1425 than cancer cells without the biomarker, as shown below. This sensitivity was consistent across multiple cancer cells lines.

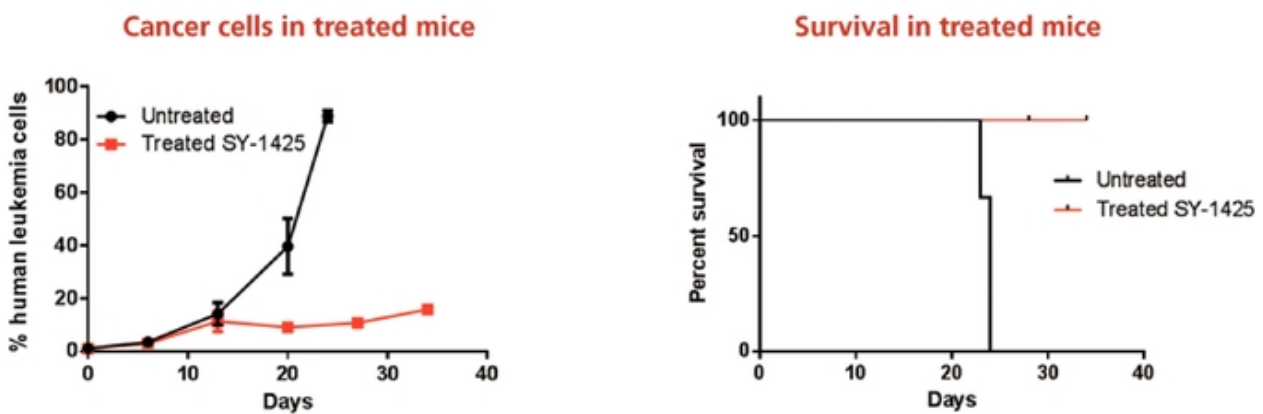


Our Preclinical Data

We have conducted multiple preclinical studies of SY-1425 in AML, excluding APL, and in breast cancer. In certain studies, we use mouse models in which mice are implanted with human tumors, which are referred to as patient-derived xenograft models, or PDX models. In PDX models of AML, SY-1425 was observed to be effective in reducing the growth of tumors and prolonging survival in mice with tumors with the *RARA* biomarker, but did not appear to stop tumor growth or prolong survival in mice whose tumors did not appear to have the biomarker.

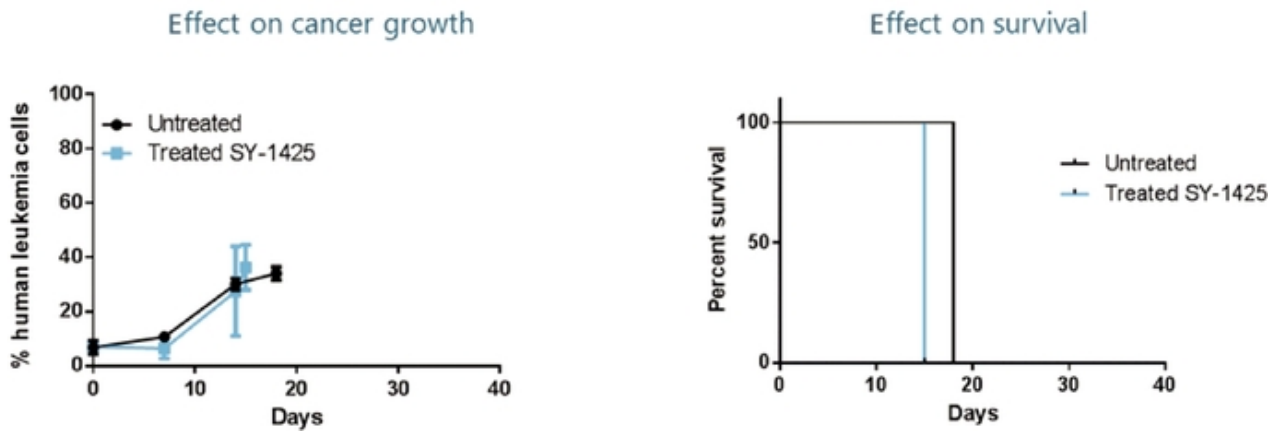
As shown below, in a PDX model derived from AML patient tumor cells with the *RARA* biomarker, referred to as biomarker-positive AML, half of the mice were treated with SY-1425, and the other half of the mice went untreated. In the untreated group, the cancer progressed, as measured by the percentage of human leukemia cells in the blood. Correspondingly, high levels of these cancer cells were measured in the bone marrow and spleen of the untreated mice. None of the untreated mice in the study survived beyond 25 days. In contrast, the cancer was observed to be controlled in the mice treated with SY-1425, as measured by the levels of human leukemia cancer cells detected in the blood. Similarly, low levels of these cancer cells were measured in the bone marrow and spleen. Notably, all of the mice treated with SY-1425 survived until the end of the 35-day study.

RARA Biomarker-Positive Model in AML



In contrast, as shown below, in a PDX model without the *RARA* biomarker, SY-1425 was observed to have no effect on tumor control or survival. In both the treated and untreated groups, the cancer progressed, as measured by the percentage of human leukemia cells detected in the blood. Correspondingly, high levels of these cancer cells were measured in the bone marrow and spleen in both groups of mice. None of the untreated mice survived beyond 20 days. These data demonstrate a strong link between the *RARA* biomarker and sensitivity to SY-1425, and provide meaningful evidence that patients with the *RARA* biomarker may be promising candidates for a clinical trial of SY-1425.

RARA Biomarker-Negative Model in AML



We have also compared the activity of SY-1425 to the activity of ATRA in the *RARA* biomarker-positive PDX model. We observed superior anti-tumor activity and survival with SY-1425 compared to ATRA, with ATRA-treated mice demonstrating similar survival to the untreated mice.

Additionally, in our preclinical studies in breast cancer, we observed a strong link between SY-1425 activity and breast cancer tumors with the *RARA* biomarker. SY-1425 was observed to result in significant tumor growth inhibition in PDX models derived from tumors with the *RARA* biomarker but was observed to have no effect in *RARA* biomarker-negative PDX models.

SY-1425 Clinical Development Plan

We plan to develop SY-1425 in North America and Europe for treatment of AML and MDS in genomically defined patient populations identified by our *RARA* biomarker. In the United States, we expect to submit an IND to the FDA and initiate a Phase 2 clinical trial in AML, excluding APL, and MDS in mid-2016. We expect that this Phase 2 clinical trial will be a multi-center, open-label trial exploring activity in four groups: (1) relapsed or refractory AML patients, (2) AML patients who are elderly or unfit for treatment with standard therapies, (3) high-risk relapsed or refractory MDS patients and (4) low-risk transfusion-dependent MDS patients. We anticipate that we will enroll approximately 60 to 70 patients, who will have been prospectively selected using our *RARA* biomarker. We expect the primary endpoints of the trial to be (1) overall response rate for relapsed or refractory high-risk MDS patients and for AML patients, and (2) transfusion independence for low-risk MDS patients. We also expect to measure duration of response, safety and tolerability, survival and biomarker predictability. We expect to receive data from this trial in mid-2017, or 12 months after the first patient is enrolled.

We have entered into an agreement with a third party commercial provider to continue developing our novel *RARA* biomarker into a validated laboratory test under Clinical Laboratory Improvement Amendment, or CLIA, guidelines using a well-established diagnostic platform and approach that may be used to prospectively enroll *RARA* biomarker-positive patients in our clinical trial. This CLIA

laboratory test could become the basis for a commercial companion diagnostic. We are evaluating commercial providers to lead the development of a potential commercial companion diagnostic for the *RARA* biomarker but have not yet entered in to an agreement with a third party for this work. We expect to do so in the first half of 2016.

Tamibarotene (SY-1425) has been extensively studied and has a well-established safety profile. We expect to use the same dosage used in the treatment of APL in Japan in our Phase 2 clinical trial. This same dosage for SY-1425 was previously used in a U.S. trial in relapsed and refractory APL, for which an IND was opened. We have in-licensed the IND package that was used for approval in Japan and the IND filing in the United States. We believe that this data, including established preclinical and chemistry and manufacturing controls, or CMC, data, will be sufficient for our IND application. Given the prior trials and the existing safety and efficacy data for tamibarotene, which was provided to us under our license agreement with TMRC, we believe that the FDA will permit us to initiate a Phase 2 clinical trial of SY-1425 without requiring us to conduct a Phase 1 clinical trial to assess safety and tolerability. To date, we have not had any communications with the FDA regarding our clinical development plans for SY-1425.

We chose AML and MDS for our initial indications due to high levels of observed efficacy of SY-1425 in our preclinical models, the significant unmet medical need of these patients and the potential for accelerated development. We intend to pursue additional indications, including breast cancer, in the near future. Our preclinical data in breast cancer supports the development of SY-1425 in a genomically defined subset of patients with breast cancers with our *RARA* biomarker. We plan to initiate clinical trials in these patients upon establishing proof-of-concept in AML and MDS. We also believe there are subsets of patients with other tumor types with our *RARA* biomarker and continue to research the role of the *RARA* super-enhancer in additional cancers.

Existing Clinical Data

Tamibarotene (SY-1425) is approved and marketed as Amnolake in Japan for treatment of acute recurrent or intractable APL. Given the demonstrated efficacy of the drug in acute recurrent or intractable APL, we intend to evaluate SY-1425 for treatment of APL in North America and Europe. Extensive clinical work has been conducted on tamibarotene prior to our in-licensing it from TMRC. The effectiveness of tamibarotene has been evaluated in patients with APL, including for relapsed patients and as maintenance therapy for newly diagnosed patients.

- In a Phase 2 clinical trial of tamibarotene as a single agent in patients who relapsed following treatment with ATRA, 58% achieved a complete response. The majority of these patients went on to receive a bone marrow transplant or chemotherapy after treatment with tamibarotene and maintained a complete response for at least 14 months.
- In a Phase 3 clinical trial comparing tamibarotene as an add-on therapy to arsenic trioxide, or ATO, a standard of care for APL, versus ATRA as an add-on therapy to ATO in relapsed patients, patients in the tamibarotene-treated group demonstrated:
 - An overall complete response rate of 80%, compared to 54% in the ATRA-treated group ($p=0.022$); and
 - A complete molecular remission rate of 23%, compared to 3% in the ATRA-treated group ($p=0.0275$). Complete molecular remission is achieved when there is no evidence of disease in the patient's blood cells as detected by DNA-based tests.
- In a different Phase 3 clinical trial comparing tamibarotene to ATRA as maintenance therapy in newly diagnosed APL patients, the four-year relapse-free survival rate in high-risk patients treated with tamibarotene was 87%, compared to 58% in high-risk patients treated with ATRA ($p=0.028$).

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In all these studies, tamibarotene was generally well tolerated. Adverse effects included mild or moderate dry skin, skin rash, headache and bone pain, as well as retinoic acid syndrome and elevated levels of cholesterol, lipids, liver function enzymes and white blood cells, which were severe in certain cases. One such adverse effect, retinoic acid syndrome, is referenced on the drug's label and was infrequently observed clinically. Retinoic acid syndrome is a side effect associated with retinoids and arsenic trioxide and can be mitigated by regular monitoring of clinical parameters, including white blood cell counts. A summary of four published clinical studies of tamibarotene use in APL is provided below.

Design	Number of Patients	Patient Population	Tamibarotene Treatment	Efficacy / Duration		
Phase 2 in relapsed APL ¹	25	Relapse after ATRA-induced CR	6 mg/m ² daily, discontinued at CR	CR = 58% (14/24 evaluable) (³ 14 months duration in 5 patients in conjunction with BMT, 7 patients in conjunction with CT)		
Phase 3 tamibarotene vs. ATRA as APL maintenance ²	269	Front-line following ATRA-induced CR and consolidation	Tamibarotene 6 mg/m ² vs. ATRA 45 mg/m ² 14 days every 3 months for 2 years	Overall 4-year RFS: 91% vs. 84%; 4-year RFS in high risk: 87% vs. 58% (tamibarotene vs. ATRA)		
Phase 2 in relapsed/refractory APL after ATRA and ATO ³	14	Patients with prior lines of treatment (9 with 2 prior lines, 3 with 3 prior lines and 2 with 5 prior lines)	6 mg/m ² daily for 56 day induction period then every other month as consolidation for up to one year	CR = 36% CRi = 29% mEFS = 3.5 months mOS = 9.5 months		
Phase 3, tamibarotene vs. ATRA as add-on to ATO in relapsed APL ⁴	71		6 mg/m ² /day tamibarotene, 25 mg/m ² /day ATRA add-on to 0.15 mg/kg/day ATO for 56 days		Tamibarotene	ATRA
					+ATO	+ATO
				CR	80%	54%
				CRm	23%	3%

Table legend:

CR = complete remission

CRm = complete molecular remission

CRi = complete remission with incomplete blood count recovery

RFS = relapse-free survival

mEFS = median event-free survival

mOS = median overall survival

BMT = bone marrow transplant

CT = chemotherapy

1. Tobita, et al. *Blood*, August 1997.
2. Shinagawa, et al. *Journal of Clinical Oncology*, November 2014.
3. Sanford D, et al. *British Journal of Haematology*, July 2015.
4. Wang et al, ASH presentation, December 2015.

Tamibarotene was also studied in a Phase 2 clinical trial for the treatment of unselected late-stage non-small cell lung cancer under a previous license between TMRC and a third party. This trial was terminated when interim data suggested that a primary endpoint of progression-free survival for 18 months after starting therapy would not be reached.

SY-1425 Market Opportunity

We believe that SY-1425 has the potential to address significant unmet medical need across a range of blood cancers and solid tumors. Based on our analysis of *RARA* super-enhancers in patient samples, and on *RARA* biomarker data in publicly available databases, we estimate that approximately 25% of AML and MDS patients and approximately 35% of breast cancer patients may benefit from *RARA* agonist therapy like SY-1425.

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There are an estimated 33,000 new AML diagnoses in the United States, Canada and the five largest European countries each year. AML remains an area of significant unmet medical need. In the United States, newly diagnosed patients have a 25% five-year survival rate. There has been little improvement in treatment options for AML, with typical treatment including older chemotherapeutics and stem cell transplantation.

Of the estimated 33,000 newly diagnosed patients in the countries listed above each year, nearly half of these patients, or approximately 16,000, are elderly or unfit for treatment with these invasive standard therapies, leaving this group with very few to no treatment options. Furthermore, approximately 30% or 10,000 AML patients eventually relapse or are refractory to current treatment options. In the absence of adequate therapies, these relapsed or refractory patients may be put into clinical trials for new and emerging therapies.

Based on our analysis of *RARA* super-enhancers in patient samples and on *RARA* biomarker data in publicly available databases, we believe that approximately 25% of AML patients could benefit from treatment with a *RARa* agonist such as SY-1425. Thus we estimate that in the countries listed above, approximately 4,000 patients who are elderly or unfit for current intensive treatments and 2,500 patients who eventually relapse or are refractory to current treatment options could benefit from treatment with a *RARa* agonist such as SY-1425.

There are approximately 32,000 new MDS diagnoses in the countries listed above each year, with up to one-third of these newly diagnosed patients estimated to be likely to progress to AML. In the United States, high-risk patients, who represent 23% of the total MDS patient population, have a median survival of only approximately two years, while the low-risk patient population has a median survival of approximately six years. As with AML, treatment options are limited.

Of the estimated 32,000 newly diagnosed patients in the countries listed above each year, more than half of these patients, or approximately 17,000, have low-risk transfusion-dependent MDS. Furthermore, approximately 19% or 6,000 MDS patients have high-risk relapsed or refractory MDS.

Based on *RARA* biomarker data in publicly available databases, we believe that approximately 25% of MDS patients could benefit from treatment with a *RARa* agonist such as SY-1425. Thus we estimate that in the countries listed above, approximately 4,250 patients with low-risk transfusion-dependent MDS and 1,500 patients with high-risk relapsed or refractory MDS could benefit from treatment with a *RARa* agonist such as SY-1425.

Approximately 485,000 women in the countries listed above are diagnosed with breast cancer annually, with 158,000 of these women categorized as metastatic and eligible for systemic therapies. Breast cancer is categorized and treated by the stage for risk of metastatic recurrence and by whether it is driven by estrogen receptor and progesterone receptor signaling, referred to as being hormone positive, driven by HER2 receptor signaling, referred to as being HER2+, or neither, which is referred to as being triple negative. Despite advances in treatments for hormone-positive and receptor-positive patients, the lack of similar advances in treatment options for triple negative breast cancer patients, which represent approximately 15 to 20% of all newly diagnosed breast cancer patients each year in the countries listed above, represents a significant unmet medical need. In the United States, the five-year survival rate of newly diagnosed metastatic breast cancer is approximately 26%. In the United States, 40,000 women die annually from breast cancer, making breast cancer one of the largest causes of cancer-related deaths. Based on our analysis of patient samples, we believe that approximately 35% of metastatic patients, or 55,000 patients in the countries listed above, have the *RARA* biomarker and would benefit from a product candidate like SY-1425.

There are an estimated 2,500 new APL cases diagnosed in the United States, Canada and the five largest European countries each year. Despite advances in treating APL, the disease remains associated with a significant incidence of early death due to disease-related susceptibility to bleeding or hemorrhage.

CDK7 Inhibitor Program

Overview

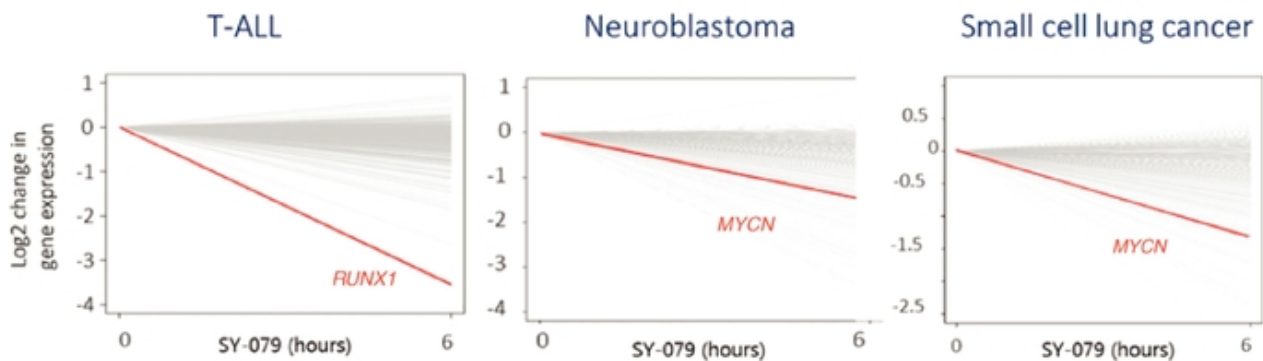
Our CDK7 inhibitor program is focused on cancers that are dependent on a high and constant expression of certain transcription factors for their growth and survival, a phenomenon known as transcriptional addiction. We have generated several first-in-class potent and highly selective small molecule inhibitors of CDK7 with evidence of *in vivo* efficacy. We expect to select our development candidate in the first half of 2016 and start IND-enabling activities soon thereafter. We plan to submit an IND in the second half of 2016 and to initiate a Phase 1/2 clinical trial in patients with acute leukemias, including AML and ALL, in the first half of 2017.

Drugging Transcriptional Kinases

Using our CDK7 inhibitor SY-079, known in the scientific literature as THZ1, our scientific founders and collaborators demonstrated that transcriptionally addicted cancers are particularly sensitive to selective inhibition of CDK7. CDK7, a member of the cyclin-dependent kinase, or CDK, family, is a transcriptional kinase that plays a central role in the expression of transcription factors in these cancers. CDK7 is associated with super-enhancers that control the expression of the transcription factors driving the cancer's growth and survival. Inhibiting CDK7 preferentially lowers the expression of disease-driving transcription factors controlled by super-enhancers, resulting in the selective killing of cancer cells over normal cells.

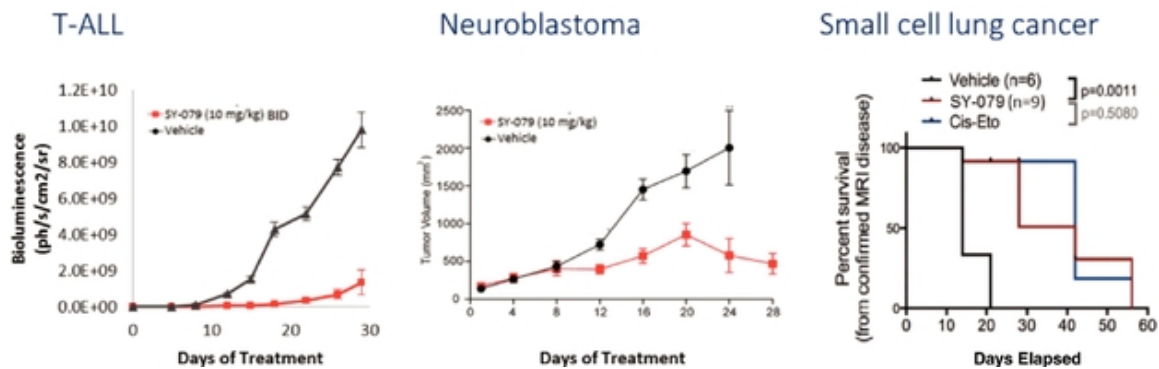
Our scientific founders and collaborators conducted preclinical studies in cell lines of T-ALL, a form of ALL that originates in T-cells, *MYCN*-amplified neuroblastoma, a form of neuroblastoma resulting from amplification of the gene *MYCN*, and small cell lung cancer. As shown in the graphic below, CDK7 inhibition resulted in reduced expression levels of the specific transcription factor contributing to each of these cancers: *RUNX1* in T-ALL and *MYCN* in neuroblastoma and small cell lung cancer. These findings have been published in *Cell*, *Nature* and *Cancer Cell*.

Impact of Inhibition of CDK7 on Expression of Oncogenic Transcription Factors Driving Transcriptionally Addicted Tumors



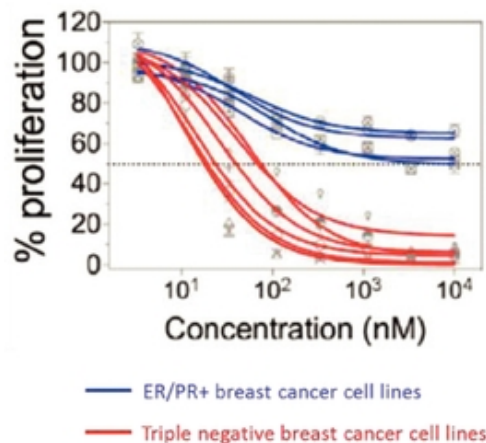
As shown below, in additional preclinical studies conducted by our scientific founders and collaborators, SY-079 also demonstrated significant anti-tumor activity in cell line-derived, or CDX, models of T-ALL and *MYCN*-amplified neuroblastoma, as well as a survival benefit similar to chemotherapy in a genetically engineered mouse model of small cell lung cancer. In the T-ALL model, the tumor size was measured by the bioluminescence, or the aggregate brightness of chemically tagged tumor cells in an imaging study. In the *MYCN*-amplified neuroblastoma model, tumor size was estimated by total volume. In the small cell lung cancer model, researchers demonstrated a survival benefit similar to chemotherapy in genetically engineered mice treated with SY-079.

Anti-Tumor Activity and Survival Benefit of SY-079 in Transcriptionally Addicted Cancers



Our scientific founders and collaborators have also demonstrated the strong potential of CDK7 inhibition, using SY-079, as a novel treatment strategy for triple negative breast cancer, a highly aggressive form of breast cancer that is transcriptionally addicted. In a PDX model of triple negative breast cancer, SY-079 selectively impacted the expression of a set of crucial genes, killing cancer cells and inhibiting tumor growth. This exemplifies our gene control approach of influencing multiple crucial genes driving cancer with one inhibitor in a targeted fashion. The graphic below illustrates the impact of increased exposure of SY-079 on cell growth on ER/PR+ breast cancer cell lines as compared to triple negative breast cancer cell lines.

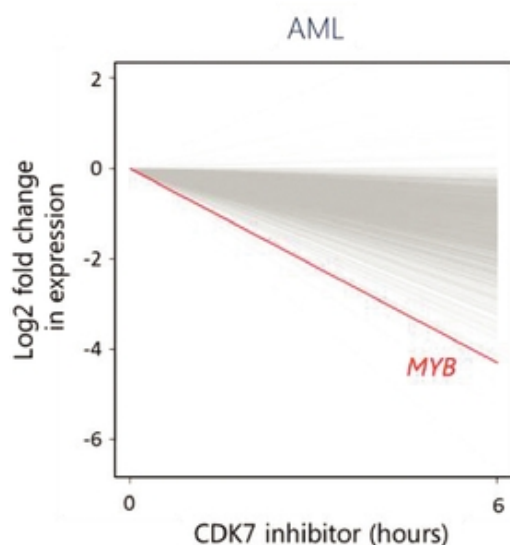
Anti-Tumor Activity of SY-079 in Triple Negative Breast Cancer



As illustrated above, SY-079 was observed to have a dramatic impact on cell growth in triple negative breast cancer cell lines, as measured by the estimated percentage of proliferating cells. The ER/PR+ breast cancer cell lines were significantly less sensitive to treatment with SY-079. These findings were published in *Cell*.

In an AML cell line treated with a CDK7 inhibitor, expression levels of genes associated with super-enhancers that we studied were observed to be more highly repressed on average than those of the genes we studied that are not associated with super-enhancers. In this same cell line, *MYB* was observed to be one of the most highly repressed genes. We believe this finding is significant because *MYB* is a transcription factor gene known to contribute to AML. Notably, we have identified super-enhancers associated with *MYB* in nearly all AML patient samples we have analyzed.

Impact of Inhibition of CDK7 on Expression of *MYB*, an Oncogenic Transcription Factor in AML



Our Preclinical Data

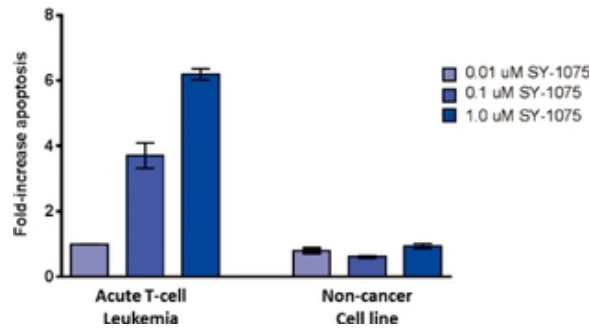
Using our internal drug discovery capabilities, we have generated several potent and selective small molecule CDK7 inhibitors with significantly enhanced drug-like characteristics beyond SY-079. We believe that selectivity is critical for a therapeutic index with CDK inhibition. CDK inhibitors known as pan-CDK inhibitors are not selective for a specific CDK. Though they have demonstrated anti-tumor activity, pan-CDK inhibitors have limited clinical utility due to dose-limiting toxicities. More recently, a selective inhibitor of CDK4/6, members of the CDK family involved in cell cycle, received accelerated approval in breast cancer, demonstrating the substantial clinical benefit of selective CDK inhibition.

In preclinical studies, our CDK7 inhibitors were observed to have significant anti-tumor activity in *in vivo* models of AML, ALL, *MYCN*-amplified neuroblastoma, small cell lung cancer and triple negative breast cancer. Our CDK7 inhibitors are covalent, meaning that they bind irreversibly and selectively to CDK7.

We have conducted a comprehensive set of biochemical and cellular experiments to characterize the potency and selectivity of our CDK7 inhibitors. In those experiments, SY-1075, a representative compound from our CDK7 inhibitor program, demonstrated high biochemical and cellular potency with a high degree of selectivity. When SY-1075 was scanned against a panel of 468 kinase assays, it was observed to demonstrate significant binding to only eight kinases, including CDK7. Notably, SY-1075 was not observed to significantly bind to other members of the CDK family.

As shown below, in a comparative assay measuring a marker of apoptosis, or programmed cell death, SY-1075 preferentially kills cancer cells in acute T-cell leukemia, with a clear dose effect, meaning that as we increased the concentration of the drug, more apoptosis was observed. However, there was relatively little effect on non-cancerous cells regardless of dose.

Impact of SY-1075 on Preferential Killing of Cancer Cells

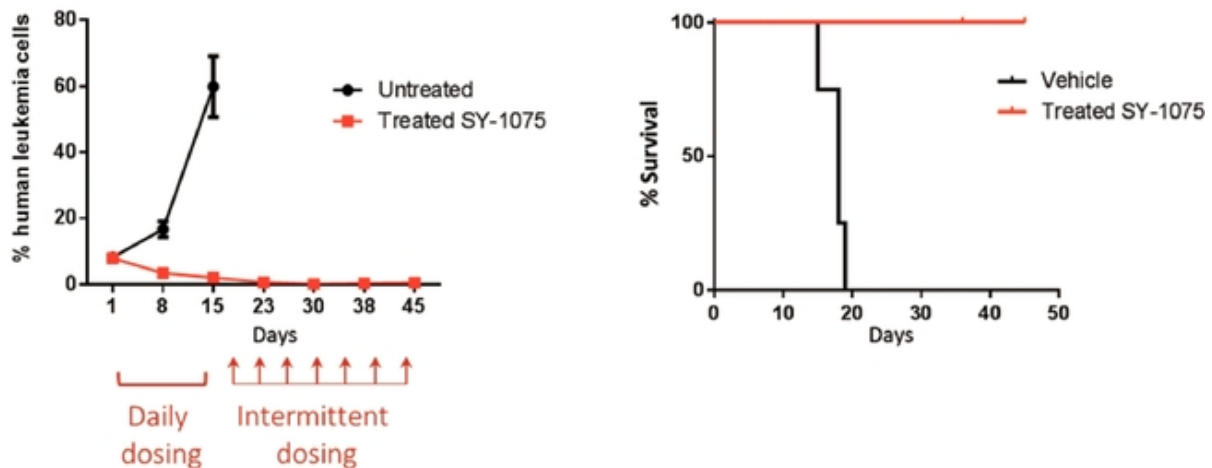


In *in vivo* studies that we conducted, our CDK7 inhibitors were observed to have complete responses and survival benefit in CDX and PDX models of AML. In one such study, which is summarized in the graphic below, SY-1075 was observed to have significant anti-tumor activity and survival benefit in a PDX model of AML. In this study, treated mice received a dose of SY-1075 daily for the first 14 days of the study and then were dosed intermittently, twice per week, through the 48th day of the study.

Mice treated with SY-1075 in this model experienced complete tumor regression, meaning that the percentage of human leukemia cells in the blood was measured at less than 1%. The treated mice showed no significant change to body weight. Maintaining stable body weight is an indicator of a promising safety profile, as well as an indicator of preclinical efficacy. In fact, at the end of the 48-day dosing period, all treated mice remained alive, and levels of human leukemia cells in the blood remained at less than 1%.

In the untreated mice, the cancer progressed, reaching levels of human leukemia cells of greater than 50% in blood and greater than 90% in tissues, at which point all mice had died of their disease or were humanely sacrificed due to excessive tumor burden.

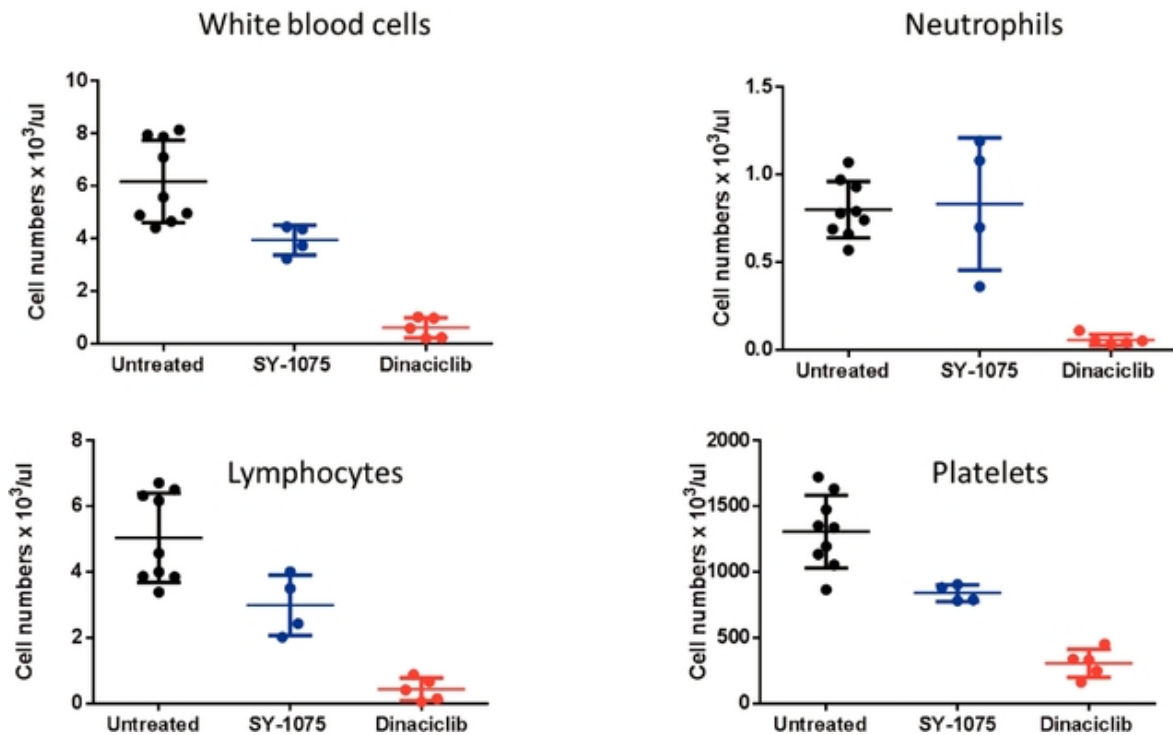
Anti-Tumor Activity and Survival Benefit of SY-1075 in PDX Model of AML



In preclinical studies, one of our CDK7 inhibitors, SY-1075, was observed to have markedly fewer negative effects on healthy cells than certain pan-CDK inhibitors. Pan-CDK inhibitors have been observed to result in blood cell death, or myelosuppression. As shown in the graphic below, when we compared the effect of SY-1075 on four types of blood cells in mice to the effect of a pan-CDK

inhibitor being developed for cancer, known as dinaciclib, the mice treated with SY-1075 did not demonstrate the same level of myelosuppression that occurred in mice treated with dinaciclib. Based on this data, we believe that our CDK7 inhibitors will have a more favorable safety profile than pan-CDK inhibitors.

Impact of SY-1075 on Blood Counts



CDK7 Clinical Development Plan

We are in the process of profiling several CDK7 inhibitors to select one as our lead development candidate in this program. We expect to nominate our lead development candidate in the first half of 2016 and start IND-enabling activities in the first half of 2016. Our goal is to submit an IND in the second half of 2016 and to initiate a Phase 1/2 clinical trial in patients with acute leukemias, including AML and ALL, in the first half of 2017. We have chosen to enroll patients with acute leukemias in our first trial based on the high degree of efficacy observed in our preclinical studies, the high degree of transcriptional dysregulation in these particular cancers, the significant unmet medical need of these patients and the potential for accelerated development. We believe there is a well-defined path to clinical proof-of-concept in acute leukemias. We then plan to expand into a broader set of molecularly defined patient populations using our gene control platform to identify patient subgroups with transcriptionally addicted cancers such as small cell lung cancer, triple negative breast cancer and *MYCN*-amplified neuroblastoma.

We are leveraging our platform to identify biomarkers that will predict patients most likely to respond to a CDK7 inhibitor. We intend to use a pharmacodynamics marker of target engagement in the tumor to guide our dosing in clinical trials.

CDK7 Market Opportunity

With our CDK7 inhibitors, we believe we have the opportunity to address significant unmet medical needs across a range of transcriptionally addicted blood cancers and solid tumors. We will initially pursue clinical development of our lead CDK7 inhibitor in AML and ALL.

There are an estimated 37,000 new AML diagnoses each year in the developed pharmaceutical markets. In the United States, newly diagnosed patients have a 25% five-year survival rate. There has been little improvement in treatment options for AML, with typical treatments including older chemotherapeutics and stem cell transplantation. AML remains an area of significant unmet medical need. Our initial clinical trial will include patients with relapsed and refractory AML and patients who are elderly or unfit for treatment with standard therapies. We estimate this population to be 29,000 patients, of which 11,000 patients have relapsed or refractory AML and of which 18,000 patients are elderly or unfit for treatment with standard therapies.

ALL is characterized by an excess of lymphoblastic cells, and approximately 12,000 patients are diagnosed annually in the developed markets. Approximately 60% of patients diagnosed with ALL are younger than 20 years old. Eighty percent of these patients are cured by current treatments such as chemotherapy and stem cell transplantation. However, only approximately 50% of patients older than 20 years old are cured, highlighting the need for more effective therapies. Our initial clinical trial will include adult recurrent or refractory patients. We estimate there are 2,500 such patients in the developed pharmaceutical markets.

Within the broader AML and ALL patient populations, using our platform we expect to discover a biomarker that could enable us to identify patient subsets most likely to benefit from our therapies. Over time, we intend to evaluate our CDK7 inhibitor program in additional transcriptionally addicted cancers, including the following:

<u>Metastatic Cancer</u>	<u>Approximate Number of Patients Diagnosed Annually in the Developed Pharmaceutical Markets</u>
Triple Negative Breast Cancer	42,000
Small Cell Lung Cancer	65,000
MYCN-amplified Neuroblastoma	200

Other Programs

We are using our platform to map gene control programs across additional cancers, inflammatory diseases and other diseases. Using these maps, we are creating a pipeline of novel preclinical drug candidates targeting transcriptional kinases, transcription factors and other transcriptional and regulatory proteins, as well as linking existing drugs to novel genomically defined patient populations.

Intellectual Property

We file patent applications directed to our gene control platform, proprietary composition of matter and product candidates in an effort to establish intellectual property positions regarding all aspects of our business, including new chemical entities, or NCEs, and uses of these NCEs in the treatment of diseases. As of January 28, 2016, we own seven pending U.S. provisional patent applications, one U.S. pending patent application, one foreign application pending in Europe, and six pending Patent Cooperation Treaty, or PCT, patent applications. In addition, as of January 28, 2016, we are exclusively licensed to four issued U.S. patents, seven U.S. pending patent applications, five issued foreign patents, 13 foreign patent applications pending in a number of jurisdictions, including Australia, Canada, China, Europe, and Japan, and one pending PCT patent application. A significant portion of

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our owned and licensed pending patent applications pertain to our product candidates, key discovery programs, specifically our CDK7 inhibitor program and transcription factor modulators, and our gene control platform.

Our intellectual property portfolio as of January 28, 2016 is summarized below. For some of our pending patent applications, prosecution has yet to commence. Prosecution is a lengthy process, during which the scope of the claims initially submitted for examination by the USPTO is often significantly narrowed by the time they issue, if they issue at all. We expect this to be the case with respect to our pending patent applications referred to below.

SY-1425

The intellectual property portfolio for SY-1425 contains two provisional patent applications directed to patient stratification methods, and methods of use for agonists of RAR α , as well as several licensed patents directed to various aspects of that compound. As of January 28, 2016, we own two pending U.S. provisional patent applications directed to this program, applications claiming priority to which, if issued, will have a statutory expiration date of 2036.

In addition, we are exclusively licensed in North America and Europe to two issued U.S. patents, and five issued foreign patent applications in Canada and Europe, directed to pharmaceutical kits and drug combinations comprising tamibarotene and certain other chemotherapeutic agents, certain formulations of tamibarotene, and crystal forms of tamibarotene and their preparation. One licensed issued U.S. patent covering formulations has a statutory expiration date of April 2028. The other licensed issued U.S. patent covering crystals has a statutory expiration date of August 2021. Patent term adjustments or patent term extensions could result in later expiration dates for each of these patents. We do not have composition of matter patent protection with respect to SY-1425.

CDK7

The intellectual property portfolio for our CDK7 inhibitor program contains patent applications directed to compositions of matter for our three lead compounds and analogs, compositions of matter for CDK7 inhibitors having different structural features (*i.e.*, different compound families), as well as methods of use for these novel compounds. As of January 28, 2016, we own six pending PCT patent applications directed to this program. Any U.S. or non-U.S. patents issuing from applications claiming priority to the pending PCT applications covering our compounds and related methods of use will have a statutory expiration date of either April 2035 or October 2035. Patent term adjustments or patent term extensions could result in later expiration dates.

We are also exclusively licensed to two pending U.S. patent applications, five pending foreign patent applications in a number of jurisdictions, including Australia, Canada, Europe, and Japan, and one pending PCT application directed to this program.

Other Programs

The intellectual property portfolio for our other programs contains patents and patent applications directed to compositions of matter for inhibiting transcription factors in multiple compound families, methods of treating various diseases through inhibition of specific transcription factor(s), and patient stratification and treatment methods based on the identification of new disease targets. As of January 28, 2016, we own five pending U.S. provisional patent applications and were exclusively licensed to one issued U.S. patent and three U.S. and two pending foreign patent applications in Europe directed to our other programs. The licensed U.S. patent has a statutory expiration date of July 2032. Any U.S. or non-U.S. patents issuing from the pending applications or applications claiming priority to the pending provisional applications covering transcription factor inhibitors and their use will have statutory expiration dates of February 2031, August 2032, November 2033 and June 2036. Any U.S. or non-U.S. patents issuing from the applications that claim priority to the provisional applications

covering patient stratification and treatment methods based on the identification of new disease targets will have a statutory expiration date of February 2036.

Platform

The intellectual property portfolio directed to our platform includes patent applications and patents directed to super-enhancers and their detection and uses thereof to detect novel disease targets, and methods for identifying protein binding sites in a genome. As of January 28, 2016, we own one pending U.S. patent application and one pending patent application in Europe directed to these technologies which, if issued, will have a statutory expiration date of March 2034. In addition, we have an exclusive license to one issued U.S. patent, two U.S. pending patent applications and six pending foreign patent applications in a number of jurisdictions, including Australia, Canada, China, Europe and Japan, directed to these technologies. The U.S. and foreign patent applications that we own are directed to the identification of new super-enhancer components and methods of treating diseases by targeting those novel components, and if issued, will have a statutory expiration date of March 2034. The licensed U.S. patent has a statutory expiration date of October 2033 and the licensed pending applications directed to super-enhancers and their detection and uses thereof to detect novel disease targets, if issued, will have a statutory expiration date of October 2033. The licensed U.S. and foreign patent applications directed to methods for identifying protein binding sites in a genome, if issued, will have a statutory expiration date of June 2033.

The term of individual patents depends upon the legal term for patents in the countries in which they are obtained. In most countries, including the United States, the patent term is 20 years from the earliest filing date of a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the USPTO in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier filed patent. The term of a patent that covers a drug or biological product may also be eligible for patent term extension when FDA approval is granted, provided statutory and regulatory requirements are met. See "—Government Regulation and Product Approvals—Marketing Authorization and Exclusivity" below for additional information on such exclusivity. In the future, if and when our product candidates receive approval by the FDA or foreign regulatory authorities, we expect to apply for patent term extensions on issued patents covering those drugs, depending upon the length of the clinical trials for each drug and other factors. There can be no assurance that any of our pending patent applications will issue or that we will benefit from any patent term extension or favorable adjustment to the term of any of our patents.

As with other biotechnology and pharmaceutical companies, our ability to maintain and solidify our proprietary and intellectual property position for our product candidates and technologies will depend on our success in obtaining effective patent claims and enforcing those claims, if granted. However, our pending patent applications, and any patent applications that we may in the future file or license from third parties may not result in the issuance of patents. We also cannot predict the breadth of claims that may be allowed or enforced in our patents. Any issued patents that we may receive in the future may be challenged, invalidated or circumvented. For example, we cannot be certain of the priority of inventions covered by pending third-party patent applications. If third parties prepare and file patent applications in the United States that also claim technology or therapeutics to which we have rights, we may have to participate in interference proceedings in the USPTO to determine priority of invention, which could result in substantial costs to us, even if the eventual outcome is favorable to us, which is highly unpredictable. In addition, because of the extensive time required for clinical development and regulatory review of a product candidate we may develop, it is possible that, before any of our product candidates can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby limiting protection such patent would afford the respective product and any competitive advantage such patent may provide.

In addition to patents, we rely upon unpatented trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, by executing confidentiality agreements with our collaborators and scientific advisors, and non-competition, non-solicitation, confidentiality, and invention assignment agreements with our employees and consultants. We have also executed agreements requiring assignment of inventions with selected scientific advisors and collaborators. The confidentiality agreements we enter into are designed to protect our proprietary information and the agreements or clauses requiring assignment of inventions to us are designed to grant us ownership of technologies that are developed through our relationship with the respective counterparty. We cannot guarantee, however, that these agreements will afford us adequate protection of our intellectual property and proprietary information rights.

License Agreements

We are a party to a number of license agreements under which we license patents, patent applications and other intellectual property from third parties. We enter into these agreements to augment our proprietary intellectual property portfolio. The licensed intellectual property covers some of the compounds that we are researching and developing and some of the scientific processes that we use. These licenses impose various diligence and financial payment obligations on us. We expect to continue to enter into these types of license agreements in the future.

Dana-Farber Cancer Institute, Inc.

In February 2013, we entered into a license agreement with Dana-Farber Cancer Institute, Inc., or Dana-Farber, pursuant to which we were granted an exclusive worldwide, sublicensable license under specified patents relating to CDK7 inhibitors and JNK inhibitors owned or controlled by Dana-Farber. The license is for all fields of use and subject to certain rights retained by Dana-Farber for internal non-commercial research, academic/teaching and government purposes. Subject to certain restrictions, Dana-Farber granted us an option to obtain an exclusive commercial license to certain improvements created by Dana-Farber during the first three years of the agreement, which would be negotiated in good faith and incorporated into this agreement. In connection with the agreement, we paid Dana-Farber an upfront licensing fee and a milestone payment based on our first round of funding, such payments totaling \$175,000, in addition to past patent expenses. We are obligated to pay Dana-Farber annual license maintenance fees that are creditable against other payments and royalties due under the agreement and to make milestone payments of up to an aggregate of \$3.4 million for each of the first two products in connection with the achievement of certain clinical and regulatory milestones. In addition, we are required to pay Dana-Farber a tiered royalty on net sales by us, our affiliates and sublicensees ranging from low single digit to mid-single digit percentages, subject to certain adjustments, as well as a tiered mid-single digit to low double digit percentage of sublicense income. Our royalty and sublicensing income payment obligations are further subject to apportionment between designated agreements existing among us, Dana-Farber and the Whitehead Institute for Biomedical Research, or Whitehead. We are required to meet certain diligence milestones and to use commercially reasonable efforts to, among other things, develop and commercialize one or more licensed products or processes and to make one or more licensed products or processes reasonably available to the public. The agreement contains specified diligence activities that if met on an annual basis would be deemed to satisfy some of our diligence obligations for the particular year. The agreement, unless earlier terminated by us or Dana-Farber, will remain in effect until the expiration or abandonment of the licensed patent rights. We have the right to terminate the agreement for any reason provided that we provide Dana-Farber the required notice and we pay all undisputed amounts due to Dana-Farber at the time of termination. Dana-Farber has the right to terminate the agreement if we cease doing business, or if we do not pay them the amounts owed under the agreement and fail to cure, or if we commit and fail to cure a material breach under the agreement, or if our successor

does not agree in writing to be bound by this agreement within the designated period following assignment.

Whitehead Institute for Biomedical Research and Dana-Farber Cancer Institute, Inc.

In April 2013, we entered into a license agreement with Whitehead and Dana-Farber, pursuant to which we were granted a worldwide, sublicensable with certain restrictions, license under specified patents relating to Chem-Seq or modulators of Myc/Max Screen owned or controlled by Whitehead and Dana-Farber, to make, have made, use, sell, offer for sale and import products and to perform and have performed licensed processes, in each case, in the applicable field. This license is exclusive, on a patent-by-patent basis in the designated fields, (i) during the term, with respect to patent rights relating to Myc/Max Screen, (ii) during the term, for use of Chem-Seq for human health and therapeutics, (iii) for a period of three years, with respect to Chem-Seq outside of human health and therapeutics and (iv) during the term, for other specified patent rights, with limited exceptions, including non-exclusive rights for research use reagents. We can automatically extend the period of exclusive rights with respect to Chem-Seq for an additional two years in exchange for an extension payment and we have been granted the first right for a limited extension after such period. We were granted a non-exclusive license to certain materials for the practice of our exclusive licenses. The licenses are subject to certain rights retained by Dana-Farber and Whitehead for internal non-commercial research, academic/teaching and government purposes. Subject to certain restrictions, we were granted an option to obtain an exclusive commercial license to certain improvements created by Whitehead or Dana-Farber during the first three years of the agreement. The option is exercisable within a certain period from the date of disclosure, and the license would be negotiated in good faith and incorporated into this agreement. Commencing five years after the effective date and subject to certain terms and conditions, the agreement requires us to negotiate and potentially issue mandatory sublicenses under the patent rights outside of human health and therapeutics for fields and products that are not directly competitive with products in active development or commercialization by us, our affiliates or sublicensees.

In connection with the agreement, we paid Whitehead an upfront licensing fee, and a milestone payment based on our first round of funding, such payments totaling \$100,000, in addition to past patent expenses. We are obligated to pay Whitehead annual license maintenance fees that are creditable against other payments and royalties due under the agreement and to make milestone payments of up to an aggregate of \$3.4 million in connection with the achievement of certain clinical and regulatory milestones. In addition, we are required to pay Whitehead a royalty on net sales of the various products by us, our affiliates and sublicensees ranging from low single digit to mid-single digit percentages, subject to certain adjustments, including a lower royalty on products identified through the use of certain licensed products or processes. In addition, we are required to pay a tiered mid-single digit to low double digit percentage of our and our affiliates' sublicense income and income we receive from the performance of licensed processes. Our royalty, sublicensing and licensed process income payment obligations are further subject to apportionment between designated agreements existing among us, Dana-Farber and Whitehead. In connection with the agreement, we also issued an aggregate of 367,875 shares of our common stock to Whitehead. We are required to achieve certain diligence milestones within the specified timeframes, and failure to do so may result in our license under certain patent rights being converted to non-exclusive or otherwise be deemed a material breach of the agreement. The agreement further requires that we use commercially reasonable efforts to, among other things, develop and commercialize one or more licensed products or processes and to make one or more licensed products or processes reasonably available to the public. The agreement contains specified diligence activities that if met on an annual basis would be deemed to satisfy some of our diligence obligations for the particular year. The agreement, unless earlier terminated by us, Whitehead or Dana-Farber, will remain in effect until the expiration or abandonment of the licensed patent rights. We have the right to terminate the agreement for any reason, provided that we provide Dana-Farber

and Whitehead the required notice and we pay all undisputed amounts due to Whitehead and Dana-Farber at the time of termination. Whitehead and Dana-Farber have the right to terminate the agreement if we cease doing business, or if we do not pay them the amounts owed under the agreement and fail to cure, or if we commit and fail to cure a material breach under the agreement, or if our successor does not agree in writing to be bound by this agreement within the designated period following assignment.

Whitehead Institute for Biomedical Research

In April 2013, we entered into a license agreement with Whitehead, which we refer to as the Whitehead license agreement, pursuant to which we were granted a worldwide license under specified patents relating to super-enhancers owned or controlled by Whitehead. This license is exclusive in all fields until April 2016, and can remain exclusive thereafter, on a field-by-field basis, as long as we can demonstrate that we are using commercially reasonable efforts in the applicable field, and if we are not using such commercially reasonable efforts in such applicable field, our license rights would become non-exclusive with respect to such field. We were also granted a non-exclusive license to use certain Whitehead materials in connection with the practice of the licensed Whitehead patents. In connection with the Whitehead license agreement, we paid Whitehead an upfront licensing fee of \$30,000. In connection with the agreement, we also issued an aggregate of 275,907 shares of our common stock to Whitehead. We are obligated to pay Whitehead annual license maintenance fees that are creditable against other payments and royalties due under the agreement. In addition, we are required to pay Whitehead a tiered royalty on our net sales ranging from low single digit to mid-single digit percentages, a lower royalty on products identified through the use of licensed products or processes, and a tiered mid-single digit to low double digit percentage of sublicense income, which steps down depending on time, development stage of the products or processes and payments made to Whitehead, and patent expenses of Whitehead in connection with the licensed patents. We are required to use commercially reasonable efforts to, among other things, develop and commercialize one or more licensed products or processes and to make one or more licensed products or products reasonably available to the public. The Whitehead license agreement, unless earlier terminated by us or Whitehead, will remain in effect until the expiration or abandonment of the licensed patent rights. We have the right to terminate the Whitehead license agreement for any reason upon three months' notice to Whitehead, provided that we pay all undisputed amounts due to Whitehead at the time of termination. Whitehead has the right to terminate the Whitehead license agreement immediately if we cease doing business, or if we do not pay Whitehead the amounts owed under the agreement or commit a material breach under the agreement, Whitehead has the right to terminate after we have had an opportunity to cure the breach.

TMRC

In September 2015, we entered into a license agreement with TMRC, which we refer to as the TMRC license agreement, pursuant to which TMRC granted us an exclusive license, with the right to sublicense, under TMRC patent rights, data, regulatory filings and other intellectual property for the North American and European development and commercialization of SY-1425 (tamibarotene) products for the treatment of human cancer indications. Under the TMRC license agreement, we have agreed to pay TMRC single-digit royalties based on net sales if TMRC's patents cover our product, and to make payments to TMRC upon meeting specified clinical and regulatory milestones in an aggregate amount of approximately \$13.0 million per indication. In addition, pursuant to the TMRC license agreement, we and TMRC have agreed to use commercially reasonable efforts to negotiate and enter into a supply agreement pursuant to which we would agree to purchase all of our requirements of active pharmaceutical ingredient for clinical and commercial development of SY-1425 from TMRC. Under the TMRC license agreement, we must use commercially reasonable efforts to, among other things, commence development activities within one year, to develop SY-1425 in at least one cancer

indication, and, following marketing approval, to market the product. The license agreement expires on the expiration of the subject patent rights or 15 years after the date of first commercial sale of product, whichever is later. The TMRC license agreement may be terminated by either party if the other party is in breach and the breach is not cured within a required amount of time or if the other party is in bankruptcy. We have the right to terminate the agreement in the event that we and TMRC have not entered into the supply agreement within 60 days of the date of the agreement. If we have reason to do so, we may also terminate the agreement after one year at our sole discretion.

Competition

The pharmaceutical and biotechnology industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technology, development experience, and scientific knowledge provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and 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.

We compete in the segments of the pharmaceutical, biotechnology and other related markets that address gene control and cancer. There are other companies working to develop therapies in the fields of gene control and cancer. These companies include divisions of large pharmaceutical companies and biotechnology companies of various sizes.

The most common methods of treating patients with cancer are surgery, radiation and drug therapy, including chemotherapy, hormone therapy and targeted 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. While our product candidates may compete with many existing drug and other therapies, they may also be used in combination with or as an adjunct to these therapies. Some of the currently approved drug therapies are branded and subject to patent protection, and others are available on a generic basis. Many of these approved drugs are well-established therapies and are widely accepted by physicians, patients and third-party payors. In general, although there has been considerable progress over the past few decades in the treatment of cancer and the currently marketed therapies provide benefits to many patients, these therapies all are limited to some extent in their efficacy and frequency of adverse events. As a result, the level of morbidity and mortality from cancer remains high.

In addition to currently marketed therapies, there are also a number of medicines in late stage clinical development to treat cancer. These medicines in development 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 market approval.

Many of our competitors may have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved medicines than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and diagnostic industries may result in even more resources being concentrated among a smaller number of our competitors. 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 necessary for, our programs. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

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.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize medicines that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any medicines that we may develop. Our competitors also may obtain FDA or other regulatory approval for their medicines 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. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic medicines. There are many generic medicines currently on the market for the indications that we are pursuing, and additional medicines are expected to become available on a generic basis over the coming years. If our therapeutic product candidates are approved, we expect that they will be priced at a significant premium over competitive generic medicines.

If the drug candidates of our priority programs are approved for the indications for which we are currently planning clinical trials, they will compete with the drugs discussed below and will likely compete with other drugs currently in development.

SY-1425

We plan to initially develop SY-1425, our RARa agonist, for patients with relapsed or refractory AML or MDS or low-risk transfusion-dependent MDS, or AML patients who are elderly or unfit for treatment with standard therapies. We will select patients for our clinical trials based on high-levels of RARa as measured by our proprietary biomarker. There has been little advancement in treatment options for patients with these cancers. Typical treatment includes chemotherapy followed by stem cell transplantation. SY-1425 may face competition from other drug candidates currently in clinical development for relapsed or refractory AML and MDS. Several companies are developing drugs for AML, including Daiichi Sankyo Company, Limited, Boehringer Ingelheim GmbH, Agios Pharmaceuticals, Inc., Novartis AG, Astellas Pharma Inc. and Karyopharm Therapeutics Inc. We believe that SY-1425 will be the only selective RARa agonist in clinical development for relapsed or refractory AML in North America and Europe. Because the mechanism of action is different than the others currently on the market and in development, we believe that SY-1425 could be first-in-class and could be used in combination with other therapies, which could minimize competition, assuming that data from a registration-enabling trial warrants such use. We are aware of only one other selective RARa program, being pursued by IO Therapeutics, Inc. This program appears to be in clinical development.

CDK7 Inhibitor Program

The clinical development of our CDK7 inhibitor program will initially focus on patients with relapsed or refractory AML or recurrent or refractory ALL.

The competitive landscape for AML is described above. In ALL, patients are typically treated with older chemotherapeutics. Targeted therapies such as kinase inhibitors, including imatinib and dasatinib, and monoclonal antibodies, including rituximab and blinatumamab, have been developed and used successfully for certain patient populations within ALL. If our CDK7 inhibitor program receives marketing approval, it may face competition from other drug candidates currently in development for relapsed and refractory ALL from several companies including Amgen Inc., Novartis and Juno Therapeutics, Inc.

We believe that our CDK7 inhibitor program will be the only selective mechanism of its kind in clinical development. Because the mechanism of action is different than the others currently on the market and in development, we believe that it could be first-in-class and used in combination with other therapies, which could minimize competition, assuming that data from a registration-enabling trial warrants such use. We are aware of only one other CDK7 inhibitor program, being pursued by a

German academic group, Lead Discovery Center. This program appears to be in early preclinical development.

Sales and Marketing

We hold North American and European commercialization rights to SY-1425 and worldwide rights to our CDK7 inhibitor program and all of our other preclinical programs. Subject to receiving marketing approval, we intend to build a focused sales and marketing organization in the United States and potentially in Europe to sell our products. We believe that such an organization will be able to address the community of physicians who are key specialists in treating the patient populations for which our product candidates are being developed.

We also plan to build a marketing and sales management organization to create and implement marketing strategies for any products that we market through our own sales organization and to oversee and support our sales force. The responsibilities of the marketing organization would include developing educational initiatives with respect to approved products and establishing relationships with researchers and practitioners in relevant fields of medicine.

Outside of the United States and potentially Europe, where appropriate, we may elect in the future to utilize strategic partners, distributors or contract sales forces to assist in the commercialization of our products. In certain instances, we may consider building our own commercial infrastructure.

Manufacturing

We do not currently own or operate manufacturing facilities for the production of clinical or commercial quantities of our product candidates. Although we intend to rely on third-party contract manufacturers to produce our product candidates and any products we may develop in the future, we have recruited personnel with experience to manage these third-party contract manufacturers. Under the TMRC license agreement, we agreed to enter into negotiations for a supply agreement obligating us to purchase all of our clinical and commercial requirements for active pharmaceutical ingredients for SY-1425 from TMRC. We anticipate entering into this agreement prior to the commencement of our Phase 2 clinical trial. We believe we currently have access to sufficient active pharmaceutical ingredients to create the drug supply for our Phase 2 clinical trial.

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 and regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. The failure to comply with 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,

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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 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 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.

Human Clinical Trials 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. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to a proposed clinical trial and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA can place an IND on clinical hold at any point in development, and depending upon the scope of the hold, clinical trial(s) may not restart until resolution of the outstanding concerns to the FDA's satisfaction.

In addition, 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 a 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. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health for public dissemination on their ClinicalTrials.gov website.

Human clinical trials are typically conducted in four 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 may be conducted after initial marketing approval. These studies are used to gain additional experience from the 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. The FDA or the sponsor or the data monitoring committee 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

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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, purity, and potency 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.

Review of an NDA by 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, and the sponsor of an approved NDA is also subject to annual product and establishment user fees. These fees are typically increased annually. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for drugs with orphan designation and a waiver for certain small businesses, an exception from the establishment fee when the establishment does not engage in manufacturing the drug during a particular fiscal year, and an exception from the product fee for a drug that is the same as another drug approved under an abbreviated pathway.

The FDA conducts a preliminary review of an NDA generally within 60 calendar days of its receipt and strives to inform 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. Under that agreement, 90% of applications seeking approval of New Molecular Entities, or NMEs, are meant to be reviewed within ten months from the date on which FDA accepts the NDA for filing, and 90% of applications for NMEs that have been designated for "priority review" are meant to be reviewed within six months of the filing date. For applications seeking approval of drugs that are not NMEs, the ten-month and six-month review periods run from the date that FDA receives the application. 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 (e.g., 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 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 product for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the product 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. Products 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 product, 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 product.

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 product, 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 products 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 product's clinical benefit. As a result, a product 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 product from the market on an expedited basis. All promotional materials for product 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.

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

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments to the FDCA, Congress established an abbreviated regulatory scheme authorizing 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, the strength of the drug and the conditions of use 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 therapeutically 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, a new chemical entity, or 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).

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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 the 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, 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 Food and Drug Safety and Innovation Act, or 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 any 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 and until FDA promulgates a regulation stating otherwise, 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. With regard to patents, the six-month pediatric exclusivity period will not attach to any patents for which an ANDA or 505(b)(2) applicant submitted a paragraph IV patent certification, unless the NDA sponsor or patent owner first obtains a court determination that the patent is valid and infringed by the proposed product.

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 drug

designation before submitting an NDA for the drug and rare disease or condition. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan drug designation does not shorten the goal dates under the Prescription Drug User Fee Act, or PDUFA, for the regulatory review and approval process, although it does convey certain advantages such as tax benefits and exemption from the PDUFA application fee.

If a product with orphan designation receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor's marketing application for the same drug for the same indication for seven years, except in certain limited circumstances. Orphan exclusivity does not block the approval of a different drug for the same rare disease or condition, nor does it block the approval of the same drug for different indications. If a drug designated as an orphan drug ultimately receives marketing approval for an indication broader than what was designated in its orphan drug 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 drug 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.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension, also known as patent term restoration, 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. Patent term extension is generally available only for drug products whose active ingredient has not previously been approved by the FDA. 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 extension 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 United States PTO reviews and approves the application for any patent term extension in consultation with the FDA.

Review and Approval of Drugs in Europe and other Foreign Jurisdictions

In addition to regulations in the United States, a manufacturer is subject to a variety of regulations in foreign jurisdictions to the extent they choose to sell any drug products in those foreign countries. Even if a manufacturer obtains FDA approval of a product, it must still obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. For other countries outside of the European Union, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary.

Clinical Trial Approval in the European Union

Pursuant to the currently applicable Clinical Trials Directive 2001/20/EC and the Directive 2005/28/EC on Good Clinical Practice, an applicant must obtain the approval from the competent national authority of the EU Member State in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion. In April 2014, the European Union adopted a new Clinical Trials Regulation (EU) No 536/2014, which is set to replace the current Clinical Trials

Directive 2001/20/EC. The new Clinical Trials Regulation will overhaul the current system of approvals for clinical trials in the European Union, and it intended to simplify and streamline the approval of clinical trials in the European Union. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial will be required to submit a single application for approval of a clinical trial to a reporting EU Member State, or RMS, through an EU Portal. The new Regulation also aims to streamline and simplify the rules on safety reporting for clinical trials.

Marketing Authorization and Exclusivity

In the European Union, marketing authorizations for medicinal products may be obtained through different procedures founded on the same basic regulatory process. The centralized procedure provides for the grant of a single marketing authorization that is valid for all EU Member States. The centralized procedure is compulsory for medicinal products produced by certain biotechnological processes, products designated as orphan medicinal products, and products with a new active substance indicated for the treatment of certain diseases. On the other hand, a decentralized procedure provides for approval by one or more other concerned EU Member States of an assessment of an application for marketing authorization conducted by one EU Member State, known as the reference EU Member State. In accordance with the mutual recognition procedure, the sponsor applies for national marketing authorization in one EU Member State. Upon receipt of this authorization the sponsor can then seek the recognition of this authorization by other EU Member States.

A marketing authorization is valid for five years, in principle, and it may be renewed after five years on the basis of a reevaluation of the risk-benefit balance by the EMA or by the competent authority of the relevant EU Member State. Once renewed, the marketing authorization is valid for an unlimited period, unless the European Commission or the relevant competent authority of the EU Member State decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal period. Any marketing authorization that is not followed by the marketing of the medicinal product on the EU market (in the case of the centralized procedure) or on the market of the EU Member State which delivered the marketing authorization within three years after authorization ceases to be valid.

In the European Union, innovative medicinal products authorized in the European Union on the basis of a full marketing authorization are entitled to eight years of data exclusivity. During this period, applicants for authorization of generics of these innovative products cannot rely on data contained in the marketing authorization dossier submitted for the innovative medicinal product. Innovative medicinal products are also entitled to ten years' market exclusivity. During this ten year period no generic of this medicinal product can be placed on the EU market. The overall ten-year period will be extended to a maximum of eleven 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 authorization, is held to bring a significant clinical benefit in comparison with existing therapies.

Regulatory Requirements after Marketing Authorization

As in the U.S., both marketing authorization holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA and the competent authorities of the individual EU Member States both before and after grant of the manufacturing and marketing authorizations. The holder of an EU marketing authorization for a medicinal product must, for example, comply with EU pharmacovigilance legislation and its related regulations and guidelines which entail many requirements for conducting pharmacovigilance, or the assessment and monitoring of the safety of medicinal products. The manufacturing process for medicinal products in the European Union is also highly regulated and regulators may shut down manufacturing facilities that they believe do not comply with regulations. Manufacturing requires a manufacturing authorization, and the manufacturing

authorization holder must comply with various requirements set out in the applicable EU laws, including compliance with EU cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients.

In the European Union, the advertising and promotion of approved products are subject to EU Member States' laws governing promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. In addition, other legislation adopted by individual EU Member States may apply to the advertising and promotion of medicinal products. These laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics, or SmPC, as approved by the competent authorities. Promotion of a medicinal product that does not comply with the SmPC is considered to constitute off-label promotion, which is prohibited in the European Union.

Orphan Drug Designation and Exclusivity in the European Union

Under the relevant EU Regulations, a product can be designated as an orphan medicinal product by the European Commission if its sponsor can establish: that the product is intended for the diagnosis, prevention or treatment of (1) a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the European Union when the application is made, or (2) a life-threatening, seriously debilitating or serious and chronic condition in the European Union and that without incentives the medicinal product is unlikely to be developed. 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 Union or, if such method exists, the medicinal product will be of significant benefit to those affected by that condition. Once authorized, orphan medicinal products are entitled to ten years of market exclusivity in all EU Member States, along with a range of other benefits. However, marketing authorization may also be granted to a similar medicinal product with the same orphan indication if this product is safer, more effective or otherwise clinically superior to the original orphan medicinal product.

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 at least 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 foreign government authorities. Even if our product candidate is 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

candidate could reduce physician utilization and/or patient acceptance 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 candidate 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 regulatory marketing approval for a product and may require us to conduct a clinical trial that compares the cost effectiveness of our product candidate 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 or so called health technology assessments, 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 health care 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, i.e., 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 data privacy and security 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 United States 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 be 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, on certain types of people and entities 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 Education Reconciliation Act, or collectively the Affordable Care Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the United States 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 certain health care providers or marketing expenditures. 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.

By way of example, the United States and state governments continue to propose and pass legislation designed to reduce the cost of healthcare. In March 2010, the United States Congress enacted the Affordable Care Act, which, among other things, includes changes to the coverage and payment for products under government health care programs. Among the provisions of the Affordable Care Act 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, although this fee would not apply to sales of certain products approved exclusively for orphan indications;
- 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 and extending rebate liability to prescriptions for individuals enrolled in Medicare Advantage plans;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expansion of the types of entities eligible for the 340B drug discount program;
- establishment of 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;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- the 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. However, the IPAB implementation has been not been clearly defined. The Affordable Care Act provided that under certain circumstances, IPAB recommendations will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings; and
- establishment of the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Funding has been allocated to support the mission of the Center for Medicare and Medicaid Innovation from 2011 to 2019.

Other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. For example, in August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee

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on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least \$1.2 trillion for fiscal years 2012 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 of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2024 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. Such reforms could have an adverse effect on anticipated revenues from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop product candidates.

Employees

As of January 28, 2016 we had 48 full-time employees, including 23 employees with M.D. or Ph.D. degrees. Of these full-time employees, 37 employees are engaged in research and development activities and 11 employees are engaged in general and administrative activities. None of our employees is represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

Facilities

We occupy approximately 21,488 rentable square feet of office and laboratory space in Cambridge, Massachusetts under a lease that expires on October 31, 2020. We have an option to extend the lease term for five additional years. We believe that this office and laboratory space is sufficient to meet our current needs and that suitable additional space will be available as and when needed.

Legal

We are not currently party to any legal proceedings.

MANAGEMENT

The following table sets forth the name, age as of January 28, 2016 and position of each of our executive officers and directors.

<u>Name</u>	<u>Age</u>	<u>Position</u>
Nancy Simonian, M.D.	55	President, Chief Executive Officer and Director
Kyle D. Kovalanka	47	Chief Operating Officer
Eric R. Olson, Ph.D.	58	Chief Scientific Officer
David A. Roth, M.D.	53	Chief Medical Officer
Jorge Conde	38	Chief Financial Officer and Chief Product Officer
Jonathan Garen	50	Chief Business Officer
Stéphane Bancel(1)(2)	43	Director
Marsha H. Fanucci(3)	62	Director
Amir Nashat, Ph.D.	43	Director
Robert Nelsen(3)	52	Director
Vicki L. Sato, Ph.D.(1)(2)	67	Director
Phillip A. Sharp, Ph.D.(1)	71	Director
Richard A. Young, Ph.D.(2)(3)	61	Director

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

Executive Officers

Nancy Simonian, M.D., has been our chief executive officer since July 2012. From 2001 to October 2011, Dr. Simonian was employed by Takeda Pharmaceuticals Company, a pharmaceutical company, and at Millennium Pharmaceuticals, Inc., a biopharmaceutical company, prior to its acquisition by Takeda, most recently serving as chief medical officer and senior vice president of clinical, medical and regulatory affairs. From 1995 to 2001, Dr. Simonian was at Biogen, Inc., a biotechnology company, and most recently served as vice president of clinical development. She is a member of the board of directors of Seattle Genetics, Inc., a biotechnology company. Prior to joining the biopharmaceutical industry, Dr. Simonian was on the faculty of Massachusetts General Hospital and Harvard Medical School as an assistant professor of neurology. She received a B.A. in biology from Princeton University and an M.D. from the University of Pennsylvania School of Medicine. Our board of directors believes Dr. Simonian is qualified to serve on our board because of her role as our chief executive officer, her experience in the biopharmaceutical industry and her other executive leadership and board of directors experience.

Kyle D. Kovalanka has served as our chief operating officer since September 2015. Prior to joining Syros, Mr. Kovalanka served as chief business officer and principal financial and accounting officer of Blueprint Medicines Corporation, a biopharmaceutical company, from September 2013 to September 2015. From 2002 to September 2013, Mr. Kovalanka worked at Takeda and at Millennium prior to its takeover by Takeda, including as vice president, corporate strategy, business development and alliance management from 2009 to September 2013. Mr. Kovalanka holds a B.A. from Wesleyan University and an M.B.A. from The Wharton Business School of the University of Pennsylvania.

Eric R. Olson, Ph.D., has been our chief scientific officer since April 2013. He previously served as research vice president for respiratory diseases at Vertex Pharmaceuticals Incorporated, a biotechnology company, from 2001 to May 2013. Dr. Olson has also held positions as the director of antibacterials and molecular sciences departments at Warner-Lambert as well as a research scientist focused on gene expression systems with The Upjohn Company, both of which were acquired by Pfizer, Inc., a pharmaceutical company. Dr. Olson received a B.S. in microbiology and immunology from the University of Minnesota and a Ph.D. in microbiology and immunology from the University of Michigan.

David A. Roth, M.D., has been our chief medical officer since December 2015. Previously, Dr. Roth was employed by Infinity Pharmaceuticals, Inc., a pharmaceutical company, from September 2013 until September 2015, serving most recently as its executive vice president and chief medical officer and previously as its senior vice president of clinical development and medical affairs. Prior to joining Infinity, Dr. Roth was the vice president, early development in the oncology business unit of Pfizer Inc., a pharmaceutical company, from 2009 to August 2013. Prior to joining the pharmaceutical industry, Dr. Roth's experience included over 10 years in research and clinical practice as an academic hematologist, and he served on the full time faculty at Harvard Medical School and Beth Israel Deaconess Medical Center in Boston. Dr. Roth received his B.S. from the Massachusetts Institute of Technology and his M.D. from Harvard Medical School in the Harvard-MIT Division of Health Sciences and Technology, where he remains on the affiliated faculty.

Jorge Conde has been our chief financial officer and chief product officer since May 2014. Prior to joining Syros, from 2007 to May 2014, Mr. Conde served in various roles at Knome, Inc., a genomics company, including founding chief executive officer, chief financial officer and chief product officer. Prior to Knome, Mr. Conde worked in marketing and operations at MedImmune, Inc. a biopharmaceutical company which was subsequently acquired by AstraZeneca, from 2006 to 2007. He has also worked in the life sciences group at Flagship Ventures and managed the business development function at Helicos Biosciences Corporation, a DNA sequencing company. Previously, he was an investment banker at Morgan Stanley & Co. where he advised biotechnology and genomics companies on strategy, M&A and capital fundraising. Mr. Conde received a B.A. in biology from Johns Hopkins University, an M.B.A. from Harvard Business School and an M.S. from the Harvard-MIT Division of Health Sciences and Technology.

Jonathan Garen has been our chief business officer since April 2015. Previously, he served as assistant vice president of corporate development of Actavis plc, a pharmaceutical company, following Actavis' acquisition of Forest Laboratories, Inc. in 2014. Prior to the acquisition, he was assistant vice president of business development at Forest Laboratories, a pharmaceutical company, since 2003. Prior to Forest Laboratories, Mr. Garen was a director in the global licensing department at Pharmacia Corporation, a biotechnology company that was subsequently acquired by Pfizer. He was also a founder and vice president of TechEx, an online exchange service matching licensing opportunities from academic research institutions with potential life sciences licensors and investors. Mr. Garen received a B.S. in physics from the Massachusetts Institute of Technology and an M.S. in environmental sciences from Yale University.

Non-Management Directors

Stéphane Bancel has served as a member of our board of directors since November 2013. He has been president and founding chief executive officer of Moderna Therapeutics, a biotechnology company since July 2011. Mr. Bancel was previously chief executive officer of bioMérieux, a diagnostics company from 2006 to July 2011. Prior to his time at bioMérieux, Mr. Bancel was managing director of Eli Lilly in Belgium and executive director of global manufacturing strategy and supply chain at Eli Lilly in Indianapolis, Indiana. Mr. Bancel serves as a supervisory director of Qiagen N.V., a biotechnology company. Mr. Bancel holds a M.E. from École Central Paris, a M.S. in chemical engineering from the University of Minnesota and an M.B.A. from Harvard Business School. We believe Mr. Bancel is qualified to serve on our board because of his experience as a senior executive and his knowledge of our industry.

Marsha H. Fanucci has been a member of our board of directors since October 2015. Since 2009, Ms. Fanucci has been an independent consultant. From 2004 through 2009, she served as senior vice president and chief financial officer of Millennium, which was subsequently acquired by Takeda. She previously served in various other roles at Millennium, including as vice president, finance and corporate strategy and vice president, corporate development. Ms. Fanucci is a member of the boards of directors of Alnylam Pharmaceuticals, Inc., Ironwood Pharmaceuticals, Inc. and Momenta

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Pharmaceuticals, Inc. She received her B.S. in pharmacy from West Virginia University and her M.B.A. from Northeastern University. We believe Ms. Fanucci is qualified to serve on our board of directors due to her expertise with public and financial accounting matters and her experience leading financial organizations in biotechnology companies.

Amir Nashat, Ph.D., has served on our board of directors since January 2016. He is a managing partner at Polaris Venture Partners, a venture capital firm, where he has worked since 2002. Dr. Nashat also serves on the board of the Partners Innovation Fund and is a mentor with the Deshpande Center for Technological Innovation at MIT. Dr. Nashat serves on the boards of directors of Fate Therapeutics, Inc. and BIND Therapeutics, Inc. Dr. Nashat received a Ph.D. in chemical engineering from the Massachusetts Institute of Technology, and an M.S. and B.S. in materials science and mechanical engineering from the University of California, Berkeley. We believe Dr. Nashat is qualified to serve on our board of directors because of his experience on the boards of directors of other publicly traded companies and his experience as an investor in biotechnology and life sciences companies.

Robert Nelsen has served on our board of directors since our inception in November 2011. He currently serves as our lead independent director. Mr. Nelsen was a co-founder of ARCH Venture Partners, a venture capital firm, and has served in various capacities for ARCH and affiliated entities since 1986. He is currently a managing director of ARCH Venture Corporation. Mr. Nelsen is a director of Agios Pharmaceuticals, Inc., Bellerophon Therapeutics, Inc., Juno Therapeutics, Inc. and Sage Therapeutics, Inc., as well as a director of various private companies. Mr. Nelsen also serves as a trustee of the Fred Hutchinson Cancer Research Institute, a trustee of the Institute for Systems Biology, and a director of the National Venture Capital Association. Mr. Nelsen received a B.S. with majors in biology and economics from the University of Puget Sound and an M.B.A. from the University of Chicago. We believe Mr. Nelsen is qualified to serve on our board of directors due to his extensive experience as an investor in, and director of, early stage biopharmaceutical and life sciences companies.

Vicki L. Sato, Ph.D., has served on our board of directors since August 2013. She has been a professor of management practice at Harvard Business School since September 2006 and was a professor in the Department of Molecular and Cell Biology at Harvard University from July 2005 until October 2015. She was previously president of Vertex. Dr. Sato is a member of the boards of directors of Bristol Myers Squibb Company, PerkinElmer Corporation and BorgWarner, Inc. Prior to becoming president of Vertex, she was the chief scientific officer and senior vice president of research and development. She joined Vertex in 1992, after serving as vice president of research at Biogen Inc., a biotechnology company. Dr. Sato received her A.B. from Radcliffe College and her A.M. and Ph.D. degrees from Harvard University. She conducted her postdoctoral work at both the University of California Berkeley and Stanford Medical Center. We believe Dr. Sato is qualified to serve on our board of directors because of her experience as a senior executive and as a director of several life sciences companies, and because of her knowledge of our industry.

Phillip A. Sharp, Ph.D., has served on our board of directors since December 2012. Dr. Sharp has been an institute professor at the Massachusetts Institute of Technology since 1999. Much of Dr. Sharp's scientific work has been conducted at MIT's Center for Cancer Research (now the Koch Institute), which he joined in 1974 and directed from 1985 to 1991. He subsequently led the Department of Biology from 1991 to 1999 before assuming the directorship of the McGovern Institute from 2000 to 2004. Dr. Sharp is the winner of the 1993 Nobel Prize in Physiology or Medicine. Dr. Sharp has served on the board of directors of Alnylam Pharmaceuticals, Inc., a biopharmaceutical company, since 2002. He earned his B.A. from Union College in 1966 and a Ph.D. in chemistry from the University of Illinois, Champaign-Urbana in 1969. He did his postdoctoral training at the California Institute of Technology. We believe Dr. Sharp is qualified to serve on our board of directors due to his scientific expertise and his experience as a director of a publicly traded company.

Richard A. Young, Ph.D., has served on our board of directors since our inception in November 2011. He is also one of our scientific co-founders and a member of our scientific advisory board. He

has been a member of the Whitehead Institute and professor of Biology at the Massachusetts Institute of Technology since 1984. In May 2012, he was elected into the National Academy of Sciences. Dr. Young has served as an advisor to *Science* magazine and the World Health Organization. Dr. Young received his Ph.D. in molecular biophysics and biochemistry from Yale University. We believe Dr. Young is qualified to serve on our board of directors because of his scientific expertise and his role as one of our scientific co-founders.

Board Composition and Election of Directors

Board Composition

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

Our directors were elected to and currently serve on the board of directors pursuant to a voting agreement among us and our stockholders. This agreement will terminate upon the closing of this offering, after which there will be no further contractual obligations regarding the election of our directors.

In accordance with the terms of our restated certificate of incorporation and amended and restated bylaws that will become effective upon the closing 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 Stéphane Bancel, Amir Nashat, Ph.D., and Robert Nelsen, and their term will expire at the first annual meeting of stockholders held after the closing of this offering;
- the class II directors will be Vicki L. Sato, Ph.D., Phillip A. Sharp, Ph.D. and Richard A. Young, Ph.D., and their term will expire at the second annual meeting of stockholders held after the closing of this offering; and
- the class III directors will be Nancy Simonian, M.D. and Marsha H. Fanucci, and their term will expire at the third annual meeting of stockholders held after the closing of this offering.

Our restated certificate of incorporation and amended and restated bylaws that will become effective upon the closing of this offering provide that the authorized number of directors may be changed only by resolution of our board of directors. Our restated certificate of incorporation and amended and restated bylaws will also provide that our directors may be removed only for cause by the affirmative vote of the holders of 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.

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 under the Securities Exchange Act of 1934, as amended, or the Exchange Act. Audit committee members must also satisfy the independence criteria set forth in Rule 10A-3 under the Exchange Act, and compensation committee members must also satisfy the independence criteria set forth in Rule 10C-1 under the Exchange Act and be a non-employee member of our board of directors as defined in Rule 16b-3 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

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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 December 2015, our board of directors undertook a review of the composition of our board of directors and its committees and the independence of each director. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board of directors has determined that each of Stéphane Bancel, Marsha H. Fanucci, Robert Nelsen, Vicki L. Sato, Ph.D., Phillip A. Sharp, Ph.D. and Richard A. Young, Ph.D. is an "independent director" as defined under applicable NASDAQ rules. In making such determination, our board of directors considered the relationships that each such non-employee director has with our company and all other facts and circumstances that our board of directors deemed relevant in determining his or her independence, including the beneficial ownership of our capital stock by each non-employee director. Dr. Simonian is not deemed to be an independent director under these rules because she 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 Marsha H. Fanucci, Robert Nelsen and Richard A. Young, Ph.D., and Ms. Fanucci is the chair of the audit committee. Effective at the time of this offering, 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;
- overseeing 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;

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- 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 Securities and Exchange Commission, or 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.

In December 2015, our board of directors determined that Ms. Fanucci and Mr. Nelsen satisfy the independence criteria for audit committee members set forth in Rule 10A-3 under the Exchange Act. Dr. Young is not an independent director for the purpose of membership in our audit committee under Rule 10A-3 because he receives consulting fees from us.

Under applicable NASDAQ rules, we are permitted to phase-in our compliance with the independence requirements for our audit committee. The phase-in periods with respect to director independence allow us to have only one independent member on our audit committee upon the listing date of our common stock, a majority of independent members on our audit committee within 90 days of the listing date and a fully independent audit committee within one year of the listing date. We are taking advantage of these phase-in rules with respect to Dr. Young's service on our audit committee, and we expect that by the first anniversary of our listing on The NASDAQ Global Market, our audit committee will comply with the applicable independence requirements.

Our board of directors has determined that Marsha H. Fanucci 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.

Compensation Committee

The members of our compensation committee are Phillip A. Sharp, Ph.D., Stéphane Bancel and Vicki L. Sato, Ph.D., and Dr. Sharp is the chair of the compensation committee. Effective at the time of this offering, 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;
- overseeing and administering our cash and equity incentive plans;
- reviewing and making recommendations to our board of directors with respect to director compensation and management succession planning;
- 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 members of our compensation committee meet the requirements for independence under Rule 10C-1 under the Exchange Act and the criteria to be non-employee directors as defined in Rule 16b-3 under the Exchange Act and outside directors as defined in Section 162(m) of the Internal Revenue Code of 1986, as amended.

Nominating and Corporate Governance Committee

The members of our nominating and corporate governance committee are Vicki L. Sato, Ph.D., Stéphane Bancel and Richard A. Young, Ph.D., and Dr. Sato is the chair of the nominating and corporate governance committee. Effective at the time of this offering, 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;
- reviewing and making recommendations to our board of directors with respect to our board leadership structure and board committee structure;
- making recommendations to our board of directors with respect to accepting director resignations;
- reviewing and making recommendations to our board of directors with respect to management succession planning;
- developing and recommending to our board of directors corporate governance principles; and
- overseeing an annual evaluation of our board of directors and an annual review of succession planning for senior executives.

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

Prior to the closing of this offering, we will 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. Following this offering, we will post a copy of the code on the Corporate Governance section of our website, which is located at www.syros.com. Our board of directors will be responsible for overseeing the code of business conduct and ethics and must approve any waivers of the code for directors, officers and employees. If we make any substantive amendments to, or grant any waivers from, the code of business conduct and ethics for any officer or director, we will disclose the nature of such amendment or waiver on our website or in a current report on Form 8-K.

EXECUTIVE COMPENSATION

This section describes the material elements of compensation awarded to, earned by or paid to each of our named executive officers in 2014 and 2015. Our named executive officers for 2015 are Nancy Simonian, M.D., Kyle D. Kovalanka and David A. Roth, M.D. This section also provides qualitative information regarding the manner and context in which compensation is awarded to and earned by our 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 2014 and 2015.

<u>Name and Principal Position</u>	<u>Year</u>	<u>Salary (\$)</u>	<u>Bonus (\$)</u>	<u>Option Awards \$(1)</u>	<u>All Other Compensation \$(2)</u>	<u>Total (\$)</u>
Nancy Simonian, M.D.	2015	425,000	—	723,248	270	1,148,518
President and Chief Executive Officer(3)	2014	425,000	—	43,540	263	468,803
Kyle D. Kovalanka(4) Chief Operating Officer	2015	106,692	122,500	1,262,638	68	1,491,898
David A. Roth, M.D.(5) Chief Medical Officer	2015	26,064	—	1,437,272	—	1,463,336

- (1) The amounts reported in the "Option Awards" column reflect the aggregate grant date fair value of stock-based compensation awarded during the year computed in accordance with the provisions of Financial Accounting Standards Board Accounting Standard Codification, or ASC, Topic 718. Unlike the calculations contained in our consolidated financial statements, this calculation does not give effect to any estimate of forfeitures related to service-based vesting, but assumes that the named executive officer will perform the requisite service for the award to vest in full. See Note 11 to our financial statements included elsewhere in this prospectus regarding assumptions underlying the valuation of equity awards.
- (2) The amounts reported in the "All Other Compensation" column reflect, for each named executive officer, the cost to us of life insurance premiums paid for the named executive officer.
- (3) Dr. Simonian also serves as a member of our board of directors but does not receive any additional compensation for her service as a director.
- (4) Mr. Kovalanka commenced employment with us on September 21, 2015. Amounts shown represent compensation earned by Mr. Kovalanka during that partial year of employment.
- (5) Dr. Roth commenced employment with us on December 7, 2015. Amounts shown represent compensation earned by Dr. Roth during that partial year of employment.

Narrative to Summary Compensation Table

In 2014 and 2015, we paid a base salary of \$425,000 to Dr. Simonian. Mr. Kovalanka commenced employment with us in September 2015. In 2015, we paid him a base salary of \$106,692 for his partial year of employment, and his annualized base salary was \$380,000. Dr. Roth commenced employment with us in December 2015. In 2015, we paid him a base salary of \$26,064 for his partial year of employment, and his annualized base salary was \$380,000. We use base salaries to recognize the experience, skills, knowledge and responsibilities required of all our employees, including our named

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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. Our offer letters with our executive officers provide that they will be eligible for annual performance-based bonuses up to a specific percentage of their salary, subject to approval by our board of directors. No such bonuses were paid in 2014. In 2015, we paid a sign-on bonus of \$122,500 to Mr. Kovalanka.

In 2015, we also made equity incentive grants to our executive officers, including Dr. Simonian, Mr. Kovalanka and Dr. Roth. Dr. Simonian was granted three options to purchase up to 376,382, up to 161,430 and up to 161,429 shares of common stock, respectively. The first and second grants will vest as to 25% of the shares on February 5, 2016 and June 9, 2016, respectively, with the remaining shares vesting in equal monthly installments thereafter through February 5, 2019 and June 9, 2019, respectively. Dr. Simonian's third grant vests upon the achievement of performance-based criteria, with 50% of the shares vesting upon the closing of this offering and the remaining 50% of the shares vesting upon the earlier to occur of clinical proof-of-concept studies for a company drug candidate and a significant development or partnership deal, in each case as determined by our board of directors, and in any event will vest in full on June 9, 2021. Mr. Kovalanka was granted two options to purchase up to 709,697 and up to 258,072 shares of common stock, respectively. The first grant will vest as to 25% of the shares on September 21, 2016, with the remaining shares vesting in equal monthly installments thereafter through September 21, 2019. Mr. Kovalanka's second grant vests upon the achievement of performance-based criteria, with 40% of the shares vesting upon the closing of this offering, 40% vesting upon the execution by us of a collaboration agreement and 20% of the shares vesting upon clinical proof-of-concept for a company drug candidate, in each case as determined by our board of directors, and in any event will vest in full on September 21, 2021. Dr. Roth was granted two options to purchase up to 645,179 and up to 193,553 shares of common stock, respectively. The first grant will vest as to 25% of the shares on December 7, 2016, with the remaining shares vesting in equal monthly installments thereafter through December 7, 2019. Dr. Roth's second grant vests upon the achievement of performance-based criteria, with 75% of the shares vesting upon clinical proof-of-concept for a company drug candidate and 25% of the shares vesting upon execution by us of a collaboration agreement, in each case as determined by our board of directors, and in any event will vest in full on December 7, 2021.

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

Outstanding Equity Awards at Fiscal Year End

The following table sets forth information regarding outstanding equity awards held by our named executive officers as of December 31, 2015, which consisted entirely of stock options:

Name	Number of Securities Underlying Unexercised Options Exercisable (#)	Number of Securities Underlying Unexercised Options Unexercisable (#)	Option Exercise Price (\$/share)	Option Expiration Date
Nancy Simonian, M.D.	175,898(1)	205,216(1)	0.27	5/21/2023
	140,719(2)	281,438(2)	0.27	5/21/2023
	23,437(3)	51,563(3)	0.81	10/21/2024
		376,382(4)	0.81	2/4/2025
		161,430(5)	0.81	6/8/2025
Kyle D. Kovalanka		161,429(6)	0.81	6/8/2025
		709,697(7)	1.85	9/20/2025
David A. Roth, M.D.		258,072(8)	1.85	9/20/2025
		645,179(9)	2.42	12/22/2025
		193,553(10)	2.42	12/22/2025

- (1) This option was granted on May 22, 2013 and vested as to 25% of the shares on July 2, 2013 with the remaining shares vesting in equal monthly installments thereafter through July 2, 2016.
- (2) This option was granted on May 22, 2013 and vests upon the achievement of performance-based criteria, and in any event will vest in full on July 2, 2018.
- (3) This option was granted on October 22, 2014 and vested as to 25% of the shares on September 29, 2015 with the remaining shares vesting in equal monthly installments thereafter through September 29, 2018.
- (4) This option was granted on February 5, 2015 and vests as to 25% of the shares on February 5, 2016 with the remaining shares vesting in equal monthly installments thereafter through February 5, 2019.
- (5) This option was granted on June 9, 2015 and vests as to 25% of the shares on June 9, 2016 with the remaining shares vesting in equal monthly installments thereafter through June 9, 2019.
- (6) This option was granted on June 9, 2015 and vests upon the achievement of performance-based criteria, and in any event will vest in full on June 9, 2021.
- (7) This option was granted on September 21, 2015 and vests as to 25% of the shares on September 21, 2016 with the remaining shares vesting in equal monthly installments thereafter through September 21, 2019.
- (8) This option was granted on September 21, 2015 and vests upon the achievement of performance-based criteria, and in any event will vest in full on September 21, 2021.
- (9) This option was granted on December 23, 2015 and vests as to 25% of the shares on December 7, 2016 with the remaining shares vesting in equal monthly installments thereafter through December 7, 2019.
- (10) This option was granted on December 23, 2015 and vests upon the achievement of performance-based criteria, and in any event will vest in full on December 7, 2021.

Employment and Change in Control Arrangements

We have entered into written offer letters with each of our named executive officers. These agreements set forth the terms of the named executive officer's compensation, including his or her initial base salary, severance and annual cash bonus opportunity. In addition, the agreements provide that the named executive officers are eligible to participate in company-sponsored benefit programs that are available generally to all of our employees. In connection with the commencement of their employment with us, our named executive officers executed our standard invention and non-disclosure agreement and non-competition and non-solicitation agreement.

The offer letter with Dr. Simonian provides that she is eligible to receive an annual incentive bonus equal to 50% of her then-current salary, subject to the terms of the applicable bonus plans approved by our board of directors. Dr. Simonian's offer letter also provides that if her employment is terminated by us without cause, or by her with good reason, as such terms are defined in her offer letter, she will receive monthly severance payments equal to her then-current monthly salary rate for 12 months and payment of an incentive bonus pro-rated for the portion of the then-current calendar year during which she was employed by us, subject to certain conditions. In addition, in the event of a change in control of our company, as defined in the offer letter, all unvested stock options then held by Dr. Simonian will vest in full 12 months after the change in control, or earlier if her employment is terminated by us without cause or by her for good reason in contemplation of, pursuant to or following a change in control, referred to as the CIC Equity Vesting.

The offer letter with each of Mr. Kovalanka and Dr. Roth provides that if his employment is terminated by us without cause, or by him with good reason, as such terms are defined in his offer letter, he will receive monthly severance payments equal to his then-current monthly rate of salary for nine months, subject to certain conditions. Mr. Kovalanka and Dr. Roth are also eligible for the CIC Equity Vesting.

Equity Compensation Plans

The three equity incentive plans described in this section are our 2012 Equity Incentive Plan, as amended to date, or the 2012 plan, our 2016 Stock Incentive Plan, or the 2016 plan, and our 2016 Employee Stock Purchase Plan, or the 2016 ESPP. Prior to this offering, we granted awards to eligible participants under the 2012 plan. Following the effectiveness of this registration statement, we expect to grant awards to eligible participants only under the 2016 plan.

2012 Equity Incentive Plan

The 2012 plan was adopted by our board of directors and approved by our stockholders in August 2012. The 2012 plan provides for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, awards of restricted stock, restricted stock units, other stock-based awards and cash-based awards. Our employees, officers, directors, consultants and advisors are eligible to receive awards under our 2012 plan; however, incentive stock options may only be granted to our employees. A maximum of 10,311,306 shares of our common stock are authorized for issuance under the 2012 plan.

The type of award granted under our 2012 plan and the terms of such award are set forth in the applicable award agreement.

Pursuant to the terms of the 2012 plan, our board of directors (or a committee delegated by our board of directors) administers the plan and, subject to any limitations set forth in the plan, selects the recipients of awards and determines:

- the number of shares of our common stock covered by options and the dates upon which the options become exercisable;

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- the type of options to be granted;
- the duration of options, which may not be in excess of ten years;
- 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 methods of payment of the exercise price of options; and
- the number of shares of our common stock subject to any stock appreciation rights, awards of restricted stock, restricted stock units or other stock-based awards and the terms and conditions of such awards and of any cash-based awards, including conditions for repurchase, measurement price, issue price and 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 2012 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 2012 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 2012 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 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 each outstanding other stock-based award.

Upon a merger or other reorganization event (as defined in the 2012 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 2012 plan as to all or any (or any portion of) outstanding awards other than awards of restricted stock:

- provide that all outstanding awards will be assumed, or substantially equivalent awards will be substituted, by the acquiring or successor corporation (or an affiliate thereof);
- upon written notice to a participant, provide that all of the participant's vested but unexercised awards will terminate immediately prior to the consummation of such reorganization event 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 such reorganization event;

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- in the event of a reorganization event pursuant to which holders of shares 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 our liquidation or dissolution, awards will convert into the right to receive liquidation proceeds (if applicable, net of the exercise, measurement or purchase price thereof and any applicable tax withholdings); or
- any combination of the foregoing.

Our board of directors is not obligated by the 2012 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 that are subject to Section 409A of the Internal Revenue Code of 1986, as amended, or the Code, 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 our liquidation or dissolution, the repurchase and other rights with respect to outstanding awards of restricted stock 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. However, our board of directors may provide 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, either initially or by amendment. Upon the occurrence of a reorganization event involving our 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 2012 plan will 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.

As of January 28, 2016, there were options to purchase 8,208,947 shares of our common stock outstanding under the 2012 plan, at a weighted-average exercise price of \$1.04 per share.

No award may be granted under the 2012 plan on or after the effectiveness of the registration statement for this offering. Our board of directors may amend, suspend or terminate the 2012 plan at any time, except that stockholder approval may be required to comply with applicable law or stock market requirements.

2016 Stock Incentive Plan

Our board of directors has adopted, and we expect our stockholders to approve, the 2016 plan, which will become effective immediately prior to the effectiveness of the registration statement for this offering. The 2016 plan will provide 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 effectiveness of the 2016 plan, the number of shares of our common stock that will be reserved

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for issuance under the 2016 plan will be the sum of (1) 11,700,000 shares plus; (2) the number of shares reserved for issuance (up to 8,815,298 shares) equal to the sum of the number of shares of our common stock then available for issuance under the 2012 plan and the number of shares of our common stock subject to outstanding awards under the 2012 plan that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by us at their original issuance price pursuant to a contractual repurchase right; plus (3) an annual increase, to be added the first day of each fiscal year, beginning with the fiscal year ending December 31, 2017 and continuing until, and including, the fiscal year ending December 31, 2026, equal to the lowest of 6,000,000 shares of our common stock, 4.0% of the number of shares of our common stock outstanding on the first day of the 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 2016 plan; however, incentive stock options may only be granted to our employees.

Pursuant to the terms of the 2016 plan, our board of directors (or a committee delegated by our board of directors) administers the plan and, subject to any limitations set forth in the plan, will select the recipients of awards and determine:

- the number of shares of our common stock covered by options and the dates upon which those options become exercisable;
- the type of options to be granted;
- the duration of options, which may not be in excess of ten years;
- 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 methods of payment of the exercise price of options; and
- the number of shares of our common stock subject to and the terms and conditions of any stock appreciation rights, awards of restricted stock, restricted stock units or other stock-based awards, including conditions for repurchase, measurement price, issue price and 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 2016 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 2016 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 2016 plan;
- the share counting rules 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 measurement price of each outstanding stock appreciation right;

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- the number of shares and 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 each outstanding other stock-based award.

Upon a merger or other reorganization event (as defined in our 2016 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 2016 plan, as to all or any (or any portion of) outstanding awards, other than awards of restricted stock:

- provide that all outstanding awards will be assumed or substantially equivalent awards will be substituted by the acquiring successor corporation (or an affiliate thereof);
- upon written notice to a participant, provide that all of the participant's unvested and/or unexercised awards will terminate immediately prior to the consummation of such reorganization event 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 such reorganization event;
- in the event of a reorganization event pursuant to which holders of shares 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 our liquidation or dissolution, awards will convert into the right to receive liquidation proceeds (if applicable, net of the exercise, measurement or purchase price thereof and any applicable tax withholdings); or
- any combination of the foregoing.

Our board of directors is not obligated by the 2016 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 our liquidation or dissolution, the repurchase and other rights with respect to outstanding awards of restricted stock 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. However, our board of directors may provide 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, either initially or by amendment. Upon the occurrence of a reorganization event involving our liquidation or dissolution, all restrictions and conditions on each outstanding restricted stock award will automatically be deemed terminated or

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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 2016 plan will 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 Code or NASDAQ rules, our board of directors may amend, modify or terminate any outstanding award under the 2016 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 2016 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 2016 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 2016 plan) and grant in substitution therefor new awards under the 2016 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 NASDAQ rules.

No award may be granted under the 2016 plan after ten years from the effectiveness of the 2016 plan. Our board of directors may amend, suspend or terminate the 2016 plan at any time, except that stockholder approval will be required to comply with applicable law or stock market requirements.

2016 Employee Stock Purchase Plan

Our board of directors has adopted, and we expect our stockholders to approve, the 2016 ESPP, to become effective upon the closing of this offering. The 2016 ESPP will be administered by our board of directors or by a committee appointed by our board of directors. The 2016 ESPP initially will provide participating employees with the opportunity to purchase up to an aggregate of 2,200,000 shares of our common stock. The number of shares of our common stock reserved for issuance under the 2016 ESPP will automatically increase on the first day of each fiscal year, commencing on January 1, 2017 and ending on December 31, 2025, in an amount equal to the least of (i) 4,400,000 shares of our common stock, (ii) 1.0% of the total number of shares of our common stock outstanding on the first day of the applicable year, and (iii) an amount determined by our board of directors.

All of our employees or employees of any designated subsidiary, as defined in the 2016 ESPP, are eligible to participate in the 2016 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 2016 ESPP; and

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- such person was our employee or an employee of a designated subsidiary on the first day of the applicable offering period under the 2016 ESPP.

No employee may purchase shares of our common stock under the 2016 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 2016 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 2016 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 2016 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 2016 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 2016 ESPP, and the employee's accumulated payroll deductions will be refunded. An employee's rights under the 2016 ESPP terminate upon voluntary withdrawal from an offering under the 2016 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 2016 ESPP, the share limitations under the 2016 ESPP, and the purchase price for an offering period under the 2016 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 2016 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 2016 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 2016 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 2016 ESPP or any portion thereof. We will obtain stockholder approval for any amendment if such approval is required by Section 423 of the Code. Further, our board of directors may not make any amendment that would cause the 2016 ESPP to fail to comply with Section 423 of the Code. The 2016 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 Code. In general, all of our employees are eligible to participate, beginning on the first day of the quarter 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 2015, and have the amount of the reduction contributed to the 401(k) plan.

Limitations on Liability and Indemnification

Our restated certificate of incorporation that will become effective upon the closing 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 or other duty as a director. However, these provisions do not eliminate or limit the liability of any of our directors:

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

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

directors will be further limited to the greatest extent permitted by the General Corporation Law of the State of Delaware.

In addition, our restated certificate of incorporation that will become effective upon the closing 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 have entered into indemnification agreements with each of our directors, and we intend to enter into indemnification agreements with all of our directors and executive officers prior to the closing of this offering. These indemnification agreements may 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 Trading 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 subsequent 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

In September 2015, we adopted a director compensation program to be effective for periods prior to our initial public offering, pursuant to which non-founder, non-investor, non-employee members of our board of directors will receive annual cash compensation of \$17,500 for service on our board of directors. This fee is payable in arrears in four equal quarterly installments on the last day of each quarter, provided that the amount of such payment will be prorated for any portion of such quarter that the director is not serving on our board of directors. Prior to the adoption of this program, during 2014, we paid Dr. Sato an annual retainer of \$25,000 in return for her service on our board of directors, and in 2015 we paid Dr. Sato an annual retainer of \$15,000. In September 2015, we granted options to purchase 27,500 shares of our common stock to each of Dr. Sato, Dr. Sharp and Mr. Bancel and in October 2015, we granted an option to purchase 55,000 shares of our common stock to Ms. Fanucci, in return for their service on our board of directors. The options were granted at an exercise price per share of \$1.85, which equalled the fair market value of our common stock on the date of grant, vest as to 25% of the shares underlying the option on the first anniversary of the date of grant, with the remainder of the shares underlying the option vesting in equal monthly installments for an additional three years, and have a term of 10 years. No other directors have received compensation from us for their service on our board of directors. We also reimburse our non-employee directors for

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reasonable travel and out-of-pocket expenses incurred in connection with attending board of director and committee meetings.

In January 2016, our board of directors also approved a director compensation program to be effective at the closing of this offering. Under this director compensation program, we will pay our non-employee directors a cash retainer for service on the board of directors and for service on each committee on which the director is a member. The chair of each committee and the chair of the board of directors will receive higher retainers for such service. These fees will be payable in arrears in four equal quarterly installments on the last day of each quarter, provided that the amount of such payment will be prorated for any portion of such quarter that the director is not serving on our board of directors, on such committee or in such position, and no fee shall be payable in respect of any period prior to the time of this offering. The fees paid to non-employee directors for service on the board of directors and for service on each committee of the board of directors on which the director is a member will be as follows:

	Base	Incremental— Chair	Incremental— Non-Chair
Board of Directors	\$ 35,000	\$ 30,000	
Audit Committee		\$ 15,000	\$ 7,500
Compensation Committee		\$ 10,000	\$ 5,000
Nominating and Corporate Governance Committee		\$ 7,000	\$ 3,500

In addition, under this director compensation program, on or around the closing of this offering for current directors, or upon their election to the board for new directors, we will grant to our non-employee directors an initial grant of an option to purchase 22,000 shares of our common stock, with an exercise price equivalent to fair market value of a share of common stock at the time of grant, which option will vest as to 16.66% of the shares on the six month anniversary of the date of grant and as to the remainder of the shares monthly thereafter until the third anniversary of the date of grant, subject to continued service, with full acceleration upon a change in control of us. The option will have a term of 10 years. Immediately following each annual meeting of our stockholders, we will grant to each director who has served on our board of directors for at least six months as of the time of such grant an option to purchase 11,000 shares of our common stock, with an exercise price equivalent to fair market value of a share of common stock at the time of grant, which option will vest as to 50% of the shares on the six-month anniversary of the date of grant and as to the remainder of the shares monthly thereafter until the first anniversary of the date of grant, subject to continued service, with full acceleration upon a change in control of us. The option will have a term of 10 years.

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

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

TRANSACTIONS WITH RELATED PERSONS

Since January 1, 2013, we have engaged in the following transactions in which the amount involved exceeded \$120,000 and any of our directors or executive officers or beneficial holders of more than 5% of any class of our voting securities, or any immediate family member of the foregoing persons, or any person who was in any of those categories at the time of such transaction, 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 A Preferred Stock Financings

In April and November 2013, we issued and sold an aggregate of 12,100,000 shares of our Series A-2 preferred stock at a price per share of \$1.00, for an aggregate purchase price of \$12.1 million. The following table sets forth the number of shares of our Series A-2 preferred stock purchased by our directors, executive officers and 5% stockholders and their affiliates and the aggregate purchase price paid for such shares.

<u>Name</u>	<u>Shares of Series A-2 Preferred Stock Purchased</u>	<u>Aggregate Purchase Price</u>
Entities affiliated with Flagship Ventures	5,000,000	\$ 5,000,000
ARCH Venture Fund VII, L.P.	5,000,000	\$ 5,000,000
Phillip A. Sharp, Ph.D.	1,000,000	\$ 1,000,000
WuXi PharmaTech Healthcare Fund I, L.P.	500,000	\$ 500,000
Nancy Simonian, M.D.	250,000	\$ 250,000
Stéphane Bancel	100,000	\$ 100,000
Total	11,850,000	\$ 11,850,000

In March and August 2014, we issued and sold an aggregate of 15,750,000 shares of our Series A-3 preferred stock at a price per share of \$1.00, for an aggregate purchase price of \$15.75 million. The following table sets forth the number of shares of our Series A-2 preferred stock purchased by our directors, executive officers and 5% stockholders and their affiliates and the aggregate purchase price paid for such shares.

<u>Name</u>	<u>Shares of Series A-3 Preferred Stock Purchased</u>	<u>Aggregate Purchase Price</u>
Entities affiliated with Flagship Ventures	7,500,000	\$ 7,500,000
ARCH Venture Fund VII, L.P.	7,500,000	\$ 7,500,000
WuXi PharmaTech Healthcare Fund I, L.P.	500,000	\$ 500,000
Total	15,500,000	\$ 15,500,000

Series B Preferred Stock Financings

In October 2014, we issued and sold an aggregate of 16,893,931 shares of our Series B preferred stock at a price per share of \$3.1461, for an aggregate purchase price of \$53.1 million. The following table sets forth the number of shares of our Series B preferred stock purchased by our directors,

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executive officers and 5% stockholders and their affiliates and the aggregate purchase price paid for such shares.

<u>Name</u>	Shares of Series B Preferred Stock	
	Purchased	Aggregate Purchase Price
Entities affiliated with Fidelity	6,357,077	\$ 19,999,999
Polaris Partners VII, L.P.	3,178,539	\$ 10,000,001
Entities affiliated with Flagship Ventures	2,224,976	\$ 6,999,997
ARCH Venture Fund VII, L.P.	1,589,269	\$ 4,999,993
WuXi PharmaTech Healthcare Fund I, L.P.	953,561	\$ 2,999,998
Total	14,303,422	\$ 44,999,988

In January 2016, we issued and sold an aggregate of 12,714,150 shares of our Series B preferred stock at a price per share of \$3.1461, for an aggregate purchase price of \$40.0 million. The following table sets forth the number of shares of our Series B preferred stock purchased by our directors, executive officers and 5% stockholders and their affiliates and the aggregate purchase price paid for such shares.

<u>Name</u>	Shares of Series B Preferred Stock	
	Purchased	Aggregate Purchase Price
Entities affiliated with Deerfield Management	6,357,077	\$ 20,000,000
Entities affiliated with Fidelity	1,589,269	\$ 4,999,999
WuXi PharmaTech Healthcare Fund II, L.P.	1,589,269	\$ 4,999,999
Entities affiliated with Polaris	1,271,415	\$ 3,999,999
Total	10,807,030	\$ 33,999,997

Robert Nelsen, a member of our board of directors, is a general partner at ARCH Venture Fund VII, L.P. Douglas Cole, M.D., who was a member of our board of directors at the time of the Series A and October 2014 Series B preferred stock financings, is a general partner at Flagship Ventures and is the spouse of Dr. Simonian. Amir Nashat, Ph.D., a member of our board of directors, is a managing partner at Polaris.

Investors' Rights Agreement

We are a party to an amended and restated investors' rights agreement, dated as of October 9, 2014, as amended, which we refer to as our investors' rights agreement, with holders of our preferred stock, including entities affiliated with Flagship Ventures, ARCH Venture Fund VII, L.P., entities affiliated with Fidelity, entities affiliated with Deerfield Management, entities affiliated with Polaris, entities affiliated with WuXi PharmaTech, Nancy Simonian, M.D., Phillip A. Sharp, Ph.D., and Stéphane Bancel. The investors' rights agreement provides these holders the right, following the closing 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.

Services Agreement with WuXi

We are party to a services agreement with WuXi AppTec (Hong Kong) Limited, or WuXi, an affiliate of our 5% stockholder WuXi PharmaTech, pursuant to which we engage WuXi to provide external research and preclinical development services. Prior to this agreement, we were party to a similar services agreement with WuXi. During the years ended December 31, 2013, 2014 and 2015, we

paid WuXi \$0.2 million, \$1.1 million and \$3.1 million, respectively, for services provided under these agreements.

Employment Agreements

See the "Executive Compensation—Employment and Change in Control Agreements" section of this prospectus for a further discussion of these arrangements.

Equity Grants to Directors and Executive Officers

We have granted stock options and stock awards to certain of our directors and named executive officers. For more information regarding the stock options and stock awards granted to our directors and named executive officers see "Executive Compensation."

Indemnification Agreements

Our restated certificate of incorporation that will become effective upon the closing of this offering provides that we will indemnify our directors and officers to the fullest extent permitted by Delaware law. In addition, we have entered into indemnification agreements with each of our directors, and we intend to enter into indemnification agreements with all of our directors and executive officers prior to the closing of this offering. See "Executive Compensation—Limitations of Liability and Indemnification" for additional information regarding these agreements.

Policies and Procedures for Related Person Transactions

Our board of directors will adopt written policies and procedures, which will become effective at the closing of this offering, for the review of any transaction, arrangement or relationship in which our company is 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 chief financial officer. The policy calls for the proposed related person transaction to be reviewed and approved by our audit committee. Whenever practicable, the reporting, review and approval will occur prior to entry into the transaction. If advance review and approval is not practicable, the committee will review, and, in its discretion, may ratify the related person transaction. The policy also permits the 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;

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- 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.

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 January 28, 2016 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 69,507,802 shares of our common stock outstanding as of January 28, 2016, assuming the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 59,958,081 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 overallotment option.

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 January 28, 2016 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 investing power with respect to all of the shares of our common stock beneficially owned by them, subject to community property laws, where applicable. Except as otherwise

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set forth below, the address of the beneficial owner is c/o Syros Pharmaceuticals, Inc., 620 Memorial Drive, Suite 300, Cambridge Massachusetts 02139.

<u>Name of Beneficial Owner</u>	<u>Shares Beneficially Owned</u>	<u>Percentage of Shares Beneficially Owned</u>	
		<u>Before Offering</u>	<u>After Offering</u>
5% Stockholders			
Entities affiliated with Flagship Ventures	16,524,976(1)	23.8%	
ARCH Venture Fund VII, L.P.	15,889,269(2)	22.9%	
Entities affiliated with Fidelity	7,946,346(3)	11.4%	
Entities affiliated with Deerfield Management	6,357,077(4)	9.1%	
Entities affiliated with Polaris	4,449,954(5)	6.4%	
Entities affiliated with WuXi Pharmatech	4,042,830(6)	5.8%	
Named Executive Officers and Directors			
Nancy Simonian, M.D.	1,993,415(7)	2.8%	
Kyle D. Kuvalanka	103,228(8)	*	
David A. Roth, M.D.	—	*	
Stéphane Bancel	179,931(9)	*	
Marsha H. Fanucci	—	—	
Amir Nashat, Ph.D.	4,449,954(10)	6.4%	
Robert Nelsen	15,889,269(11)	22.9%	
Vicki L. Sato, Ph.D.	41,630(12)	*	
Phillip A. Sharp, Ph.D.	1,118,231(13)	1.6%	
Richard A. Young, Ph.D.	2,000,000	2.9%	
<i>All Executive Officers and Directors as a Group (13 persons)</i>	26,442,512(14)	37.2%	

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

- (1) Consists of 800,000 shares of common stock held by Flagship VentureLabs IV, LLC ("Flagship VentureLabs"), 12,579,981 shares of common stock issuable upon the conversion of preferred stock held by Flagship Ventures Fund IV, L.P. ("Flagship Fund IV") and 3,144,995 shares of common stock issuable upon the conversion of preferred stock held by Flagship Ventures Fund IV-Rx, L.P. ("Flagship Fund IV-Rx" and together with Flagship VentureLabs and Flagship IV, the "Flagship Funds"). Flagship Fund IV is a member of Flagship VentureLabs and also serves as its manager. The general partner of each of Flagship Fund IV and Flagship Fund IV-Rx is Flagship Ventures Fund IV General Partner LLC ("Flagship Fund IV GP"). Stéphane Bancel is a director of Syros and a limited partner of Flagship Fund IV and a member of Flagship Fund IV GP. Mr. Bancel disclaims beneficial ownership of such shares. Noubar B. Afeyan, Ph.D. and Edwin M. Kania Jr. are the managers of Flagship Fund IV GP. Flagship Fund IV GP and each of these individuals may be deemed to share voting and investment power with respect to all shares held by the Flagship Funds. Each of the foregoing persons disclaims beneficial ownership of the shares except to the extent of any pecuniary interest therein. The address of such stockholder is One Memorial Drive, 7th Floor, Cambridge, Massachusetts 02142.
- (2) Consists of 800,000 shares of common stock and 15,089,269 shares of common stock issuable upon the conversion of preferred stock held of record by ARCH Venture Fund VII, L.P., or ARCH VII. ARCH Venture Partners VII, L.P., or the GPLP, as the sole general partner of ARCH VII, may be deemed to beneficially own the shares held of record by ARCH VII. The GPLP disclaims beneficial ownership of all shares held of record by ARCH VII in which the GPLP does not have an actual pecuniary interest. ARCH Venture Partners VII, LLC, or the GPLLC, as the sole

general partner of the GPLP, may be deemed to beneficially own certain of the shares held of record by ARCH VII. The GPLLC disclaims beneficial ownership of all shares held of record by ARCH VII in which it does not have an actual pecuniary interest. Keith Crandell, Clinton Bybee and Robert Nelsen are the managing directors of the GPLLC, and may be deemed to share voting and dispositive power over the shares held of record by ARCH VII. The managing directors disclaim beneficial ownership of all shares held of record by ARCH VII in which they do not have an actual pecuniary interest. ARCH Venture Fund VII, L.P. has an address at 8725 West Higgins Road, Suite 290, Chicago, Illinois 60631.

- (3) Consists of shares of common stock issuable upon the conversion of preferred stock, 4,558,440 of which are held of record by Powhatan & Co., LLC fbo Fidelity Mt. Vernon Street: Fidelity Growth Company Fund, 234,635 of which are held of record by Bangle & Co fbo Fidelity Advisor Series VII: Fidelity Advisor Biotechnology Fund, 885,931 of which are held of record by Mag & Co fbo Fidelity Growth Company Comingled Pool, 1,138,582 of which are held of record by Mag & Co fbi Fidelity Select Portfolios: Biotechnology Portfolio and 1,128,758 of which are held of record by WAVELENGTH + Co fbo Fidelity Mt. Vernon Street Trust: Fidelity Series Growth Company Fund. These accounts are managed by direct or indirect subsidiaries of FMR LLC. Edward C. Johnson 3d is a Director and the Chairman of FMR LLC and Abigail P. Johnson is a Director, Vice Chairman and the President of FMR LLC. Members of the family of Edward C. Johnson 3d, including Abigail P. Johnson, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders' voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC. Neither FMR LLC nor Edward C. Johnson 3d nor Abigail P. Johnson has the sole power to vote or direct the voting of the shares owned directly by the various investment companies registered under the Investment Company Act ("Fidelity Funds") advised by Fidelity Management & Research Company ("FMR Co"), a wholly owned subsidiary of FMR LLC, which power resides with the Fidelity Funds' Board of Trustees. Fidelity Management & Research Company carries out the voting of the shares under written guidelines established by the Fidelity Funds' Board of Trustees. The address for Fidelity Select Portfolios: Biotechnology Portfolio is Brown Brothers Harriman & Co., 525 Washington Blvd., Jersey City NJ 07310. The address for Fidelity Advisor Series VII: Fidelity Advisor Biotechnology Fund is State Street Bank & Trust, PO Box 5756, Boston, Massachusetts 02206. The address for Fidelity Growth Company Commingled Pool is Brown Brothers Harriman & Co., 525 Washington Blvd., Jersey City NJ 07310. The address for Fidelity Mt. Vernon Trust: Fidelity Series Growth Company Fund is State Street Bank & Trust, PO Box 5756, Boston, Massachusetts 02206. The address for Fidelity Mt. Vernon Street Trust: Fidelity Growth Company Fund is BNY Mellon, 525 William Penn Place Rm 0400, Pittsburgh, PA 15259.
- (4) Consists of shares of common stock issuable upon the conversion of preferred stock, 1,907,123 of which are held by Deerfield Special Situations Fund, L.P. and 4,449,954 of which are held by Deerfield Private Design Fund III, L.P. Deerfield Mgmt, L.P. is the general partner of Deerfield Special Situations Fund, L.P. and Deerfield Mgmt III, L.P. is the general partner of Deerfield Private Design Fund III, L.P. Deerfield Management Company, L.P. is the investment manager of each of Deerfield Special Situations Fund, L.P. and Deerfield Private Design Fund III, L.P. Mr. James E. Flynn is the sole member of the general partner of each of Deerfield Mgmt, L.P., Deerfield Mgmt III, L.P. and Deerfield Management Company, L.P. Deerfield Mgmt, L.P., Deerfield Mgmt III, L.P., Deerfield Management Company, L.P. and Mr. James E Flynn may be deemed to beneficially own the securities held by Deerfield Special Situations Fund, L.P. and

Deerfield Private Design Fund III, L.P. The address of each such entity is 780 Third Avenue, 37th Floor, New York, New York 10017.

- (5) Consists of shares of common stock issuable upon the conversion of preferred stock, 4,366,825 of which are held by Polaris Partners VII, L.P. and 83,129 of which are held by Polaris Partners Entrepreneurs' Fund VII, L.P. The general partner of Polaris Partners VII, L.P. and Polaris Partners Entrepreneurs' Fund VII, L.P. is Polaris Management Co. VII, L.L.C. ("Polaris Management"), and Polaris Management may be deemed to have sole voting and investment power over such shares. Polaris Management disclaims beneficial ownership of these shares, except to the extent of its pecuniary interest therein. The address of such stockholders is One Marina Park Drive, 10th Floor, Boston, Massachusetts 02210.
- (6) Consists of shares of common stock issuable upon the conversion of preferred stock, 2,453,561 of which are held by WuXi PharmaTech Healthcare Fund I, L.P. and 1,589,269 of which are held by WuXi Healthcare Ventures II, L.P. The general partner of WuXi PharmaTech Healthcare Fund I, L.P. is WuXi PharmaTech Investments (Cayman) Inc. Edward Hu is a director of WuXi PharmaTech Investments (Cayman) Inc. and may be deemed to have voting and investment power over the shares held by WuXi PharmaTech Healthcare Fund I, L.P. The general partner of WuXi Healthcare Ventures II, L.P. is WuXi Healthcare Management, LLC. Wei Li is a director of WuXi Healthcare Management, LLC and may be deemed to have voting and investment power over the shares held by WuXi Healthcare Ventures II, L.P. Each such person and entity disclaims beneficial ownership over such shares, except with respect to their pecuniary interest therein. The address of each such entity is 222 Third Street, Suite 1100, Cambridge, Massachusetts 02142.
- (7) Consists of (i) 250,000 shares of common stock issuable upon the conversion of preferred stock, (ii) 1,166,794 shares of common stock and (iii) 576,621 shares of common stock issuable upon the exercise of options that vest on or prior to March 28, 2016.
- (8) Consists of shares of common stock issuable upon the exercise of options that vest on or prior to March 28, 2016.
- (9) Includes 100,000 shares of common stock issuable upon the conversion of preferred stock.
- (10) See footnote 5.
- (11) See footnote 2.
- (12) Consists of shares of common stock issuable upon the exercise of options that vest on or prior to March 28, 2016.
- (13) Consists of (i) 550,000 shares of common stock issuable upon the conversion of preferred stock held of record by Dr. Sharp, (ii) 150,000 shares of common stock issuable upon the conversion of preferred stock held of record by Ann H. Sharp and Christine S. Carey, as Trustees of the Phillip A. Sharp 2008 Irrevocable Trust f/b/o Christine S. Carey, (iii) 150,000 shares of common stock issuable upon the conversion of preferred stock held of record by Ann H. Sharp and Helena S. Gordon, as Trustees of the Phillip A. Sharp 2008 Irrevocable Trust f/b/o Helena H. Sharp, (iv) 150,000 shares of common stock issuable upon the conversion of preferred stock held of record by Ann H. Sharp and Sarah S. Brokaw, as Trustees of the Phillip A. Sharp 2008 Irrevocable Trust f/b/o Sara S. Brokaw and (v) 118,231 shares of common stock issuable upon the exercise of options that vest on or prior to March 28, 2016.
- (14) Includes 20,889,223 shares of common stock issuable upon conversion of preferred stock and 1,506,564 shares of common stock issuable upon the exercise of options that vest on or prior to March 28, 2016.

DESCRIPTION OF CAPITAL STOCK

General

Following the closing of this offering, our authorized capital stock will consist of 200,000,000 shares of common stock, par value \$0.001 per share, and 10,000,000 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 restated certificate of incorporation and the amended and restated bylaws that will be in effect upon the closing 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 January 28, 2016, we had outstanding 9,549,721 shares of common stock. These shares of common stock were held by 31 stockholders of record. As of January 28, 2016, there would have been outstanding 69,507,802 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. These shares of common stock would have been held by 57 stockholders of record.

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

As of January 28, 2016, there were outstanding 59,958,081 shares of preferred stock, consisting of 2,500,000 shares of Series A-1 preferred stock, 12,100,000 shares of Series A-2 preferred stock, 15,750,000 shares of Series A-3 preferred stock and 29,608,081 shares of Series B preferred stock. All currently outstanding shares of preferred stock will be converted into an aggregate of 59,958,081 shares of common stock upon the closing of this offering.

Under the terms of our restated certificate of incorporation that will become effective upon the closing 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

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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 January 28, 2016, options to purchase 8,350,322 shares of our common stock at a weighted-average exercise price of \$1.02 per share were outstanding, of which options to purchase 1,956,861 shares of our common stock were exercisable, at a weighted-average exercise price of \$0.36 per share, and options to purchase 526,420 shares of common stock were available for future issuance under our 2012 Equity Incentive Plan.

Registration Rights

Our investor's rights agreement provides specified holders of our currently outstanding preferred stock, including some of our directors and 5% stockholders and their respective affiliates and entities affiliated with our officers and directors, the right, following the closing of this offering, to require us to register the shares of common stock that will be issued upon conversion of the preferred stock 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 effective date of the registration statement for this offering, subject to specified limitations set forth in the investor's rights agreement, at any time the holders of 25% of then outstanding registrable securities, as defined in the investor's rights agreement, acting together, may demand in writing that we register their registrable securities under the Securities Act so long as the total amount of registrable shares requested to be registered has an anticipated aggregate offering price to the public, net of selling expenses, as defined in the investors' rights agreement, that would exceed \$5.0 million. We are not obligated to effect 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, the holders of at least 25% of the registrable securities then outstanding may demand in writing that we register on Form S-3 registrable shares 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, net of selling expenses, as defined in the investors' rights agreement, of at least \$2.0 million. We are not obligated to effect a registration statement pursuant to this demand provision on more than two occasions in any twelve-month period, subject to specified exceptions.

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 securities under the Securities Act, either for our own account or for the account of any of our stockholders that are not holders of registrable shares, solely for cash and on a form that would also permit the registration of registrable shares, the holders of our registrable shares are entitled to notice of registration and, subject to specified exceptions, we will be required to register the registrable shares then held by them that they request that we register.

Expenses

Pursuant to the investor's 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 of one counsel representing the selling stockholders, other than

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any underwriting discounts and commissions, related to any demand or incidental registration. The investor's 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 closing of this offering our restated certificate of incorporation and our amended and restated 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 closing of this offering, our restated certificate of incorporation and our amended and restated 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 closing of this offering, our restated 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 closing of this offering, our restated certificate of incorporation and our amended and restated 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 closing of this offering, our amended and restated 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 closing 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

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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 a sale involving us and the "interested stockholder" of 10% or more 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 upon the closing 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 upon closing of this offering, our restated 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 restated certificate of incorporation or amended and restated bylaws, or (4) any action asserting a claim against our company governed by the internal affairs doctrine. Although our restated 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 "SYRS."

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 a liquid 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 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 equity securities.

Based upon the 9,549,721 shares of our common stock that were outstanding on January 28, 2016, 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 59,958,081 shares of common stock upon the closing of this offering, and assuming no exercise by the underwriters of their overallotment option and no exercise of options outstanding as of January 28, 2016.

Of the shares to be outstanding immediately after the closing of this offering, we expect that the _____ shares to be sold in this offering will be freely tradable without restriction under the Securities Act unless purchased by our "affiliates," as that term is defined in Rule 144 under the Securities Act. The remaining 69,507,802 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 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 69,507,802 shares of our common stock will be eligible for sale under Rule 144, including shares eligible for resale

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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 1,580,939 shares of our common stock will be eligible for sale in accordance with Rule 701, subject to satisfying applicable vesting schedules.

Lock-Up Agreements

We, and each of our executive officers and directors and the holders of substantially all of our outstanding stock have agreed that, without the prior written consent of Cowen and Company, LLC and Piper Jaffray & Co., 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: directly or indirectly, (i) offer, sell, assign, transfer, pledge, contract to sell, or otherwise dispose of, or announce the intention to otherwise dispose of, any shares of common stock or securities convertible into or exercisable or exchangeable for common stock; (ii) enter into any swap, hedge or similar agreement or arrangement that transfers in whole or in part, the economic risk of ownership of the common stock or securities convertible into or exercisable or exchangeable for common stock, whether now owned or hereafter acquired by the undersigned or with respect to which the undersigned has or hereafter acquires the power of disposition; or (iii) engage in any short selling of the common stock or securities convertible into or exercisable or exchangeable for common stock. These restrictions are subject to customary exceptions, including transfers made by an individual as gifts, to members of the individual's immediate family or a trust for the benefit of the individual or his or her immediate family, or by will, intestacy or operation of law; and transfers by an entity to its stockholders or other owners, to an affiliate, or in connection with a sale of the entity. See "Underwriting" for additional information.

Registration Rights

Subject to the lock-up agreements described above, upon the closing of this offering, the holders of an aggregate of 62,122,135 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 January 28, 2016, we had outstanding options to purchase 8,350,322 shares of our common stock, of which options to purchase 1,956,861 shares were vested. 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 and options and other awards issuable pursuant to the 2016 stock incentive plan, the 2016 ESPP and our 2012 equity incentive plan. 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 general discussion of material U.S. federal income and estate tax considerations relating to 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 pass-through entity) 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 such 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 own 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 Internal Revenue Code of 1986, as amended, or the Code, existing 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 (generally, property held for investment) for U.S. federal income tax purposes. 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;

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

THIS DISCUSSION IS FOR GENERAL INFORMATION ONLY AND IS NOT, AND IS NOT INTENDED TO BE, LEGAL OR TAX ADVICE. PROSPECTIVE INVESTORS SHOULD CONSULT THEIR OWN 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, and will be 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 discussion below under the headings "Information Reporting and Backup Withholding" and "FATCA."

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, will be 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). 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) on its "effectively connected earnings and profits," subject to certain adjustments.

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 own 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 discussion 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 recognized in the taxable year of the disposition, 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, at any time 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. If we are a U.S. real property holding corporation and either our common stock is not regularly traded on an established securities market or a non-U.S. holder holds more than 5% of our outstanding common stock, directly or indirectly, during the applicable testing period, such non-U.S. holder's proceeds received on the disposition of shares of our common stock generally will be subject to withholding at a rate of 10% and such non-U.S. holder will generally be taxed on any gain in the same manner as gain that is effectively connected with the conduct of a U.S. trade or business, except that the branch profits tax generally will not apply.

Information Reporting and Backup Withholding

We must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. 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

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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 not a U.S. person, 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, currently at a rate of 28%, 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, whether 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 from backup withholding. 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 own 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

The Foreign Account Tax Compliance Act, or FATCA, generally imposes 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 U.S. holders of debt or equity interests in such foreign entity or (iii) the foreign entity is otherwise exempt from 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 own 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 general information only. It is not legal or tax advice. Prospective investors should consult their own 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

We and the underwriters for the offering named below have entered into an underwriting agreement with respect to the shares of common stock being offered. Subject to the terms and conditions of the underwriting agreement, each underwriter has severally agreed to purchase from us the number of shares of common stock set forth opposite its name below. Cowen and Company, LLC and Piper Jaffray & Co. are the representatives of the underwriters.

<u>Underwriter</u>	<u>Number of Shares</u>
Cowen and Company, LLC	
Piper Jaffray & Co.	
JMP Securities LLC	
Wedbush Securities Inc.	
Total	

The underwriting agreement provides that the obligations of the underwriters are subject to certain conditions precedent and that the underwriters have agreed, severally and not jointly, to purchase all of the shares of common stock sold under the underwriting agreement if any of these shares are purchased, other than those shares covered by the overallotment option described below. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against specified liabilities, including liabilities under the Securities Act, and to contribute to payments the underwriters may be required to make in respect thereof.

The underwriters are offering the shares of common stock, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel and other conditions specified in the underwriting agreement. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Overallotment Option to Purchase Additional Shares

We have granted to the underwriters an option to purchase up to _____ additional shares of common stock at the public offering price, less the underwriting discount, in this offering of common stock. This option is exercisable for a period of 30 days. The underwriters may exercise this option solely for the purpose of covering overallotments, if any, made in connection with the sale of common stock offered hereby. To the extent that the underwriters exercise this option, the underwriters will purchase additional shares from us in approximately the same proportion as shown in the table above.

Discounts and Commissions

The following table shows the public offering price, underwriting discount and proceeds, before expenses, to us. These amounts are shown assuming both no exercise and full exercise of the underwriters' overallotment option.

We estimate that the total expenses of this offering of common stock, excluding underwriting discounts and commissions, will be approximately \$ _____ and are payable by us. We have also agreed to reimburse the underwriters for certain of their expenses as set forth in the underwriting agreement, including legal fees incurred in the qualification of this offering and the concurrent offering of notes

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with the Financial Regulatory Authority, or FINRA, in an amount of up to \$30,000, which amount is deemed to be underwriting compensation by FINRA.

	Total		
	Per Share	Without Overallotment	With Overallotment
Initial public offering price	\$	\$	\$
Underwriting discounts and commissions			
Proceeds, before expenses, to Syros	\$	\$	\$

The underwriters propose to offer the shares of common stock to the public at the public offering price set forth on the cover of this prospectus. The underwriters may offer the shares of common stock to securities dealers at the public offering price less a concession not in excess of \$ per share. If all of the shares are not sold at the public offering price, the underwriters may change the offering price and other selling terms. Sales of shares of common stock made outside of the United States may be made by affiliates of certain of the underwriters. Certain of the underwriters may sell shares to the public through one or more of their affiliates as selling agents.

Discretionary Accounts

The underwriters do not intend to confirm sales of the shares of common stock to any accounts over which they have discretionary authority.

Market Information

Prior to this offering, there has been no public market for shares of our common stock. The initial public offering price will be determined by negotiations between us and the representatives of the underwriters. In addition to prevailing market conditions, the factors to be considered in these negotiations include:

- the history of, and prospects for, our company and the industry in which we compete;
- our past and present financial information;
- 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 our common stock may not develop, or if such a market develops, may not be sustained. 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.

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

Price Stabilization, Short Positions and Penalty Bids

In connection with this offering of common stock, the underwriters may engage in stabilizing transactions, overallotment transactions, syndicate covering transactions, penalty bids and purchases to cover positions created by short sales.

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- Stabilizing transactions permit bids to purchase shares of common stock so long as the stabilizing bids do not exceed a specified maximum, and are engaged in for the purpose of preventing or retarding a decline in the market price of the common stock while the offering is in progress.
- Overallotment transactions involve sales by the underwriters of shares of common stock in excess of the number of shares the underwriters are obligated to purchase. This creates a syndicate short position which may be either a covered short position or a naked short position. In a covered short position, the number of shares over-allotted by the underwriters is not greater than the number of shares that they may purchase in the overallotment option. In a naked short position, the number of shares involved is greater than the number of shares in the overallotment option. The underwriters may close out any short position by exercising their overallotment option and/or purchasing shares in the open market.
- Syndicate covering transactions involve purchases of common stock in the open market after the distribution has been completed in order to cover syndicate short positions. In determining the source of shares to close out the short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared with the price at which they may purchase shares through exercise of the overallotment option. If the underwriters sell more shares than could be covered by exercise of the overallotment option and, therefore, have a naked short position, the position can be closed out only by buying shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that after pricing there could be downward pressure on the price of the shares in the open market that could adversely affect investors who purchase in the offering.
- Penalty bids permit the representatives to reclaim a selling concession from a syndicate member when the common stock originally sold by that syndicate member is purchased in stabilizing or syndicate covering transactions to cover syndicate short positions.

These stabilizing transactions, syndicate covering transactions and penalty bids 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 in the open market may be higher than it would otherwise be in the absence of these transactions. Neither we nor the underwriters make any representation or prediction as to the effect that the transactions described above may have on the price of shares of our common stock. These transactions may be effected on The NASDAQ Global Market, in the over-the-counter market or otherwise and, if commenced, may be discontinued at any time.

Lock-Up Agreements

Pursuant to certain "lock-up" agreements, we and our executive officers, directors and stockholders, have agreed, subject to certain exceptions, not to offer, sell, assign, transfer, pledge, contract to sell, or otherwise dispose of or announce the intention to otherwise dispose of, or enter into any swap, hedge or similar agreement or arrangement that transfers, in whole or in part, the economic consequence of ownership of, directly or indirectly, or make any demand or request or exercise any right with respect to the registration of, or file with the SEC a registration statement under the Securities Act relating to, any common stock or securities convertible into or exchangeable or exercisable for any common stock without the prior written consent of Cowen and Company, LLC and Piper Jaffray & Co., for a period of 180 days after the date of the underwriting agreement.

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. The lock-up agreements include customary exceptions.

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Cowen and Company, LLC and Piper Jaffray & Co., in their sole discretion, may release our common stock and other securities subject to the lock-up agreements described above in whole or in part at any time. When determining whether or not to release our common stock and other securities from lock-up agreements, Cowen and Company, LLC and Piper Jaffray & Co. will consider, among other factors, the holder's reasons for requesting the release, the number of shares for which the release is being requested and market conditions at the time of the request. In the event of such a release or waiver for one of our directors or officers, Cowen and Company, LLC and Piper Jaffray & Co. shall provide us with notice of the impending release or waiver at least three business days before the effective date of such release or waiver and we will announce the impending release or waiver by issuing a press release at least two business days before the effective date of the release or waiver.

Electronic Offer, Sale and Distribution of Shares

A prospectus in electronic format may be made available on the websites maintained by one or more of the underwriters or selling group members, if any, participating in this offering and one or more of the underwriters participating in this offering may distribute prospectuses electronically. The representatives may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the underwriters and selling group members that will make internet distributions on the same basis as other allocations. Other than the prospectus in electronic format, the information on these websites is not part of this prospectus or the registration statement of which this prospectus forms a part, has not been approved or endorsed by us or any underwriter in its capacity as underwriter, and should not be relied upon by investors.

Other Relationships

Certain of the underwriters and their affiliates have provided, and may in the future provide, various investment banking, commercial banking and other financial services for us and our affiliates for which they have received, and may in the future receive, customary fees.

Selling Restrictions

No action has been taken in any jurisdiction except the United States that would permit a public offering of our common stock, or the possession, circulation or distribution of this prospectus or any other material relating to us or our common stock in any jurisdiction where action for that purpose is required. Accordingly, the shares may not be offered or sold, directly or indirectly, and neither this prospectus nor any other offering material or advertisements in connection with the shares may be distributed or published, in or from any country or jurisdiction except in compliance with any applicable rules and regulations of any such country or jurisdiction.

Canada

The securities 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 securities 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

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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.

United Kingdom

Each of the underwriters has, separately and not jointly, represented and agreed that:

- it has not made or will not make an offer of the securities to the public in the United Kingdom within the meaning of section 102B of the Financial Services and Markets Act 2000 (as amended), or the FSMA, except to legal entities which are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities or otherwise in circumstances which do not require the publication by us of a prospectus pursuant to the Prospectus Rules of the Financial Services Authority, or FSA;
- it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of section 21 of FSMA) to persons 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 or in circumstances in which section 21 of FSMA does not apply to us; and
- it has complied with and will comply with all applicable provisions of FSMA with respect to anything done by it in relation to the securities in, from or otherwise involving the United Kingdom.

Switzerland

The securities will not be offered, directly or indirectly, to the public in Switzerland and this prospectus does not constitute a public offering prospectus as that term is understood pursuant to article 652a or 1156 of the Swiss Federal Code of Obligations.

Israel

In the State of Israel this prospectus shall not be regarded as an offer to the public to purchase shares of common stock under the Israeli Securities Law, 5728—1968, which requires a prospectus to be published and authorized by the Israel Securities Authority, if it complies with certain provisions of Section 15 of the Israeli Securities Law, 5728—1968, including, *inter alia*, if: (i) the offer is made, distributed or directed to not more than 35 investors, subject to certain conditions (the "Addressed Investors"); or (ii) the offer is made, distributed or directed to certain qualified investors defined in the First Addendum of the Israeli Securities Law, 5728—1968, subject to certain conditions (the "Qualified Investors"). The Qualified Investors shall not be taken into account in the count of the Addressed Investors and may be offered to purchase securities in addition to the 35 Addressed Investors. The company has not and will not take any action that would require it to publish a prospectus in accordance with and subject to the Israeli Securities Law, 5728—1968. We have not and will not distribute this prospectus or make, distribute or direct an offer to subscribe for our common stock to any person within the State of Israel, other than to Qualified Investors and up to 35 Addressed Investors.

Qualified Investors may have to submit written evidence that they meet the definitions set out in of the First Addendum to the Israeli Securities Law, 5728—1968. In particular, we may request, as a

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condition to be offered common stock, that Qualified Investors will each represent, warrant and certify to us and/or to anyone acting on our behalf: (i) that it is an investor falling within one of the categories listed in the First Addendum to the Israeli Securities Law, 5728—1968; (ii) which of the categories listed in the First Addendum to the Israeli Securities Law, 5728—1968 regarding Qualified Investors is applicable to it; (iii) that it will abide by all provisions set forth in the Israeli Securities Law, 5728—1968 and the regulations promulgated thereunder in connection with the offer to be issued common stock; (iv) that the shares of common stock that it will be issued are, subject to exemptions available under the Israeli Securities Law, 5728—1968: (a) for its own account; (b) for investment purposes only; and (c) not issued with a view to resale within the State of Israel, other than in accordance with the provisions of the Israeli Securities Law, 5728—1968; and (v) that it is willing to provide further evidence of its Qualified Investor status. Addressed Investors may have to submit written evidence in respect of their identity and may have to sign and submit a declaration containing, *inter alia*, the Addressed Investor's name, address and passport number or Israeli identification number.

European Economic Area

In relation to each Member State of the European Economic Area, or the EEA, which has implemented the European Prospectus Directive (each, a "Relevant Member State"), an offer of our shares may not be made to the public in a Relevant Member State other than:

- to any legal entity which is a qualified investor, as defined in the European Prospectus Directive;
- to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150 natural or legal persons (other than qualified investors as defined in the European Prospectus Directive), subject to obtaining the prior consent of the relevant dealer or dealers nominated by us for any such offer; or
- in any other circumstances falling within Article 3(2) of the European Prospectus Directive;

provided that no such offer of our shares shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the European Prospectus Directive or supplement prospectus pursuant to Article 16 of the European Prospectus Directive.

For the purposes of this description, the expression an "offer to the public" in relation to the securities 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 securities to be offered so as to enable an investor to decide to purchase or subscribe for the securities, as the expression may be varied in that Relevant Member State by any measure implementing the European Prospectus Directive in that member state, and the expression "European Prospectus Directive" means Directive 2003/71/EC (and amendments hereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State) and includes any relevant implementing measure in each Relevant Member State. The expression 2010 PD Amending Directive means Directive 2010/73/EU.

We have not authorized and do not authorize the making of any offer of securities through any financial intermediary on our behalf, other than offers made by the underwriters and their respective affiliates, with a view to the final placement of the securities as contemplated in this document. Accordingly, no purchaser of the shares, other than the underwriters, is authorized to make any further offer of shares on our behalf or on behalf of the underwriters.

Hong Kong

The contents of this document have not been reviewed or approved by any regulatory authority in Hong Kong. This document does not constitute an offer or invitation to the public in Hong Kong to acquire shares. Accordingly, unless permitted by the securities laws of Hong Kong, no person may issue or have in its possession for the purposes of issue, this document or any advertisement, invitation or

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document relating to the shares, 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 in Hong Kong other than in relation to shares which are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" (as such term is defined in the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) ("SFO") and the subsidiary legislation made thereunder); or in circumstances which do not result in this document being a "prospectus" as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32, Laws of Hong Kong) ("CO"); or which do not constitute an offer or an invitation to the public for the purposes of the SFO or the CO. The offer of the shares is personal to the person to whom this document has been delivered, and a subscription for shares will only be accepted from such person. No person to whom a copy of this document is issued may issue, circulate or distribute this document in Hong Kong, or make or give a copy of this document to any other person. You are advised to exercise caution in relation to the offer. If you are in any doubt about any of the contents of this document, you should obtain independent professional advice.

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 the shares may not be circulated or distributed, nor may the shares 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 pursuant to Section 274 of the Securities and Futures Act, Chapter 289 of Singapore ("SFA"), (ii) to a relevant person (as defined in Section 275(2) of the SFA), 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 shares are subscribed or purchased pursuant to an offer made in reliance on Section 275 of the SFA by a relevant person which is:

- (a) a corporation (which is not an accredited investor) 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 is an accredited investor;

shares, debentures and units of shares, and debentures of that corporation, or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferable for six months after that corporation or that trust has acquired the shares under Section 275 except:

- (1) to an institutional investor or to a relevant person (as defined in Section 275(2) of the SFA), or any person pursuant to Section 275(1A) of the SFA (in the case of that corporation) or Section 276(4)(i)(B) of the SFA (in the case of that trust);
- (2) where no consideration is or will be given for the transfer; or
- (3) where the transfer is by operation of law.

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. The underwriters have been represented in this offering by Cooley LLP.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements at December 31, 2013 and 2014, and for each of the years then ended, as set forth in their report. We have included our consolidated financial statements in the prospectus and elsewhere in the registration statement in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

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 a 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. For further information with respect to us and our common stock, we refer you to the registration statement and to the exhibits and schedules to the registration statement. Statements contained in this prospectus about the contents of any contract, agreement or other document 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 to such contract, agreement or document.

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, DC 20549. You can request copies of the registration statement by writing to the Public Reference Section of the SEC 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 the closing of this offering, we will be subject to the information reporting requirements of the Exchange Act, and we will file reports, proxy statements and other information with the SEC. We plan to fulfill our obligations with respect to such requirements by filing periodic reports and other information with the SEC. We intend to furnish our stockholders with annual reports containing consolidated financial statements certified by an independent registered public accounting firm. We also maintain a website at www.syros.com. Our website is not a part of this prospectus.

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Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders of
Syros Pharmaceuticals, Inc.

We have audited the accompanying consolidated balance sheets of Syros Pharmaceuticals, Inc. (the "Company") as of December 31, 2013 and 2014, and the related consolidated statements of operations and comprehensive loss, convertible preferred stock and stockholders' (deficit) equity, and cash flows for each of the years then ended. 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 in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also 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.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Syros Pharmaceuticals, Inc. at December 31, 2013 and 2014, and the consolidated results of its operations and its cash flows for each of the years then ended, in conformity with U.S. generally accepted accounting principles.

Boston, Massachusetts
November 20, 2015

/s/ Ernst & Young LLP

Syros Pharmaceuticals, Inc.

Consolidated Balance Sheets

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

	<u>December 31,</u>		<u>September 30, 2015</u>	
	<u>2013</u>	<u>2014</u>	<u>Actual</u>	<u>Pro Forma</u>
	(unaudited)			
Assets				
Current assets:				
Cash and cash equivalents	\$ 3,801	\$ 60,393	\$ 44,985	\$ 84,817
Prepaid expenses and other current assets	112	150	303	303
Total current assets	3,913	60,543	45,288	85,120
Property and equipment, net	938	881	4,061	4,061
Other long term assets	—	—	210	210
Restricted cash	70	70	483	483
Total assets	<u>\$ 4,921</u>	<u>\$ 61,494</u>	<u>\$ 50,042</u>	<u>\$ 89,874</u>
Liabilities, convertible preferred stock and stockholders' (deficit) equity				
Current liabilities:				
Accounts payable	\$ 594	\$ 928	\$ 1,649	\$ 1,649
Accrued expenses	280	287	2,492	2,492
Deferred rent, current portion	36	37	215	215
Capital lease obligations, current portion	—	—	111	111
Total current liabilities	910	1,252	4,467	4,467
Deferred rent, net of current portion	36	—	1,496	1,496
Restricted stock liability, net of current portion	2	1	—	—
Capital lease obligations, net of current portion	—	—	246	246
Commitments and contingencies (Note 8)				
Series A convertible preferred stock, \$0.001 par value; 32,000,000 shares authorized at December 31, 2013 and 30,350,000 shares authorized at December 31, 2014 and September 30, 2015 (unaudited), 14,600,000 shares issued and outstanding at December 31, 2013, 30,350,000 shares issued and outstanding at December 31, 2014 and September 30, 2015 (unaudited) and no shares issued and outstanding at September 30, 2015 (pro forma) (unaudited); (aggregated liquidation preference of \$31,238 and \$32,544 at December 31, 2014 and September 30, 2015 (unaudited), respectively)				
	13,266	29,015	29,015	—
Series B convertible preferred stock, \$0.001 par value; no shares authorized, issued and outstanding at December 31, 2013, 16,893,931 shares authorized, issued and outstanding at December 31, 2014 and September 30, 2015 (unaudited) and no shares issued and outstanding at September 30, 2015 (pro forma) (unaudited); (aggregated liquidation preference of \$53,846 and \$56,230 at December 31, 2014 and September 30, 2015 (unaudited), respectively)				
	—	52,998	52,998	—
Stockholders' (deficit) equity:				
Preferred stock, \$0.001 par value; no shares authorized or outstanding actual; 10,000,000 shares authorized, no shares issued and outstanding pro forma and pro forma as adjusted				
	—	—		
Common stock, \$0.001 par value; 47,000,000 shares authorized at December 31, 2013 and 64,571,908 shares authorized at December 31, 2014 and September 30, 2015 (unaudited), 5,173,782, 6,150,065 and 8,384,486 shares issued and outstanding at December 31, 2013 and 2014 and September 30, 2015 (unaudited), respectively, and 68,542,567 shares issued and outstanding at September 30, 2015 (pro forma) (unaudited)				
	5	6	8	69
Additional paid-in capital	966	1,917	4,636	127,068
Accumulated deficit	(10,264)	(23,695)	(42,824)	(43,472)
Total stockholders' (deficit) equity	(9,293)	(21,772)	(38,180)	83,665
Total liabilities, convertible preferred stock and stockholders' (deficit) equity	<u>\$ 4,921</u>	<u>\$ 61,494</u>	<u>\$ 50,042</u>	<u>\$ 89,874</u>

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

Syros Pharmaceuticals, Inc.**Consolidated Statements of Operations and Comprehensive Loss**

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

	Year Ended December 31,		Nine Months Ended September 30,	
	2013	2014	2014	2015
Revenue	\$ —	\$ —	\$ —	\$ 317
Operating expenses:				
Research and development	6,266	10,923	7,901	16,030
General and administrative	2,367	2,512	1,843	3,418
Total operating expenses	8,633	13,435	9,744	19,448
Loss from operations	(8,633)	(13,435)	(9,744)	(19,131)
Other income (expense), net	(32)	4	2	2
Net loss and comprehensive loss	\$ (8,665)	\$ (13,431)	\$ (9,742)	\$ (19,129)
Accrued dividends on preferred stock	(594)	(2,211)	(1,074)	(3,690)
Net loss applicable to common stockholders	\$ (9,259)	\$ (15,642)	\$ (10,816)	\$ (22,819)
Net loss per share applicable to common stockholders—basic and diluted	\$ (2.25)	\$ (2.74)	\$ (1.93)	\$ (3.26)
Weighted-average number of common shares used in net loss per share applicable to common stockholders—basic and diluted	4,110,716	5,718,844	5,599,543	6,997,532
Pro forma net loss per share—basic and diluted (unaudited)		\$ (0.37)		\$ (0.36)
Weighted-average number of common shares used in pro forma net loss per share—basic and diluted (unaudited)		35,901,743		54,250,987

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

Syros Pharmaceuticals, Inc.

Consolidated Statements of Convertible Preferred Stock and Stockholders' (Deficit) Equity

(amounts in thousands except share data)

	Series A Convertible Preferred Stock		Series B Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Deficit	Stockholders' (Deficit) Equity
	# of Shares	Amount	# of Shares	Amount	# of Shares	Amount			
Balance at December 31, 2012	2,500,000	\$ 1,208	—	\$ —	2,400,000	\$ 2	\$ 123	\$ (1,599)	\$ (1,474)
Issuance of Series A convertible preferred stock, net of issuance costs of \$42	12,100,000	12,058	—	—	—	—	—	—	—
Issuance of common stock	—	—	—	—	643,782	1	22	—	23
Exercise of stock options and vesting of restricted stock awards	—	—	—	—	2,130,000	2	—	—	2
Stock-based compensation expense	—	—	—	—	—	—	821	—	821
Net loss	—	—	—	—	—	—	—	(8,665)	(8,665)
Balance at December 31, 2013	14,600,000	13,266	—	—	5,173,782	5	966	(10,264)	(9,293)
Issuance of Series A convertible preferred stock, net of issuance costs of \$1	15,750,000	15,749	—	—	—	—	—	—	—
Issuance of Series B convertible preferred stock, net of issuance costs of \$152	—	—	16,893,931	52,998	—	—	—	—	—
Exercise of stock options and vesting of restricted stock awards	—	—	—	—	976,283	1	14	—	15
Stock-based compensation expense	—	—	—	—	—	—	937	—	937
Net loss	—	—	—	—	—	—	—	(13,431)	(13,431)
Balance at December 31, 2014	30,350,000	29,015	16,893,931	52,998	6,150,065	6	1,917	(23,695)	(21,772)
Exercise of stock options and vesting of restricted stock awards (unaudited)	—	—	—	—	2,234,421	2	334	—	336
Stock-based compensation expense (unaudited)	—	—	—	—	—	—	2,385	—	2,385
Net loss (unaudited)	—	—	—	—	—	—	—	(19,129)	(19,129)
Balance at September 30, 2015 (unaudited)	<u>30,350,000</u>	<u>29,015</u>	<u>16,893,931</u>	<u>52,998</u>	<u>8,384,486</u>	<u>8</u>	<u>4,636</u>	<u>(42,824)</u>	<u>(38,180)</u>
Issuance of Series B convertible preferred stock, net of issuance costs of \$168	—	—	12,714,150	39,832	—	—	—	—	—
Conversion of Series A convertible preferred stock into common stock (unaudited)	(30,350,000)	(29,015)	—	—	30,350,000	30	28,985	—	29,015
Conversion of Series B convertible preferred stock into common stock (unaudited)	—	—	(29,608,081)	(92,830)	29,608,081	31	92,799	—	92,830
Stock-based compensation expense for stock-based awards that vest upon initial public offering	—	—	—	—	200,000	—	648	(648)	—
Pro forma balance at September 30, 2015 (unaudited)	<u>—</u>	<u>\$ —</u>	<u>—</u>	<u>\$ —</u>	<u>68,542,567</u>	<u>\$ 69</u>	<u>\$ 127,068</u>	<u>\$ (43,472)</u>	<u>\$ 83,665</u>

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

Syros Pharmaceuticals, Inc.

Consolidated Statements of Cash Flows

(amounts in thousands)

	Year Ended December 31,		Nine Months Ended September 30,	
	2013	2014	2014	2015
	(unaudited)			
Operating Activities				
Net loss	\$ (8,665)	\$ (13,431)	\$ (9,742)	\$ (19,129)
Adjustments to reconcile net loss to net cash used in operating activities:				
Depreciation	170	258	187	373
Non-cash interest expense	33	—	—	—
Stock-based compensation expense	821	937	587	2,385
Changes in operating assets and liabilities:				
Prepaid expenses and other current assets	(89)	(38)	(12)	(153)
Other long term assets	—	—	—	(210)
Restricted cash	(20)	—	—	(413)
Accounts payable	361	334	88	721
Accrued expenses	136	7	451	1,536
Deferred rent and lease incentive	59	(36)	(25)	61
Net cash used in operating activities	<u>(7,194)</u>	<u>(11,969)</u>	<u>(8,466)</u>	<u>(14,829)</u>
Investing Activities				
Purchases of property and equipment	(878)	(201)	(187)	(883)
Net cash used in investing activities	<u>(878)</u>	<u>(201)</u>	<u>(187)</u>	<u>(883)</u>
Financing Activities				
Payments of capital lease obligations	—	—	—	(32)
Proceeds from issuance of convertible preferred stock, net of issuance costs				
	10,021	68,747	15,749	—
Proceeds from issuance of common stock	24	15	15	336
Net cash provided by financing activities	<u>10,045</u>	<u>68,762</u>	<u>15,764</u>	<u>304</u>
Increase (decrease) in cash and cash equivalents	1,973	56,592	7,111	(15,408)
Cash and cash equivalents				
Beginning of period	1,828	3,801	3,801	60,393
End of period	<u>\$ 3,801</u>	<u>\$ 60,393</u>	<u>\$ 10,912</u>	<u>\$ 44,985</u>
Supplemental disclosure of cash flow information:				
Cash paid for interest	\$ —	\$ —	\$ —	\$ 12
Non-cash investing and financing activities				
Issuance of Series A convertible preferred stock through conversion of convertible notes	\$ 2,036	\$ —	\$ —	\$ —
Property and equipment received but unpaid as of period end	\$ —	\$ —	\$ —	\$ 669
Assets acquired under capital lease	\$ —	\$ —	\$ —	\$ 389
Assets acquired through lease incentive	\$ —	\$ —	\$ —	\$ 1,612

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

Syros Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements

**(Information as of September 30, 2015 and for the nine months ended
September 30, 2014 and 2015 is unaudited)**

1. Nature of Business

Syros Pharmaceuticals, Inc. (the "Company"), formerly known as LS22, Inc., a Delaware corporation formed in November 2011, is a biopharmaceutical company seeking to discover and develop medicines that control the expression of genes with the aim of treating cancer and other serious diseases. The Company has built a proprietary platform to identify crucial genes that become dysregulated in diseased cells in order to create medicines that return cells to a non-diseased state.

The Company is subject to a number of risks similar to those of other early stage companies, including dependence on key individuals; risks inherent in the development and commercialization of medicines to treat human disease; competition from other companies, many of which are larger and better capitalized; risks relating to obtaining and maintaining necessary intellectual property protection; and the need to obtain adequate additional financing to fund the development of its product candidates. If the Company is unable to raise capital when needed or on attractive terms, it would be forced to delay, reduce, eliminate or out-license certain of its research and development programs or future commercialization efforts.

The Company has an accumulated deficit as of September 30, 2015 of approximately \$42.8 million and will require substantial additional capital for research and product development. The future success of the Company is dependent upon its ability to develop its product candidates, and ultimately upon its ability to attain profitable operations. At September 30, 2015, the Company believes that its cash and cash equivalents, totaling \$45.0 million, will be sufficient to allow the Company to fund its current operating plan for a period of at least the next 12 months. Thereafter, the Company will be required to obtain additional funding and intends to pursue a public offering of its common stock to fund future operations. However, if the Company is unable to complete a sufficient public offering in a timely manner it would need to pursue other financing alternatives, such as private financing of debt or equity or collaboration agreements. There can be no assurances, however, that the current operating plan will be achieved or that additional funding will be available on terms acceptable to the Company, or at all.

2. Summary of Significant Accounting Policies

The following is a summary of significant accounting policies followed in the preparation of these financial statements.

Basis of Presentation

The Company's financial statements have been prepared in accordance with accounting principles generally accepted in the United States ("U.S. GAAP") and include all adjustments necessary for the fair presentation of the Company's financial position and results of its operations for the periods presented. Any reference in these notes to applicable guidance is meant to refer to the authoritative United States generally accepted accounting principles as found in the Accounting Standards Codification ("ASC") and Accounting Standards Updates ("ASU") of the Financial Accounting Standards Board ("FASB").

Principles of Consolidation

The accompanying consolidated financial statements include the accounts of Syros Pharmaceuticals, Inc. and its wholly owned subsidiary, Syros Securities Corporation, which is a

Syros Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

**(Information as of September 30, 2015 and for the nine months ended
September 30, 2014 and 2015 is unaudited)**

2. Summary of Significant Accounting Policies (Continued)

Massachusetts subsidiary formed by the Company in December 2014 to exclusively engage in buying, selling and holding securities on its own behalf. All intercompany transactions and balances have been eliminated.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts in the financial statements and accompanying notes. Management considers many factors in selecting appropriate financial accounting policies and in developing the estimates and assumptions that are used in the preparation of the financial statements. Management must apply significant judgment in this process. In addition, other factors may affect estimates, which include, but are not limited to, expected business and operational changes, sensitivity and volatility associated with the assumptions used in developing estimates and whether historical trends are expected to be representative of future trends. Management's estimation process often may yield a range of potentially reasonable estimates and management must select an amount that falls within that range of reasonable estimates. On an ongoing basis, the Company's management evaluates its estimates, which include, but are not limited to, estimates related to revenue recognition, stock-based compensation expense, including estimating the fair value of the Company's common stock (the "Common Stock"), accrued expenses and income taxes. Actual results may differ from those estimates or assumptions.

Unaudited Interim Financial Information

The unaudited interim financial statements as of September 30, 2015 and for the nine months ended September 30, 2014 and 2015 and the related interim information contained within the notes to the financial statements are unaudited. The interim unaudited financial statements have been prepared on the same basis as the annual audited financial statements and, in the opinion of management, reflect all adjustments, which include only normal recurring adjustments, necessary for the fair presentation of the Company's consolidated financial position as of September 30, 2015, and the consolidated statements of operations and comprehensive loss and its cash flows for the nine months ended September 30, 2014 and 2015. The financial data and other information disclosed in these notes as of and for the nine months ended September 30, 2014 and 2015 are unaudited. The results for the nine months ended September 30, 2015 are not necessarily indicative of results to be expected for the year ending December 31, 2015, or any other future annual or interim periods.

Unaudited Pro Forma Financial Information

Upon the closing of a qualified initial public offering, all of the Company's outstanding convertible preferred stock will automatically convert into Common Stock and certain of the Company's restricted stock and performance-based stock option awards will vest. The accompanying unaudited pro forma consolidated balance sheet and statement of convertible preferred stock and stockholders' (deficit) equity as of September 30, 2015 assumes (1) the completion of the Company's Series B preferred stock financing in January 2016 in which it issued and sold an aggregate of 12,714,150 shares of Series B Preferred Stock for an aggregate purchase price of \$40 million, (2) the conversion of all outstanding convertible preferred stock, including the shares of Series B preferred stock that the Company issued in

Syros Pharmaceuticals, Inc.**Notes to Consolidated Financial Statements (Continued)**

**(Information as of September 30, 2015 and for the nine months ended
September 30, 2014 and 2015 is unaudited)**

2. Summary of Significant Accounting Policies (Continued)

January 2016 into an aggregate of 59,958,081 shares of common stock, and (3) the vesting of certain restricted stock and performance-based stock option awards as if this proposed initial public offering was completed on September 30, 2015. In the accompanying consolidated statements of operations and comprehensive loss, unaudited pro forma basic and diluted net loss per share attributable to common stockholders has been prepared to give effect to the automatic conversion of all outstanding shares of convertible preferred stock and vesting of certain restricted stock and performance-based stock option awards as if this proposed initial public offering had occurred on the later of the beginning of the reporting period or the issuance date of the convertible preferred stock or performance-based award. Accordingly, 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 excludes the effects of dividends on preferred stock and includes additional compensation expense related to the vesting of certain of the Company's restricted stock and performance-based stock option awards.

Segment Information

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker, or decision making group, in making decisions on how to allocate resources and assess performance. The Company's chief operating decision maker is the Chief Executive Officer. The Company and the chief operating decision maker view the Company's operations and manage its business in one operating segment. The Company operates only in the United States.

Comprehensive Loss

Comprehensive loss is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. For the years ended December 31, 2013 and 2014 and for the nine months ended September 30, 2014 and 2015, comprehensive loss was equal to net loss.

Cash and Cash Equivalents

The Company considers all highly liquid instruments that have original maturities of three months or less when acquired to be cash equivalents. Cash equivalents, which consist of money market funds that invest in U.S. Treasury obligations, are stated at fair value. The Company maintains its bank accounts at one major financial institution. Cash and cash equivalents consist of the following (in thousands):

	December 31,		September 30, 2015
	2013	2014	
Cash and cash equivalents:			
Cash	\$ 155	\$ 54,981	\$ 6
Money market funds	3,646	5,412	44,979
Total	<u>\$ 3,801</u>	<u>\$ 60,393</u>	<u>\$ 44,985</u>

Syros Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

**(Information as of September 30, 2015 and for the nine months ended
September 30, 2014 and 2015 is unaudited)**

2. Summary of Significant Accounting Policies (Continued)

Off-Balance Sheet Risk and Concentrations of Credit Risk

The Company has no financial instruments with off-balance sheet risk, such as foreign exchange contracts, option contracts, or other foreign hedging arrangements. Financial instruments that potentially subject the Company to concentrations of credit risk primarily consist of cash and cash equivalents. The Company's cash is held in accounts at a financial institution that may exceed federally insured limits. The Company has not experienced any credit losses in such accounts and does not believe it is exposed to any significant credit risk on these funds.

Fair Value of Financial Instruments

ASC Topic 820, *Fair Value Measurement* ("ASC 820"), establishes a fair value hierarchy for instruments measured at fair value that distinguished between assumptions based on market data (observable inputs) and the Company's own assumptions (unobservable inputs). Observable inputs are inputs that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumption about the inputs that market participants would use in pricing the asset or liability, and are developed based on the best information available in the circumstances.

ASC 820 identified fair value as the exchange price, or exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As a basis for considering market participant assumptions in fair value measurements, ASC 820 established a three-tier fair value hierarchy that distinguishes between the following:

Level 1—Quoted market prices (unadjusted) in active markets for identical assets or liabilities.

Level 2—Inputs other than quoted prices included within Level 1 that are either directly or indirectly observable, such as quoted market prices, interest rates and yield curves.

Level 3—Unobservable inputs developed using estimates or assumptions developed by the Company, which reflect those that a market participant would use.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized as Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

The carrying amounts reflected in the balance sheets for cash and cash equivalents, prepaid expenses, other current assets, accounts payable and accrued expenses approximate their fair values, due to their short-term nature.

Property and Equipment

Property and equipment consists of laboratory equipment, computer equipment, furniture and fixtures and leasehold improvements, all of which are stated at cost, less accumulated depreciation. Expenditures for maintenance and repairs that do not improve or extend the lives of the respective

Syros Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

**(Information as of September 30, 2015 and for the nine months ended
September 30, 2014 and 2015 is unaudited)**

2. Summary of Significant Accounting Policies (Continued)

assets are recorded to expense as incurred. Major betterments are capitalized as additions to property and equipment. Depreciation is recognized over the estimated useful lives of the assets using the straight-line method.

Construction-in-progress is stated at cost, which relates to the cost of research equipment not yet placed into service. No depreciation expense is recorded on construction-in-progress until such time as the relevant assets are completed and put into use.

Impairment of Long-Lived Assets

The Company continually evaluates long-lived assets for potential impairment when events or changes in circumstances indicate the carrying value of the assets may not be recoverable. Recoverability is measured by comparing the book values of the assets to the expected future net undiscounted cash flows that the assets are expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the book values of the assets exceed their fair value. The Company has not recognized any impairment losses from inception through September 30, 2015.

Other Long Term Assets

Other long term assets consists of deferred issuance costs, which includes direct incremental legal and accounting fees relating to the Company's proposed initial public offering of common stock. Deferred issuance costs are capitalized as incurred. The deferred issuance costs will be offset against proceeds upon the consummation of the offering. In the event the offering is terminated, deferred issuance costs will be expensed. Approximately \$210,000 of deferred issuance costs were incurred and capitalized as of September 30, 2015. No amounts were capitalized as of December 31, 2014 and 2013. Such costs are included within non-current assets on the balance sheet.

Revenue Recognition

To date, the Company's only source of revenue has been the research agreement with a multinational pharmaceutical company (Note 13).

The Company recognizes revenue in accordance with ASC Topic 605, *Revenue Recognition* ("ASC 605"). Accordingly, revenue is recognized when all of the following criteria are met:

- Persuasive evidence of an arrangement exists;
- Delivery has occurred or services have been rendered;
- The seller's price to the buyer is fixed or determinable; and
- Collectability is reasonably assured.

Amounts received prior to satisfying the revenue recognition criteria are recognized as deferred revenue in the Company's consolidated balance sheets. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified in current liabilities. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion.

Syros Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

**(Information as of September 30, 2015 and for the nine months ended
September 30, 2014 and 2015 is unaudited)**

2. Summary of Significant Accounting Policies (Continued)

The Company analyzes arrangements with multiple deliverables based on the guidance in ASC Topic 605-25, *Revenue Recognition—Multiple Element Arrangements* ("ASC 605-25"). Pursuant to the guidance in ASC 605-25, the Company evaluates multiple element arrangements to determine (1) the deliverables included in the arrangement and (2) whether the individual deliverables represent separate units of accounting or whether they must be accounted for as a combined unit of accounting. This evaluation involves subjective determinations and requires management to make judgements about the individual deliverables and whether such deliverables are separate from other aspects of the contractual relationship. Deliverables are considered separate units of accounting provided that: (i) the delivered item(s) has value to the customer on a standalone basis and (ii) if the arrangement includes a general right of return relative to the delivered item(s), delivery or performance of the undelivered item(s) is considered probable and substantially within control of the Company. The Company's research agreement contains a single unit of accounting.

The Company recognizes arrangement consideration allocated to each unit of accounting when all of the revenue recognition criteria in ASC 605 are satisfied for that particular unit of accounting. In the event that a deliverable does not represent a separate unit of accounting, the Company would recognize revenue from the combined unit of accounting over the contractual or estimated performance period for the undelivered items, which is typically the term of its research and development obligations. If there is no discernible pattern of performance or objectively measurable performance measures do not exist, then the Company would recognize revenue under the arrangement on a straight-line basis over the period it expects to complete its performance obligations or upon completion when the final act is of such significance to the overall arrangement that performance has not substantively occurred until the completion of that act. Conversely, if the pattern of performance over which the service is provided to the customer can be determined and objectively measurable performance measures exist, then the Company would recognize revenue under the arrangement using the proportional performance method.

The Company recognizes service revenue under its research agreement based upon the completed performance method of revenue recognition as it is unable to reasonably estimate the period of performance of the services and the delivery of the final study report is significant to the arrangement.

Research and Development

Expenditures relating to research and development are expensed in the period incurred. Research and development expenses consist of both internal and external costs associated with the development of the Company's gene control platform and gene control medicines, with initial focus on cancer. Research and development costs include salaries and benefits, materials and supplies, external research and preclinical expenses, stock-based compensation expense and facilities costs. Facilities costs primarily include the allocation of rent, utilities and depreciation.

In certain circumstances, the Company is required to make nonrefundable advance payments to vendors for goods or services that will be received in the future for use in research and development activities. In such circumstances, the nonrefundable advance payments are deferred and capitalized, even when there is no alternative future use for the research and development, until related goods or services are provided.

Syros Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

**(Information as of September 30, 2015 and for the nine months ended
September 30, 2014 and 2015 is unaudited)**

2. Summary of Significant Accounting Policies (Continued)

The Company records accruals for estimated ongoing research costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes progress of the work being performed, including the phase or completion of the event, invoices received and costs. Significant judgements and estimates may be made in determining the accrued balances at the end of any reporting period. Actual results could differ from the Company's estimates.

The Company may in-license the rights to develop and commercialize product candidates. For each in-license transaction the Company evaluates whether it has acquired processes or activities along with inputs that would be sufficient to constitute a "business" as defined under U.S. GAAP. A "business" as defined under U.S. GAAP consists of inputs and processes applied to those inputs that have the ability to create outputs. Although businesses usually have outputs, outputs are not required for an integrated set of activities to qualify as a business. When the Company determines that it has not acquired sufficient processes or activities to constitute a business, any up-front payments, as well as milestone payments, are immediately expensed as research and development in the period in which they are achieved.

Stock-Based Compensation Expense

The Company accounts for its stock-based compensation awards in accordance with ASC Topic 718, *Compensation—Stock Compensation* ("ASC 718"). ASC 718 requires all stock-based payments to employees and directors, including grants of restricted stock and stock options, to be recognized as expense in the consolidated statements of operations based on their grant date fair values. Grants of restricted stock and stock options to other service providers, referred to as non-employees, are required to be recognized as expense in the consolidated statements of operations based on their vesting date fair values. The Company estimates the fair value of options granted using the Black-Scholes option-pricing model. The Company uses the value of its common stock to determine the fair value of restricted stock awards.

The use of the Black-Scholes option-pricing model requires management to apply significant judgement and make estimates, including:

Expected volatility—Since the Company is privately held as of the date of these financial statements, it does not have relevant historical data to support its expected volatility. As such, the Company has used an average of expected volatility based on the volatilities of a representative group of publicly traded biopharmaceutical companies with similar characteristics to the Company, including stage of product development, length of trading history and life science industry focus. The expected volatility was determined using an average of the historical volatilities of the representative group of companies for a period equal to the expected term of the option grant. The Company intends to consistently apply this process using the same representative companies until a sufficient amount of historical information regarding the volatility of the Company's own share price becomes available or until circumstances change, such that the identified entities are no longer representative companies. In the latter case, more suitable, similar entities whose share prices are publicly available would be utilized in the calculation.

Risk-free interest rate—The risk-free interest rate is based on the U.S. Treasury yield curve in effect at the time of grant commensurate with the expected life assumption.

Syros Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

**(Information as of September 30, 2015 and for the nine months ended
September 30, 2014 and 2015 is unaudited)**

2. Summary of Significant Accounting Policies (Continued)

Expected term—The Company uses the "simplified method" as prescribed by the Securities and Exchange Commission ("SEC") Staff Accounting Bulletin No. 107, *Share-Based Payment* to estimate the expected term of stock option grants made to employees. Under this approach, the weighted-average expected life is presumed to be the average of the contractual term (ten years) and the vesting term (generally four years) of the Company's stock options, taking into consideration multiple vesting tranches. The Company utilizes this method as the Company has insufficient historical information regarding stock option exercises to provide a basis for an estimate. For options granted to non-employees, the Company utilizes the contractual term of the arrangement as the basis for the expected term assumption.

Fair value of the underlying common shares—The fair value of the underlying common shares was determined using the option-pricing method, or OPM or a hybrid of the probability-weighted expected return method, or PWERM, and the OPM, and was approved by its board of directors.

Dividends—The Company has never paid, and does not anticipate paying, any cash dividends in the foreseeable future, and therefore uses an expected dividend yield of zero.

The amount of stock-based compensation expense recognized during a period is based on the fair value of the portion of the awards that are ultimately expected to vest. Forfeitures are estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. The term "forfeitures" is distinct from "cancellations" or "expirations" and represents only the unvested portion of the surrendered option. The Company evaluates its forfeiture rate at each reporting period. Ultimately, the actual expense recognized over the vesting period will be for only those options that vest.

The Company expenses the fair value of its stock-based awards to employees on a straight-line basis over the associated service period, which is generally the vesting period. For stock-based awards granted to consultants and non-employees, compensation expense is recognized over the period during which services are rendered by such consultants and non-employees until completed. At the end of each financial reporting period prior to completion of the service, the fair value of these awards is remeasured using the then-current fair value of such awards.

For stock-based awards that contain performance-based milestones, the Company records stock-based compensation expense in accordance with the accelerated attribution model. Management evaluates when the achievement of a performance-based milestone is probable based on the expected satisfaction of the performance conditions as of the reporting date. For certain of the Company's performance-based awards, notwithstanding any vesting in accordance with the achievement of performance-based milestones, such awards vest in full on the sixth anniversary of the vesting commencement date.

Income Taxes

The Company accounts for income taxes in accordance with ASC Topic 740, *Income Taxes* ("ASC 740"). The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the Company's financial statements or tax returns. Under this method, deferred tax assets and liabilities are determined based on differences between the

Syros Pharmaceuticals, Inc.**Notes to Consolidated Financial Statements (Continued)**

**(Information as of September 30, 2015 and for the nine months ended
September 30, 2014 and 2015 is unaudited)**

2. Summary of Significant Accounting Policies (Continued)

financial statement carrying amounts and the tax bases of the assets and liabilities using the enacted tax rates in effect in the years in which the differences are expected to reverse. A valuation allowance against deferred tax assets is recorded if, based on the weight of the available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

The Company accounts for uncertain tax positions using a more-likely-than-not threshold for recognizing and resolving uncertain tax positions. The evaluation of uncertain tax positions is based on factors including, but not limited to, changes in the law, the measurement of tax positions taken or expected to be taken in tax returns, the effective settlement of matters subject to audit, new audit activity, and changes in facts or circumstances related to a tax position.

Net Loss per Share and Unaudited Pro Forma Net Loss per Share

Basic net loss per share applicable to common stockholders is calculated by dividing net loss applicable to common stockholders by the weighted average shares outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share applicable to common stockholders is calculated by adjusting the weighted average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period, determined using the treasury-stock method and the if-converted method. For purposes of the diluted net loss per share applicable to common stockholders calculation, convertible preferred stock, stock options, and unvested restricted stock are considered to be common stock equivalents but are excluded from the calculation of diluted net loss per share applicable to common stockholders, as their effect would be anti-dilutive; therefore, basic and diluted net loss per share applicable to common stockholders were the same for all periods presented.

The following common stock equivalents were excluded from the calculation of diluted net loss per share applicable to common stockholders for the periods indicated because including them would have had an anti-dilutive effect.

	<u>As of December 31,</u>		<u>As of September 30,</u>	
	<u>2013</u>	<u>2014</u>	<u>2014</u>	<u>2015</u>
Convertible preferred stock	14,600,000	47,243,931	30,350,000	47,243,931
Outstanding stock options	3,985,851	4,987,881	4,646,191	7,088,929
Unvested restricted common stock	3,154,931	2,233,283	2,479,931	1,243,296
	<u>21,740,782</u>	<u>54,465,095</u>	<u>37,476,122</u>	<u>55,576,156</u>

Unaudited pro forma net loss per share applicable to common stockholders is computed using the weighted-average number of common shares outstanding after giving effect to the conversion of all convertible preferred stock into shares of common stock and the vesting of certain restricted stock awards, which occurs upon the closing of the initial public offering, as if such conversion or vesting had occurred at the beginning of the period presented, or the date of original issuance, if later. Accordingly, the pro forma basic and diluted net loss per share applicable to common stockholders does not include the effects of the cumulative preferred stock dividends and includes compensation expense for certain restricted stock and performance-based stock option awards with vesting contingent upon an initial public offering of the Company's common stock. Shares to be sold in the initial public offering are

Syros Pharmaceuticals, Inc.**Notes to Consolidated Financial Statements (Continued)**

**(Information as of September 30, 2015 and for the nine months ended
September 30, 2014 and 2015 is unaudited)**

2. Summary of Significant Accounting Policies (Continued)

excluded from the unaudited pro forma basic and diluted loss per share applicable to common stockholders calculations.

Unaudited pro forma net loss per share applicable to common stockholders is computed as follows (in thousands except for share and per share information):

	Year Ended December 31, 2014	Nine Months Ended September 30, 2015
Numerator:		
Net loss applicable to common stockholders	\$ (15,642)	\$ (22,819)
Plus: Accrued dividends on preferred stock	2,211	3,690
Net loss	(13,431)	(19,129)
Stock-based compensation expense for stock-based awards with vesting contingent upon initial public offering	—	(648)
Pro forma net loss	<u>\$ (13,431)</u>	<u>\$ (19,777)</u>
Denominator:		
Weighted-average number of common shares used in net loss per share applicable to common stockholders—basic and diluted	5,718,844	6,997,532
Pro forma adjustment to reflect assumed conversion of convertible preferred stock	30,182,899	47,243,931
Pro forma adjustment to reflect shares outstanding as a result of restricted stock awards that vest upon initial public offering	—	9,524
Weighted-average number of common shares used in pro forma net loss per share—basic and diluted	<u>35,901,743</u>	<u>54,250,987</u>
Pro forma basic and diluted net loss per share	<u>\$ (0.37)</u>	<u>\$ (0.36)</u>

The 12,714,150 shares of Series B Preferred Stock issued in January 2016 are not reflected in the weighted-average number of common shares outstanding because the issuance of these securities occurred after September 30, 2015.

Recent Accounting Pronouncements

In May 2014, the FASB issued ASU No. 2014-09, *Revenue From Contracts With Customers* ("ASU 2014-09"). ASU 2014-09 amends ASC 605, *Revenue Recognition*, by outlining a single comprehensive model for entities to use in accounting for revenue arising from contracts with customers. ASU 2014-09 will be effective for the Company for interim and annual periods beginning after December 15, 2017. The Company is evaluating the impact that this ASU may have on its financial statements, if any.

Syros Pharmaceuticals, Inc.**Notes to Consolidated Financial Statements (Continued)**

**(Information as of September 30, 2015 and for the nine months ended
September 30, 2014 and 2015 is unaudited)**

2. Summary of Significant Accounting Policies (Continued)

In June 2014, the FASB issued ASU 2014-10, *Development Stage Entities* (Topic 915) ("ASU 2014-10"), which removes the definition of a development stage entity from the ASC, thereby removing the financial reporting distinction between development stage entities and other reporting entities. Accordingly, ASU 2014-10 eliminates the requirements for development stage entities to (1) present inception-to-date information in the statements of operations, cash flows and shareholders' equity, (2) label financial statements as those of a development stage entity, (3) disclose a description of the development stage activities in which the entity is engaged and (4) disclose in the first year in which the entity is no longer a development stage entity that in prior years it had been in the development stage. ASU 2014-10 is effective for public business entities for annual periods beginning after December 15, 2014, with early adoption permitted. The Company early adopted the provisions of ASU 2014-10 in these financial statements.

In August 2014, the FASB issued ASU No. 2014-15, *Presentation of Financial Statements—Going Concern* ("ASU 2014-15") which provides new guidance on management's responsibility in evaluating whether or not there is substantial doubt about a company's ability to continue as a going concern within one year from the date the financial statements are issued each reporting period. ASU 2014-15 is effective for annual periods ending after December 15, 2016. Early adoption is permitted. The Company is in the process of evaluating the new guidance and determining the expected effect on its financial statements.

3. Fair Value Measurements

Assets and liabilities measured at fair value on a recurring basis are as follows (in thousands):

<u>Description</u>	<u>December 31, 2013</u>	<u>Active Markets (Level 1)</u>	<u>Observable Inputs (Level 2)</u>	<u>Unobservable Inputs (Level 3)</u>
Money market funds, included in cash equivalents	\$ 3,646	\$ 3,646	\$ —	\$ —

<u>Description</u>	<u>December 31, 2014</u>	<u>Active Markets (Level 1)</u>	<u>Observable Inputs (Level 2)</u>	<u>Unobservable Inputs (Level 3)</u>
Money market funds, included in cash equivalents	\$ 5,412	\$ 5,412	\$ —	\$ —

<u>Description</u>	<u>September 30, 2015</u>	<u>Active Markets (Level 1)</u>	<u>Observable Inputs (Level 2)</u>	<u>Unobservable Inputs (Level 3)</u>
Money market funds, included in cash equivalents	\$ 44,979	\$ 44,979	\$ —	\$ —

4. Restricted Cash

At December 31, 2013 and 2014, the Company had \$70,000 in restricted cash. This amount is comprised of a \$20,000 certificate of deposit to collateralize a credit card account with the Company's primary financial institution and a \$50,000 letter of credit, which served as the security deposit on the

Syros Pharmaceuticals, Inc.**Notes to Consolidated Financial Statements (Continued)**

**(Information as of September 30, 2015 and for the nine months ended
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4. Restricted Cash (Continued)

lease of the Company's prior facility in Watertown, Massachusetts. At September 30, 2015 the Company had \$483,000 in restricted cash which serves as the security deposit on the lease of the Company's current facility in Cambridge, Massachusetts (Note 8).

5. Property and Equipment

Property and equipment consists of the following at December 31, 2013 and 2014 and September 30, 2015 (in thousands):

	Estimated useful life (in years)	December 31,		September 30,
		2013	2014	2015
Laboratory equipment	5	\$ 900	\$ 1,080	\$ 1,893
Computer equipment	3	132	173	193
Furniture and fixtures	4	56	56	400
Leasehold improvements	Shorter of 7 years or life of lease	—	—	2,376
Construction-in-progress		20	—	—
		1,108	1,309	4,862
Less: Accumulated depreciation		(170)	(428)	(801)
Total property and equipment, net		\$ 938	\$ 881	\$ 4,061

Depreciation expense, including depreciation expense for assets recorded under capital leases, amounted to \$170,000 and \$258,000 for the years ended December 31, 2013 and 2014, respectively, and \$187,000 and \$373,000 for the nine months ended September 30, 2014 and 2015, respectively. Lab equipment included assets recorded under capital leases of \$389,000 at September 30, 2015 (Note 7). Accumulated depreciation from assets recorded under capital leases was \$65,000 at September 30, 2015.

6. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	December 31,		September 30,
	2013	2014	2015
Employee compensation and benefits	\$ 121	\$ 132	\$ 354
External research and preclinical development	—	106	784
Facilities	—	—	735
Professional fees	158	48	618
Restricted stock liability	1	1	1
	\$ 280	\$ 287	\$ 2,492

Syros Pharmaceuticals, Inc.**Notes to Consolidated Financial Statements (Continued)**

**(Information as of September 30, 2015 and for the nine months ended
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7. Indebtedness***Convertible Notes***

On December 19, 2012, the Company issued convertible notes (the "Notes") to certain of its preferred stock investors in the aggregate principal amount of \$2,000,000. Under the terms of the Notes, the principal and unpaid accrued interest of the Notes would automatically convert upon the occurrence of the Company's next qualified financing. The Notes bore an interest rate of 6% per annum. On April 10, 2013, the Company completed the Series A-2 convertible preferred stock financing, which constituted a qualified financing, and the principal and unpaid accrued interest of the Notes of \$2,036,492 automatically converted to shares of Series A-2 convertible preferred stock at a conversion price equal to the price paid per share in the financing. Upon the date of the qualified financing, the Notes were converted into 2,036,492 shares of Series A-2 convertible preferred stock at a purchase price of \$1.00 per share.

Equipment Financing

In March 2015, the Company entered into a lease agreement with a vendor for certain laboratory equipment. The Company financed \$389,000 of the amount owed under the lease agreement and is required to make consecutive monthly payments of principal, plus accrued interest at 6.44%, over 36 months through March 2018. As of September 30, 2015, the Company had made payments of \$44,000, of which \$12,000 related to interest. At September 30, 2015, \$357,000 of principal was outstanding with respect to the equipment financing arrangement.

Scheduled monthly future minimum lease payments with respect to the equipment financing arrangement are as follows (in thousands):

<u>At September 30, 2015:</u>	
2015	\$ 23
2016	152
2017	172
2018	43
	<u>\$ 390</u>

8. Commitments***Operating Leases***

In October 2012, the Company entered into an operating lease for office and laboratory space in Watertown, Massachusetts (the "2012 Lease"). The lease agreement was with Alexandria Real Estate, a related party (see Note 14). The lease agreement expired in August 2015. The Company's lease agreement had escalating rent payments and the Company recorded rent expense on a straight-line basis. The Company recorded rent expense of \$265,000 for each of the years ended December 31, 2013 and 2014, and \$199,000 and \$177,000 for the nine months ended September 30, 2014 and 2015, respectively. The lease agreement required the Company to issue an original letter of credit in the

Syros Pharmaceuticals, Inc.**Notes to Consolidated Financial Statements (Continued)**

**(Information as of September 30, 2015 and for the nine months ended
September 30, 2014 and 2015 is unaudited)**

8. Commitments (Continued)

amount of \$50,000, which is included in other current assets in the accompanying balance sheets. The Company's remaining lease commitment under the 2012 Lease as of December 31, 2014 was \$206,000.

In March 2015, the Company entered into an operating lease for approximately 21,488 rentable square feet of office and laboratory space in Cambridge, Massachusetts (the "2015 Lease"), with a lease term commencing in August 2015 and ending in October 2020, assuming occupancy in August 2015. The Company has an option to extend the lease for five additional years. The Company's lease agreement has escalating rent payments and the Company records rent expense on a straight-line basis over the term of the lease, including any rent-free periods. The Company recorded rent expense of \$99,000 for the nine months ended September 30, 2015 related to the 2015 Lease. The lease agreement required the Company to issue an original letter of credit in the amount of \$483,000, which is included in restricted cash in the accompanying balance sheet at September 30, 2015.

The 2015 Lease includes certain lease incentives in the form of tenant allowances. The Company has capitalized the improvements made with the tenant allowance into fixed assets and established a liability for the deferred lease incentive upon occupancy. The Company recorded these incentives as a component of deferred rent and will amortize these incentives as a reduction of rent expense over the lease term. The related fixed assets will be amortized over the lease term. The 2012 Lease and 2015 Lease require the Company to share in prorated operating expenses and property taxes based upon actual amounts incurred; those amounts are not fixed for future periods and, therefore, are not included in the future commitments listed below.

The minimum aggregated future lease commitment at September 30, 2015 is as follows (in thousands):

<u>At September 30, 2015:</u>	
2015	\$ 240
2016	1,217
2017	1,252
2018	1,288
2019	1,325
2020	1,130
	<u>\$ 6,452</u>

License Agreements*Dana-Farber Cancer Institute, Inc.*

In February 2013, the Company entered into a license agreement with Dana-Farber Cancer Institute, Inc. ("Dana-Farber") pursuant to which the Company was granted an exclusive worldwide, sublicensable license under specified patents relating to CDK7 inhibitors and JNK inhibitors owned or controlled by Dana-Farber. The Company paid a \$50,000 license initiation fee to Dana-Farber, which was recorded as research and development expense. A funding milestone payment of \$125,000 was paid in April 2014 upon the close of the Series A-3 convertible preferred stock financing. Payments totaling

Syros Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

**(Information as of September 30, 2015 and for the nine months ended
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8. Commitments (Continued)

\$3.4 million are due when the Company achieves certain clinical and regulatory milestones for any product to Dana-Farber, none of which have been achieved as of September 30, 2015. The future potential milestone payments have not been accrued as of December 31, 2013 and 2014 and September 30, 2015, respectively, as no milestones have been achieved and the agreement can be cancelled at the Company's option. Therefore, the Company had no obligation to pay any of these amounts. After the Company begins commercial sale of products in any country subject to the license, the Company will owe a tiered royalty on net sales. Royalty payments continue for the duration of the licensed patents.

In the event the Company grants a sublicense to a third party, the Company will pay a royalty equal to a percentage of the revenue it receives from the sublicense. The specific percentage payable is dependent on the stage of development of the product subject to the sublicense at the time the sublicense is granted.

Whitehead Institute for Biomedical Research and Dana-Farber

Effective April 1, 2013, the Company entered into a license agreement with the Whitehead Institute for Biomedical Research ("Whitehead") and Dana-Farber, pursuant to which the Company was granted a worldwide, sublicensable license under specified patents relating to modulators of Myc/Max Screen, relating to Chem-Seq owned or controlled by Whitehead and Dana-Farber. In April 2013, related to such license, the Company paid a \$50,000 license initiation fee to Whitehead, which was recorded as a research and development expense. A funding milestone payment of \$50,000 was paid in April 2014. Payments totaling \$3.4 million are due when the Company achieves certain clinical and regulatory milestones, none of which have been achieved as of September 30, 2015. The future potential milestone payments have not been accrued as of December 31, 2013 and 2014 and September 30, 2015, respectively, as no milestones have been achieved and the agreement can be cancelled at the Company's option, and therefore the Company had no obligation to pay any of these amounts. After the Company begins commercial sale of products in any country subject to the license, the Company will owe a tiered royalty on net sales. Royalty payments continue for the duration of the licensed patents.

In the event the Company grants a sublicense to a third party, the Company will pay a royalty equal to a percentage of the revenue it receives from the sublicense. The specific percentage payable is dependent on the stage of development of the product subject to the sublicense at the time the sublicense is granted.

Whitehead Institute for Biomedical Research

Effective April 4, 2013, the Company entered into an additional license agreement with Whitehead, pursuant to which the Company was granted a worldwide license under specified patents relating to super-enhancers owned or controlled by Whitehead. In April 2013, related to such license, the Company paid a \$30,000 license initiation fee to Whitehead, which was recorded as a research and development expense. A milestone payment of \$100,000 is due upon the issuance of a patent under patent rights in the United States for a product or licensed service in commercial development and another \$100,000 is due upon the receipt by the Company of \$1.0 million from a commercial partner or

Syros Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

**(Information as of September 30, 2015 and for the nine months ended
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8. Commitments (Continued)

licensee. These amounts have not been accrued as of December 31, 2013 and 2014 and September 30, 2015, respectively, because the milestones had not been achieved, and therefore, the Company had no obligation to pay any of these amounts. After the Company begins commercial sale of products in any country subject to the license, the Company will owe a tiered royalty on net sales. Royalty payments continue for the duration of the licensed patents.

In the event the Company grants a sublicense to a third party, the Company will pay a royalty equal to a percentage of the revenue it receives from the sublicense. The specific percentage payable is dependent on the stage of development of the product subject to the sublicense at the time the sublicense is granted.

As part of the above licensing agreements, the Company issued 643,782 shares of common stock to Whitehead in April 2013. The Company recorded \$166,740 of expenses within research and development as a result of this issuance.

TMRC Co. Ltd.

In September 2015, the Company entered into an exclusive license agreement with the Japanese oncology company TMRC Co. Ltd., ("TMRC") to develop and commercialize tamibarotene in North America and Europe for cancer. Tamibarotene is an agonist of retinoic acid receptor alpha ("RARα") and is currently marketed in Japan for acute promyelocytic leukemia, a form of acute myeloid leukemia ("AML"). The Company identified the genomic biomarker that identifies AML and myelodysplastic syndrome patient subgroup to be sensitive to or likely to respond to RARα agonist therapy through the Company's proprietary gene control target discovery platform. The Company has identified this product candidate as SY-1425.

In exchange for this license, the Company made a one-time, non-refundable upfront payment of \$500,000 in September 2015 and may make additional payments upon the successful achievement of clinical and regulatory milestones of approximately \$13.0 million per indication. In addition, the Company will pay TMRC single-digit percentage royalties, on a country-by-country, product-by-product basis, on net product sales in North America and Europe.

TMRC is expected to supply the active pharmaceutical ingredient for SY-1425 to the Company pursuant to a supply agreement that is currently being negotiated.

At any time after the first anniversary of the TMRC Agreement, the Company has the ability to terminate the agreement at its sole discretion for any reason.

The Company is responsible for all preclinical, clinical, regulatory and other activities necessary to develop and commercialize tamibarotene in North America and Europe. None of the assets acquired had alternative future uses. As no processes or activities that would constitute a "business" were acquired as part of the license agreement, the transaction was accounted for as an asset acquisition and the upfront payment of \$500,000 was recorded as research and development expense. The additional payments will also be recorded as research and development and expensed as achieved.

Syros Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

**(Information as of September 30, 2015 and for the nine months ended
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8. Commitments (Continued)

Litigation

The Company is not party to any litigation and does not have contingency reserves established for any litigation liabilities as of December 31, 2013, December 31, 2014 or September 30, 2015.

9. Convertible Preferred Stock

Series A Convertible Preferred Stock Financing

On August 8, 2012, the Company issued 2,500,000 shares of Series A-1 Convertible Preferred Stock ("Series A-1") at a purchase price of \$0.50 per share. The issuance resulted in cash proceeds of \$1,208,000, net of issuance costs of \$42,000. The Series A-1 has a liquidation preference amount of \$1,486,000 at September 30, 2015.

On various dates in 2013, the Company issued 12,100,000 shares of Series A-2 Convertible Preferred Stock ("Series A-2") at a purchase price of \$1.00 per share. The shares were issued for cash proceeds of \$10,021,000, net of issuance costs of \$42,000, and the exchange of outstanding Convertible Notes, including accrued interest, of approximately \$2,036,000, as disclosed in Note 7. The Series A-2 has a liquidation preference amount of \$13,888,000 at September 30, 2015.

On various dates in 2014, the Company issued 15,750,000 shares of Series A-3 Convertible Preferred Stock ("Series A-3") at a purchase price of \$1.00 per share. The issuances resulted in cash proceeds of \$15,749,000, net of issuance costs of \$1,000. The Series A-3 has a liquidation preference amount of \$17,170,000 at September 30, 2015.

The Series A-1, Series A-2 and Series A-3 preferred stock is collectively referred to as "Series A" or "Series A Preferred Stock."

Series B Convertible Preferred Stock Financing

In October 2014, the Company issued 16,893,931 shares of Series B Convertible Preferred Stock ("Series B") at a purchase price of \$3.1461 per share. The issuance resulted in cash proceeds of \$52,998,000, net of issuance costs of \$152,000. The Series B has a liquidation preference amount of \$56,230,000 at September 30, 2015.

The rights, preferences, and privileges of the Series A-1, Series A-2, Series A-3 and Series B (collectively the "Preferred Stock") are listed below:

Conversion

Each share of Preferred Stock shall be convertible, at the option of the holder thereof, at any time and from time to time, and without the payment of additional consideration by the holder thereof, into such number of fully paid and nonassessable shares of common stock as is determined by dividing the original issuance price by the conversion price in effect at the time of conversion. The conversion price currently in effect is the original issuance price, or \$0.50 per share for Series A-1, \$1.00 per share for Series A-2 and Series A-3 and \$3.1461 per share for Series B, in each case subject to adjustment in the

Syros Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

**(Information as of September 30, 2015 and for the nine months ended
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9. Convertible Preferred Stock (Continued)

event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Preferred Stock.

Conversion is at the option of the preferred stockholders, although conversion is automatic upon either of the consummation of an initial public offering resulting in gross proceeds of \$30.0 million and at a price of \$5.00 per share of the Common Stock or the vote or written consent of the majority of outstanding shares of the Preferred Stock.

Voting

On any matter presented to the stockholders of the Company for their action or consideration at any meeting of stockholders of the Company (or by written consent of stockholders in lieu of a meeting), each holder of outstanding shares of Preferred Stock shall be entitled to cast the number of votes equal to the number of whole shares of Common Stock into which the shares of Preferred Stock held by such holder are convertible as of the record date for determining stockholders entitled to vote on such matter. Except as provided by law or by other provisions of the Certificate of Incorporation, holders of Preferred Stock shall vote together with the holders of common stock as a single class.

The holders of Series B Preferred Stock have certain protective voting rights as defined. These protective rights require the written consent or affirmative vote of the holders of at least sixty-six and two thirds percent of the then outstanding shares of Series B before action can be taken to (i) modify, amend, or waive any provision of the Certificate of Incorporation in any way that adversely affects the holders of the Series B Preferred Stock, (ii) purchase or redeem or pay or declare any dividend or make any distribution on any shares of capital stock prior to the Series B Preferred Stock, other than repurchases in connection with the cessation of employment or service, or (iii) increase or decrease the authorized number of shares of Series B Preferred Stock.

In addition to the Series B protective rights, all holders of Preferred Stock have certain protective voting rights as defined. These protective rights require the written consent or affirmative vote of the holders of at least sixty-six and two thirds percent of the then outstanding shares of Preferred Stock before action can be taken to (i) liquidate, dissolve or wind-up the business and affairs of the Company, effect any merger or consolidation or any other deemed liquidation event, (ii) amend, alter or repeal any provision of the Certificate of Incorporation or Bylaws of the Company, (iii) create, or authorize the creation of, or issue or obligate itself to issue shares of, any additional class or series of capital stock unless such series ranks junior to the Preferred Stock with respect to the distribution of assets on the liquidation, dissolution or winding up of the Company, the payment of dividends and rights of redemption, or increase the authorized number of shares of Preferred Stock unless the same ranks junior to the Preferred Stock with respect to the distribution of assets on the liquidation, dissolution or winding up of the Company, the payment of dividends and rights of redemption, (iv) purchase or redeem or pay or declare any dividend or make any distribution on any shares of capital stock prior to the Preferred Stock, other than repurchases in connection with the cessation of employment or service.

Syros Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

**(Information as of September 30, 2015 and for the nine months ended
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9. Convertible Preferred Stock (Continued)

Dividends

Holders of the Preferred Stock are entitled to receive, before any cash is paid out or set aside for any Common Stock, dividends at the annual rate of \$0.03 per share on shares of Series A-1, \$0.06 per share on shares of Series A-2 and Series A-3 and \$0.1887 per share on shares of Series B, in each case subject to adjustment for any stock dividend, stock split, combination or other similar recapitalization. The dividends are cumulative and are payable only when, as, and if, declared by the board of directors, or liquidation, dissolution, sale or winding up of the Company. No dividends have been declared since the Company's inception. Aggregate cumulative preferred dividends at December 31, 2013, December 31, 2014 and September 30, 2015 were \$0.6 million, \$2.8 million and \$6.5 million, respectively.

Redemption

The preferred stock is redeemable upon a deemed liquidation event, provided that the Company does not effect a dissolution of the Company within ninety days after such deemed liquidation event.

The following events are considered deemed liquidation events unless the holders of at least sixty-six and two thirds percent of the outstanding shares of Preferred Stock and at least sixty-six and two thirds percent of the outstanding shares of Series B elect otherwise: (a) a merger or consolidation in which (i) the Company is a constituent party or (ii) a subsidiary of the Company is a constituent party and the Company issues shares of its capital stock pursuant to such merger or consolidation, except any such merger or consolidation in which the shares of capital stock of the Company outstanding immediately prior to such merger or consolidation continue to represent, or are converted into or exchanged for shares of capital stock that represent, immediately following such merger or consolidation, at least a majority, by voting power, of the capital stock of the surviving or resulting corporation, or the parent corporation of the surviving or resulting corporation if the surviving or resulting corporation is a wholly owned subsidiary of another corporation, or (b) the sale, lease, transfer, exclusive license or other disposition of all or substantially all the assets of the Company.

Liquidation

Holders of Series B have preference in the event of a liquidation, dissolution, sale or winding up of the Company equal to the greater of \$3.1461 per share, plus any accrued but unpaid dividends whether or not declared, plus any dividends declared but unpaid thereon or such amount per share as would have been payable had all shares of Series B been converted into Common Stock immediately prior to such liquidation, dissolution, sale or winding up of the Company. If upon any such liquidation, dissolution, sale or winding up of the Company or a deemed liquidation event, the assets of the Company available for distribution are insufficient to pay the holders of Series B the full amount to which they would be entitled, the holders of shares of Series B shall share ratably in any distribution of the assets available for distribution in proportion to the respective amounts which would otherwise be payable if all amounts payable with respect to such shares were paid in full.

After the payment of all liquidation preferences to holders of Series B, holders of Series A have preference in the event of a liquidation, dissolution, sale or winding up of the Company equal to the

Syros Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

**(Information as of September 30, 2015 and for the nine months ended
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9. Convertible Preferred Stock (Continued)

greater of the original issue price per share, or \$0.50 per share for Series A-1 and \$1.00 per share for Series A-2 and Series A-3, plus any dividends declared but unpaid thereon, or such amount per share as would have been payable had all shares of Series A been converted into Common Stock immediately prior to such liquidation, dissolution, sale or winding up of the Company. If upon any such liquidation, dissolution, sale or winding up of the Company or a deemed liquidation event, the assets of the Company available for distribution are insufficient to pay the holders of Series A the full amount to which they would be entitled, the holders of shares of Series A shall share ratably in any distribution of the assets available for distribution in proportion to the respective amounts which would otherwise be payable if all amounts payable with respect to such shares were paid in full.

Thereafter, if assets remain in the Company, the holders of the Common Stock shall receive all of the remaining assets of the Company pro rata based on the number of shares of Common Stock held by each.

As the Preferred Stock may become redeemable upon an event that is outside of the control of the Company, the Preferred Stock has been classified outside of stockholders' (deficit) equity. Since the Preferred Stock is not initially redeemable and it is not probable that it will become redeemable, the initial carrying value of the Preferred Stock has not been adjusted to redemption value.

The Company assessed the Series A and Series B Preferred Stock for any beneficial conversion features or embedded derivatives, including the conversion option, that would require bifurcation from the Series A and Series B Preferred Stock and receive separate accounting treatment. Based on the Company's determination that the Preferred Stock is an "equity host," all features of the Preferred Stock are either clearly and closely related to the equity host or did not meet the definition of a derivative, and do not require bifurcation as a derivative liability. On the date of issuance, the fair value of Common Stock into which the Series A and Series B Preferred Stock was convertible was less than the effective conversion price of the Series A and Series B Preferred Stock, and as such, there was no beneficial conversion feature at the commitment date.

10. Common Stock

Holders of the Company's common stock are entitled to one vote for each share of common stock held. Common stockholders are not entitled to receive dividends unless declared by the board of directors.

Syros Pharmaceuticals, Inc.**Notes to Consolidated Financial Statements (Continued)**

**(Information as of September 30, 2015 and for the nine months ended
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10. Common Stock (Continued)

The Company has reserved the following shares of Common Stock for the potential conversion of Preferred Stock and the issuance of Common Stock in connection with stock options:

	As of December 31,		As of
	2013	2014	September 30, 2015
Series A Preferred Stock	14,600,000	30,350,000	30,350,000
Series B Preferred Stock	—	16,893,931	16,893,931
Stock options outstanding	3,985,851	4,987,881	7,088,929
Shares available for future issuance under the 2012 Plan	1,329,218	3,822,859	384,752
Shares reserved for vesting of restricted stock awards	3,154,931	2,233,283	1,243,296
	<u>23,070,000</u>	<u>58,287,954</u>	<u>55,960,908</u>

11. Stock-Based Payments***2012 Stock Option Plan***

The Company grants restricted stock awards, incentive stock options ("ISO") and nonstatutory stock options ("NSO") under the Syros Pharmaceuticals, Inc. 2012 Equity Incentive Plan (the "2012 Plan"). As of September 30, 2015, the Company had reserved 8,711,306 shares of Common Stock under the 2012 Plan, of which 384,752 shares remained available for future issuance under the 2012 Plan. Under the 2012 Plan, stock options may not be granted at less than fair value on the date of grant.

Terms of restricted stock and stock option agreements, including vesting requirements, are determined by the board of directors, subject to the provisions of the 2012 Plan. Restricted stock awards granted by the Company generally vest based on each grantee's continued service with the Company during a specified period following grant. Stock option awards granted by the Company generally vest over four years, with 25% vesting on the one year anniversary of the vesting commencement date and 75% vesting ratably, on a monthly basis, over the remaining three years. Such awards are exercisable from the date of grant for a period of ten years. The Company also grants performance-based stock option awards and restricted stock for which vesting accelerates upon the achievement of performance-based milestones. For certain of such awards, notwithstanding any vesting in accordance with the achievement of performance-based milestones, such awards vest in full on the sixth anniversary of the vesting commencement date.

Stock Options***Performance-Based Stock Options***

The Company has granted stock options to management for which the vesting of such stock options accelerates upon the achievement of performance-based criteria. Milestone events are specific to the Company's corporate goals, including but not limited to certain preclinical and clinical development milestones and the Company's ability to execute on its corporate development and

Syros Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

(Information as of September 30, 2015 and for the nine months ended September 30, 2014 and 2015 is unaudited)

11. Stock-Based Payments (Continued)

financing strategies. Stock-based compensation expense associated with these performance-based stock options is recognized based on the accelerated attribution model. Management evaluates when the achievement of a performance-based milestone is probable based on the expected satisfaction of the performance conditions as of the reporting date. Notwithstanding any vesting in accordance with the achievement of performance-based milestones, such awards vest in full on the sixth anniversary of the vesting commencement date. During the year ended December 31, 2013, management determined that a performance-based milestone was achieved and recorded stock-based compensation expense of \$11,000. No additional milestones were deemed to be probable of achievement as of December 31, 2014. As of September 30, 2015, management determined that certain other performance-based milestones were probable of achievement and recorded additional stock-based compensation expense of \$65,000 as of September 30, 2015. As of September 30, 2015, there is \$930,000 of unrecognized stock-based compensation expense related to the performance-based stock options.

A summary of the status of stock options as of December 31, 2014 and September 30, 2015 and changes during the year ended December 31, 2014 and the nine months ended September 30, 2015 is presented below:

	Shares	Weighted-Average Exercise Price	Remaining Contractual Life (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2013	3,985,851	\$ 0.25	9.4	\$ 61
Granted	1,093,485	0.51		
Exercised	(54,635)	0.27		
Cancelled	(36,820)	0.27		
Outstanding at December 31, 2014	4,987,881	\$ 0.31	8.6	\$ 2,494
Granted	3,498,913	1.17		
Exercised	(1,244,434)	0.27		
Cancelled	(153,431)	0.19		
Outstanding at September 30, 2015	7,088,929	\$ 0.74	8.8	\$ 7,848
Exercisable at December 31, 2014	2,033,484	\$ 0.30		\$ 1,046
Vested and expected to vest at December 31, 2014	4,987,881	\$ 0.31	8.6	\$ 2,494
Exercisable at September 30, 2015	1,640,688	\$ 0.35	8.0	\$ 2,454
Vested and expected to vest at September 30, 2015	7,088,929	\$ 0.74	8.8	\$ 7,848

The intrinsic value of options exercised during the year ended December 31, 2014 was \$6,000 and during the nine months ended September 30, 2015 was \$1.6 million.

Syros Pharmaceuticals, Inc.**Notes to Consolidated Financial Statements (Continued)**

**(Information as of September 30, 2015 and for the nine months ended
September 30, 2014 and 2015 is unaudited)**

11. Stock-Based Payments (Continued)***Restricted Common Stock***

At various dates in 2012 and 2013, upon approval by its board of directors, the Company issued an aggregate of 6,079,931 shares of restricted Common Stock to certain advisors at a purchase price of \$0.001 per share. Of the restricted Common Stock issued by the Company, 6,000,000 shares begin vesting upon the achievement of certain performance objectives as well as continued service to the Company, as set forth in each grantee's individual restricted stock purchase agreement. The remaining 79,931 shares of restricted Common Stock were issued to a member of the Company's board of directors and vest over four years, based on the director's continued service to the Company, as set forth in the director's individual restricted stock purchase agreement. The shares of restricted Common Stock are subject to repurchase rights. Accordingly, the Company has recorded the proceeds from the issuance of restricted Common Stock as a liability in the accompanying balance sheets. The restricted stock liability is reclassified into stockholders' (deficit) equity as the restricted Common Stock vests.

A summary of the status of unvested restricted Common Stock as of December 31, 2014 and September 30, 2015 and changes during the year ended December 31, 2014 and the nine months ended September 30, 2015 is presented below:

	<u>Shares</u>	<u>Weighted-Average Grant Date Fair Value</u>
Unvested at December 31, 2013	3,154,931	\$ 0.10
Issued	—	—
Vested	(921,648)	0.10
Repurchased	—	—
Unvested at December 31, 2014	<u>2,233,283</u>	\$ 0.10
Issued	—	—
Vested	(989,987)	0.05
Repurchased	—	—
Unvested at September 30, 2015	<u>1,243,296</u>	\$ 0.10

The non-employee restricted Common Stock is revalued as it vests. The expense related to the restricted Common Stock issued to non-employees for the years ended December 31, 2013 and 2014 was \$0.4 million and \$0.6 million, respectively, and for the nine months ended September 30, 2014 and 2015 was \$0.4 million and \$1.6 million, respectively.

Syros Pharmaceuticals, Inc.**Notes to Consolidated Financial Statements (Continued)**

**(Information as of September 30, 2015 and for the nine months ended
September 30, 2014 and 2015 is unaudited)**

11. Stock-Based Payments (Continued)***Stock-based Compensation Expense***

The fair value of each stock option granted was estimated on the date of grant using the Black-Scholes option-pricing model based on the following weighted-average assumptions:

	<u>December 31,</u>		<u>September 30,</u>
	<u>2013</u>	<u>2014</u>	<u>2015</u>
Weighted-average risk-free interest rate	1.21%	2.00%	1.76%
Expected dividend yield	0%	0%	0%
Expected option term	6.11	7.03	6.09
Volatility	89.23%	85.51%	82.59%

The weighted-average grant date fair value per share of options granted during the year ended December 31, 2013 was \$0.19, during the year ended December 31, 2014 was \$0.39 and during the nine months ended September 30, 2015 was \$1.18.

The following table summarizes the stock-based compensation expense for stock options and restricted common stock granted to employees and non-employees recorded in the Company's statements of operations:

	<u>Year ended December 31,</u>		<u>Nine months ended September 30,</u>	
	<u>2013</u>	<u>2014</u>	<u>2014</u>	<u>2015</u>
Research and development	\$ 673	\$ 830	\$ 514	\$ 2,073
General and administrative	148	107	73	312
Total stock-based compensation expense	<u>\$ 821</u>	<u>\$ 937</u>	<u>\$ 587</u>	<u>\$ 2,385</u>

As of September 30, 2015, there was \$6.4 million of total unrecognized compensation cost related to non-vested stock options and unvested restricted Common Stock, which is expected to be recognized over a weighted-average period of 2.7 years.

Syros Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

(Information as of September 30, 2015 and for the nine months ended September 30, 2014 and 2015 is unaudited)

12. Income Taxes

A reconciliation of the expected income tax (benefit) computed using the federal statutory income tax rate to the Company's effective income tax rate is as follows:

	Year ended December 31,	
	2013	2014
Federal income tax computed at federal statutory tax rate	34.00%	34.00%
State income tax, net of federal benefit	4.80%	4.86%
Permanent items	(3.81)%	(1.94)%
Federal and state research and development credits	5.61%	4.73%
Other	0.17%	—%
Change in valuation allowance	(40.77)%	(41.65)%
Effective income tax rate	<u>0.00%</u>	<u>0.00%</u>

The principal components of the Company's deferred tax assets and liabilities consist of the following at December 31, 2013 and 2014, respectively (in thousands):

	Year ended December 31,	
	2013	2014
Deferred tax assets:		
Federal and state net operating loss carryforwards	\$ 2,945	\$ 7,969
Tax credit carryforwards	486	1,121
Intangible assets	548	430
Stock-based compensation	20	87
Other	103	83
Total deferred tax assets	4,102	9,690
Less valuation allowance	(4,102)	(9,690)
Net deferred tax assets	—	—
Deferred tax liabilities:		
Net deferred taxes	<u>\$ —</u>	<u>\$ —</u>

As of December 31, 2014 the Company had federal net operating loss ("NOL") carryforwards of approximately \$20.3 million and state net operating loss carryforwards of \$20.2 million, which are available to reduce future taxable income. The Company also had federal tax credits of approximately \$0.8 million and state tax credits of \$0.5 million, which may be used to offset future tax liabilities. The NOL and tax credit carryforwards will expire at various dates through 2034. The NOL and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service ("IRS") and state tax authorities. Net operating loss and tax credit carryforwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the Internal Revenue Code, respectively, as well as similar state provisions. This could limit the amount of

Syros Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

**(Information as of September 30, 2015 and for the nine months ended
September 30, 2014 and 2015 is unaudited)**

12. Income Taxes (Continued)

tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. The Company has not determined whether an ownership change has occurred and as such, the Company's NOLs may be limited.

ASC 740 requires a valuation allowance to reduce the deferred tax assets reported if, based on the weight of the evidence, it is more likely than not that some portion or all of the deferred tax assets will not be realized. After consideration of all the evidence, both positive and negative, the Company has recorded a valuation allowance against its deferred tax assets at December 31, 2013 and 2014, respectively, because the Company's management has determined that it is more likely than not that these assets will not be fully realized. The increase in the valuation allowance in 2014 primarily relates to the net loss incurred by the Company.

As of December 31, 2014, the Company had no federal and state net operating losses related to excess tax deductions that have been excluded from the above table. The benefit of these net operating losses will be recognized as an increase in additional paid in capital when it results in a reduction in taxes payable.

The Company has not as yet conducted a study of its research and development credit carryforwards. This study may result in an adjustment to the Company's research and development credit carryforwards. A full valuation allowance has been provided against the Company's research and development credits, and if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance. Thus, there would be no impact to the balance sheets or statements of operations if an adjustment were required.

The Company's reserves related to taxes are based on a determination of whether and how much of a tax benefit taken by the Company in its tax filings or positions is more likely than not to be realized following resolution of any potential contingencies present related to the tax benefit. At December 31, 2013 and 2014, the Company had no unrecognized tax benefits. The Company's policy is to recognize both interest and penalties related to unrecognized tax benefits in income tax expense.

The statute of limitations for assessment by the IRS, and state tax authorities remains open for all tax years. The Company files income tax returns in the U.S. federal and Massachusetts jurisdictions. There are currently no federal or state audits in process.

13. Research Agreement

In November 2014, the Company entered into a research agreement with a multinational pharmaceutical company (the "Counterparty") for purposes of mapping immune cell super-enhancers ("SE") and transcriptional targets in autoimmune disease. Under the research agreement, the Company will be responsible for the conduct of all activities under separate projects, as defined in the research agreement, associated with generating SE and transcriptional maps of the cell/tissue supplied by the pharmaceutical company. Upon the completion of each project, the Counterparty will determine whether to commence the next project under the research agreement upon written notification.

Syros Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

**(Information as of September 30, 2015 and for the nine months ended
September 30, 2014 and 2015 is unaudited)**

13. Research Agreement (Continued)

The research agreement expires on the earlier of November 30, 2016 or completion of the research program, unless otherwise terminated earlier. The research agreement terminates automatically if the Counterparty does not notify the Company that it would like to commence the next research project.

In exchange for these research services, the Company may receive funding of up to \$3.0 million over the term of the agreement. The Company will recognize revenue on a completed performance basis for each project performed under the agreement, as the Company does not have the ability to reasonably estimate the period of performance and the final study report for each project is significant to the overall arrangement. The Company recognized revenue of \$0.3 million during the nine months ended September 30, 2015 related to the pilot project of the research agreement.

14. Related Party Transactions

During the year ended December 31, 2014, the Company paid to WuXi AppTec (Hong Kong) Limited ("WuXi"), an affiliate of WuXi PharmaTech, \$1.1 million in cash for external research and preclinical development services. During the nine months ended September 30, 2015, the Company paid WuXi \$2.1 million in cash for external research and preclinical development services. In August 2012, as part of the Series A-1 Preferred Stock financing, WuXi purchased 500,000 shares of Series A-1 Preferred Stock at a purchase price of \$0.50 per share, for a total purchase value of \$250,000. In April 2013, as part of the Series A-2 Preferred Stock financing, WuXi purchased 500,000 shares of Series A-2 Preferred Stock at a purchase price of \$1.00 per share, for a total purchase value of \$500,000. In March 2014, as part of the Series A-3 Preferred Stock financing, WuXi purchased 500,000 shares of Series A-3 Preferred Stock at a purchase price of \$1.00 per share, for a total purchase value of \$500,000. In October 2014, as part of the Series B Preferred Stock financing, WuXi purchased 953,561 shares of Series B Preferred Stock at a purchase price per share of \$3.1461, for a total purchase value of \$3,000,000.

In October 2012, the Company entered into an operating lease for office and laboratory space in Watertown, Massachusetts with Alexandria Real Estate Equities ("ARE"). As part of the lease agreement, the Company granted ARE the right to participate in the Company's Series A-2 Preferred Stock financing. In April 2013, as part of the Series A-2 Preferred Stock financing, ARE purchased 250,000 shares of Series A-2 Preferred Stock at a purchase price of \$1.00 per share, for a total purchase value of \$250,000. During the year ended December 31, 2014, the Company paid to ARE \$0.5 million in cash for rent and miscellaneous facilities costs. During the nine months ended September 30, 2015, the Company paid to ARE \$0.3 million for rent and miscellaneous facilities costs.

15. Defined Contribution Plan

The Company established a defined contribution savings plan under Section 401(k) of the Internal Revenue Code. This plan covers substantially all employees who meet minimum age and service requirements and allows participants to defer a portion of their annual compensation on a pretax basis. Company contributions to the plan may be made at the discretion of the board of directors. Through September 30, 2015, no contributions had been made to the plan by the Company.

Syros Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements (Continued)

**(Information as of September 30, 2015 and for the nine months ended
September 30, 2014 and 2015 is unaudited)**

16. Subsequent Event (unaudited)

In December 2015, the Company amended the 2012 Plan to increase the number of shares reserved for issuance thereunder to 10,311,306 shares.

In December 2015, the Company amended its certificate of incorporation to increase the total number of shares authorized for issuance for all classes of stock to 66,171,908 shares.

In January 2016, the Company completed a Series B Preferred Stock financing in which it issued and sold an aggregate of 12,714,150 shares of Series B Preferred Stock for an aggregate purchase price of \$40 million, with such shares of Series B having the same rights and privileges as the shares of Series B issued in October 2014 (see Note 9. Convertible Preferred Stock). In connection with the Series B Preferred Stock issuance in January 2016, the Company amended its certificate of incorporation to increase the total number of shares authorized for issuance for all classes of stock to 78,886,062 shares.

Shares



Common Stock

PROSPECTUS

Cowen and Company

Piper Jaffray

JMP Securities

Wedbush PacGrow

, 2016

Through and including _____, 2016 (the 25th day after the date of this prospectus), all dealers that buy, sell or trade shares of our common stock, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

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, or SEC, registration fee, the Financial Industry Regulatory Authority, Inc., or FINRA, filing fee and the NASDAQ listing fee.

	<u>Amount</u>
SEC registration fee	\$ 8,686
FINRA filing fee	13,438
NASDAQ listing fee	125,000
Accounting fees and expenses	800,000
Legal fees and expenses	1,500,000
Blue sky fees and expenses (including legal fees)	*
Transfer agent and registrar fees and expenses	*
Printing and engraving expenses	300,000
Miscellaneous fees and expenses	*
Total expenses	<u> *</u>

* 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 or its stockholders 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 the closing of this offering, our restated 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

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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 closing of this offering, our restated certificate of incorporation will provide that we will indemnify each person who was or is a party or threatened to be made a party to 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 restated certificate of incorporation that will be effective upon the closing of the 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 have entered into indemnification agreements with our directors and executive officers. 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 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, 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 capital stock

In January 2013, we issued and sold 2,000,000 shares of our common stock at a price per share of \$0.001 for an aggregate purchase price of \$2,000.

In April and November 2013, we issued and sold an aggregate of 12,100,000 shares of our Series A-2 preferred stock at a price per share of \$1.00, for an aggregate purchase price of \$12.1 million.

In August 2013, we issued 643,782 shares of common stock to the Whitehead Institute for Biomedical Research pursuant to the terms of certain license agreements between us and the Whitehead Institute for Biomedical Research.

In November 2013, we issued and sold 79,931 shares of common stock pursuant to our 2012 equity incentive plan at a price per share of \$0.27 for an aggregate purchase price of \$21,581.37.

In March and August 2014, we issued and sold an aggregate of 15,750,000 shares of our Series A-3 preferred stock at a price per share of \$1.00, for an aggregate purchase price of \$15.75 million.

In October 2014, we issued and sold an aggregate of 16,893,931 shares of our Series B preferred stock at a price per share of \$3.1461, for an aggregate purchase price of \$53.1 million.

In January 2016, we issued and sold an aggregate of 12,714,150 shares of our Series B preferred stock at a price per share of \$3.1461, for an aggregate purchase price of \$40.0 million.

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

From January 1, 2013 through the date of the prospectus that is a part of this registration statement, we granted options to purchase an aggregate of 9,802,584 shares of common stock, with exercise prices ranging from \$0.27 to \$2.42 per share, to employees, directors, consultants and advisors pursuant to our 2012 equity incentive plan. From January 1, 2013 through the date of the prospectus that is a part of this registration statement, we issued an aggregate of 1,501,008 shares of common stock upon the exercise of options for aggregate consideration of \$0.4 million.

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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 and consultants, 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.

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 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 underwriter 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 SEC 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, as amended, 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 th day of _____, 2016.

SYROS PHARMACEUTICALS, INC.

By:

Nancy Simonian, M.D.
President, Chief Executive Officer and Director

SIGNATURES AND POWER OF ATTORNEY

We, the undersigned officers and directors of Syros Pharmaceuticals, Inc., hereby severally constitute and appoint Nancy Simonian, M.D., Kyle D. Kuvalanka and Jorge Conde, and each of them singly (with full power to each of them to act alone), our true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution in each of them for him and in his name, place and stead, and in any and all capacities, to sign any and all amendments (including post-effective amendments) to this registration statement (or any other registration statement for the same offering that is to be effective upon filing pursuant to Rule 462(b) under the Securities Act of 1933, as amended), 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 or necessary to be done in and about the premises, as full to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents or any of them, or their 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, as amended, this Registration Statement has been signed by the following persons in the capacities held on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
_____ Nancy Simonian, M.D.	President, Chief Executive Officer and Director (principal executive officer)	, 2016
_____ Jorge Conde	Chief Financial Officer (principal financial and principal accounting officer)	, 2016
_____ Stéphane Bancel	Director	, 2016
_____ Marsha H. Fanucci	Director	, 2016

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<u>Signature</u>	<u>Title</u>	<u>Date</u>
<hr/> Amir Nashat, Ph.D.	Director	, 2016
<hr/> Robert Nelsen	Director	, 2016
<hr/> Vicki L. Sato, Ph.D.	Director	, 2016
<hr/> Phillip A. Sharp, Ph.D.	Director	, 2016
<hr/> Richard A. Young, Ph.D.	Director	, 2016

EXHIBIT INDEX

Exhibit Number	Description of Exhibit
1.1*	Form of Underwriting Agreement
3.1**	Amended and Restated Certificate of Incorporation of the Registrant, as amended
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**	Second Amended and Restated Investors' Rights Agreement, dated as of October 9, 2014, as amended, among the Registrant and the other parties thereto
5.1*	Opinion of Wilmer Cutler Pickering Hale and Dorr LLP
10.1†	2012 Equity Incentive Plan, as amended
10.2**†	Form of Incentive Stock Option Agreement under 2012 Equity Incentive Plan
10.3**†	Form of Nonstatutory Stock Option Agreement under 2012 Equity Incentive Plan
10.4**†	Form of Restricted Stock Agreement under 2012 Equity Incentive Plan
10.5†	2016 Stock Incentive Plan
10.6†	Form of Incentive Stock Option Agreement under 2016 Stock Incentive Plan
10.7†	Form of Nonstatutory Stock Option Agreement under 2016 Stock Incentive Plan
10.8†	2016 Employee Stock Purchase Plan
10.9†	Offer Letter, dated November 13, 2012 and effective as of July 2, 2012, by and between the Registrant and Nancy Simonian, M.D., as amended
10.10†	Offer Letter, dated August 25, 2015, by and between the Registrant and Kyle D. Kovalanka, as amended
10.11†	Offer Letter, dated December 2, 2015, by and between the Registrant and David A. Roth, M.D., as amended
10.12	Form of Director and Officer Indemnification Agreement by and between the Registrant and each of Nancy Simonian, M.D., Jorge Conde, Jonathan Garen, Kyle D. Kovalanka, Eric R. Olson, David A. Roth, M.D., Stéphane Bancel, Marsha H. Fanucci, Amir Nashat, Ph.D., Robert Nelsen, Vicki L. Sato, Ph.D., Phillip A. Sharp, Ph.D. and Richard A. Young, Ph.D.
10.13**+	Exclusive License Agreement, by and between the Registrant and the Dana-Farber Cancer Institute, Inc., dated as of February 22, 2013
10.14**+	Exclusive Patent License Agreement, by and among the Registrant, the Whitehead Institute for Biomedical Research and the Dana-Farber Cancer Institute, dated as of April 1, 2013
10.15**+	Exclusive Patent License Agreement, by and between the Registrant and the Whitehead Institute for Biomedical Research, dated as of April 4, 2013

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<u>Exhibit Number</u>	<u>Description of Exhibit</u>
10.16**+	License Agreement, by and between the Registrant and TMRC Co., Ltd., dated as of September 11, 2015
10.17**	Lease, by and between the Registrant and 620 Memorial Leasehold LLC, dated as of March 13, 2015
21.1**	Subsidiaries of the Registrant
23.1*	Consent of Ernst & Young 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 filed.

+ Confidential treatment requested as to certain portions, which portions have been omitted and filed separately with the Securities and Exchange Commission.

† Indicates management contract or compensatory plan.

RESTATED CERTIFICATE OF INCORPORATION

OF

SYROS PHARMACEUTICALS, INC.

(originally incorporated on November 9, 2011 under the name LS22, Inc.)

FIRST: The name of the Corporation is Syros Pharmaceuticals, Inc.

SECOND: The address of the Corporation's registered office in the State of Delaware is Corporation Trust Center, 1209 Orange Street, in the City of Wilmington, County of New Castle, 19801. The name of its registered agent at that address is The Corporation Trust Company.

THIRD: The nature of the business or purposes to be conducted or promoted by the Corporation is to engage in any lawful act or activity for which corporations may be organized under the General Corporation Law of the State of Delaware.

FOURTH: The total number of shares of all classes of stock which the Corporation shall have authority to issue is 210,000,000 shares, consisting of (i) 200,000,000 shares of Common Stock, \$0.001 par value per share ("Common Stock"), and (ii) 10,000,000 shares of Preferred Stock, \$0.001 par value per share ("Preferred Stock").

The following is a statement of the designations and the powers, privileges and rights, and the qualifications, limitations or restrictions thereof in respect of each class of capital stock of the Corporation.

A. COMMON STOCK.

1. General. The voting, dividend and liquidation rights of the holders of the Common Stock are subject to and qualified by the rights of the holders of the Preferred Stock of any series as may be designated by the Board of Directors upon any issuance of the Preferred Stock of any series.

2. Voting. The holders of the Common Stock shall have voting rights at all meetings of stockholders, each such holder being entitled to one vote for each share thereof held by such holder; provided, however, that, except as otherwise required by law, holders of Common Stock shall not be entitled to vote on any amendment to this Certificate of Incorporation (which, as used herein, shall mean the certificate of incorporation of the Corporation, as amended from time to time, including the terms of any certificate of designations of any series of Preferred Stock) that relates solely to the terms of one or more outstanding series of Preferred Stock if the holders of such affected series are entitled, either separately or together as a class with the holders of one or more other such series, to vote thereon pursuant to this Certificate of Incorporation. There shall be no cumulative voting.

The number of authorized shares of Common Stock may be increased or decreased (but not below the number of shares thereof then outstanding) by the affirmative vote of the holders of a majority of the stock of the Corporation entitled to vote, irrespective of the provisions of Section 242(b)(2) of the General Corporation Law of the State of Delaware.

3. Dividends. Dividends may be declared and paid on the Common Stock from funds lawfully available therefor as and when determined by the Board of Directors and subject to any preferential dividend or other rights of any then outstanding Preferred Stock.

4. Liquidation. Upon the dissolution or liquidation of the Corporation, whether voluntary or involuntary, holders of Common Stock will be entitled to receive all assets of the Corporation available for distribution to its stockholders, subject to any preferential or other rights of any then outstanding Preferred Stock.

B. PREFERRED STOCK.

Preferred Stock may be issued from time to time in one or more series, each of such series to have such terms as stated or expressed herein and in the resolution or resolutions providing for the issue of such series adopted by the Board of Directors of the Corporation as hereinafter provided. Any shares of Preferred Stock which may be redeemed, purchased or acquired by the Corporation may be reissued except as otherwise provided by law.

Authority is hereby expressly granted to the Board of Directors from time to time to issue the Preferred Stock in one or more series, and in connection with the creation of any such series, by adopting a resolution or resolutions providing for the issuance of the shares thereof and by filing a certificate of designations relating thereto in accordance with the General Corporation Law of the State of Delaware, to determine and fix the number of shares of such series and such voting powers, full or limited, or no voting powers, and such designations, preferences and relative participating, optional or other special rights, and qualifications, limitations or restrictions thereof, including without limitation thereof, dividend rights, conversion rights, redemption privileges and liquidation preferences, as shall be stated and expressed in such resolutions, all to the full extent now or hereafter permitted by the General Corporation Law of the State of Delaware. Without limiting the generality of the foregoing, the resolutions providing for issuance of any series of Preferred Stock may provide that such series shall be superior or rank equally or be junior to any other series of Preferred Stock to the extent permitted by law.

The number of authorized shares of Preferred Stock may be increased or decreased (but not below the number of shares then outstanding) by the affirmative vote of the holders of a majority of the voting power of the capital stock of the Corporation entitled to vote thereon, voting as a single class, irrespective of the provisions of Section 242(b)(2) of the General Corporation Law of the State of Delaware.

FIFTH: Except as otherwise provided herein, the Corporation reserves the right to amend, alter, change or repeal any provision contained in this Certificate of Incorporation, in the manner now or hereafter prescribed by statute and this Certificate of Incorporation, and all rights conferred upon stockholders herein are granted subject to this reservation.

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SIXTH: In furtherance and not in limitation of the powers conferred upon it by the General Corporation Law of the State of Delaware, and subject to the terms of any series of Preferred Stock, the Board of Directors shall have the power to adopt, amend, alter or repeal the By-laws of the Corporation by the affirmative vote of a majority of the directors present at any regular or special meeting of the Board of Directors at which a quorum is present. The stockholders may not adopt, amend, alter or repeal the By-laws of the Corporation, or adopt any provision inconsistent therewith, unless such action is approved, in addition to any other vote required by this Certificate of Incorporation, by the affirmative vote of the holders of at least seventy-five percent (75%) of the votes that all the stockholders would be entitled to cast in any annual election of directors or class of directors. Notwithstanding any other provisions of law, this Certificate of Incorporation or the By-laws of the Corporation, and notwithstanding the fact that a lesser percentage may be specified by law, the affirmative vote of the holders of at least seventy-five percent (75%) of the votes which all the stockholders would be entitled to cast in any annual election of directors or class of directors shall be required to amend or repeal, or to adopt any provision inconsistent with, this Article SIXTH.

SEVENTH: 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, no director of the Corporation shall be personally liable to the Corporation or its stockholders for monetary damages for any breach of fiduciary duty as a director, notwithstanding any provision of law imposing such liability. No amendment to or repeal of this provision shall apply to or have any effect on the liability or alleged liability of any director of the Corporation for or with respect to any acts or omissions of such director occurring prior to such amendment or repeal. If the General Corporation Law of the State of Delaware is amended to permit further elimination or limitation of the personal liability of directors, then the liability of a director of the Corporation shall be eliminated or limited to the fullest extent permitted by the General Corporation Law of the State of Delaware as so amended.

EIGHTH: The Corporation shall provide indemnification as follows:

1. Actions, Suits and Proceedings Other than by or in the Right of the Corporation. The Corporation shall indemnify each person who was or is a party or threatened to be made a party to 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 the Corporation) by reason of the fact that he or she is or was, or has agreed to become, a director or officer of the Corporation, or is or was serving, or has agreed to serve, at the request of the Corporation, as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan) (all such persons being referred to hereafter 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), liabilities, losses, judgments, fines (including excise taxes and penalties arising under the Employee Retirement Income Security Act of 1974), and amounts paid in settlement actually and reasonably incurred by or on behalf of Indemnitee in connection with such action, suit or proceeding and any appeal therefrom, if Indemnitee acted in good faith and in a manner which Indemnitee reasonably believed to be in, or not opposed to, the best interests of the Corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful. The termination of any action, suit or proceeding by judgment, order,

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settlement, conviction or upon a plea of nolo contendere or its equivalent, shall not, of itself, create a presumption that Indemnitee did not act in good faith and in a manner which Indemnitee reasonably believed to be in, or not opposed to, the best interests of the Corporation, and, with respect to any criminal action or proceeding, had reasonable cause to believe that his or her conduct was unlawful.

2. Actions or Suits by or in the Right of the Corporation. The Corporation shall indemnify any Indemnitee who was or is a party to or threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the Corporation to procure a judgment in its favor by reason of the fact that Indemnitee is or was, or has agreed to become, a director or officer of the Corporation, or is or was serving, or has agreed to serve, at the request of the Corporation, as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan), 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 by or on behalf of Indemnitee in connection with such action, suit or proceeding and any appeal therefrom, if Indemnitee acted in good faith and in a manner which Indemnitee reasonably believed to be in, or not opposed to, the best interests of the Corporation, except that no indemnification shall be made under this Section 2 in respect of any claim, issue or matter as to which Indemnitee shall have been adjudged to be liable to the Corporation, unless, and only to the extent, that the Court of Chancery of Delaware or the court in which such action or suit was brought shall determine upon application that, despite the adjudication of such liability but in view of all the circumstances of the case, Indemnitee is fairly and reasonably entitled to indemnity for such expenses (including attorneys' fees) which the Court of Chancery of Delaware or such other court shall deem proper.

3. Indemnification for Expenses of Successful Party. Notwithstanding any other provisions of this Article EIGHTH, to the extent that an Indemnitee has been successful, on the merits or otherwise, in defense of any action, suit or proceeding referred to in Sections 1 and 2 of this Article EIGHTH, or in defense of any claim, issue or matter therein, or on appeal from any such action, suit or proceeding, Indemnitee shall be indemnified against all expenses (including attorneys' fees) actually and reasonably incurred by or on behalf of Indemnitee in connection therewith. Without limiting the foregoing, if any action, suit or proceeding is disposed of, on the merits or otherwise (including a disposition without prejudice), without (i) the disposition being adverse to Indemnitee, (ii) an adjudication that Indemnitee was liable to the Corporation, (iii) a plea of guilty or nolo contendere by Indemnitee, (iv) an adjudication that Indemnitee did not act 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 (v) with respect to any criminal proceeding, an adjudication that Indemnitee had reasonable cause to believe his or her conduct was unlawful, Indemnitee shall be considered for the purposes hereof to have been wholly successful with respect thereto.

4. Notification and Defense of Claim. As a condition precedent to an Indemnitee's right to be indemnified, such Indemnitee must notify the Corporation in writing as soon as practicable of any action, suit, proceeding or investigation involving such Indemnitee for which indemnity will or could be sought. With respect to any action, suit, proceeding or investigation of which the Corporation is so notified, the Corporation will be entitled to participate therein at its own expense and/or to assume the defense thereof at its own expense, with legal counsel

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reasonably acceptable to Indemnitee. After notice from the Corporation to Indemnitee of its election so to assume such defense, the Corporation shall not be liable to Indemnitee for any legal or other expenses subsequently incurred by Indemnitee in connection with such action, suit, proceeding or investigation, other than as provided below in this Section 4. Indemnitee shall have the right to employ his or her own counsel in connection with such action, suit, proceeding or investigation, but the fees and expenses of such counsel incurred after notice from the Corporation of its assumption of the defense thereof shall be at the expense of Indemnitee unless (i) the employment of counsel by Indemnitee has been authorized by the Corporation, (ii) counsel to Indemnitee shall have reasonably concluded that there may be a conflict of interest or position on any significant issue between the Corporation and Indemnitee in the conduct of the defense of such action, suit, proceeding or investigation or (iii) the Corporation shall not in fact have employed counsel to assume the defense of such action, suit, proceeding or investigation, in each of which cases the fees and expenses of counsel for Indemnitee shall be at the expense of the Corporation, except as otherwise expressly provided by this Article EIGHTH. The Corporation shall not be entitled, without the consent of Indemnitee, to assume the defense of any claim brought by or in the right of the Corporation or as to which counsel for Indemnitee shall have reasonably made the conclusion provided for in clause (ii) above. The Corporation shall not be required to indemnify Indemnitee under this Article EIGHTH for any amounts paid in settlement of any action, suit, proceeding or investigation effected without its written consent. The Corporation shall not settle any action, suit, proceeding or investigation in any manner which would impose any penalty or limitation on Indemnitee without Indemnitee's written consent. Neither the Corporation nor Indemnitee will unreasonably withhold or delay its consent to any proposed settlement.

5. Advance of Expenses. Subject to the provisions of Section 6 of this Article EIGHTH, in the event of any threatened or pending action, suit, proceeding or investigation of which the Corporation receives notice under this Article EIGHTH, any expenses (including attorneys' fees) incurred by or on behalf of Indemnitee in defending an action, suit, proceeding or investigation or any appeal therefrom shall be paid by the Corporation in advance of the final disposition of such matter; provided, however, that the payment of such expenses incurred by or on behalf of Indemnitee in advance of the final disposition of such matter shall be made only upon receipt of an undertaking by or on behalf of Indemnitee to repay all amounts so advanced in the event that it shall ultimately be determined by final judicial decision from which there is no further right to appeal that Indemnitee is not entitled to be indemnified by the Corporation as authorized in this Article EIGHTH; and provided further that no such advancement of expenses shall be made under this Article EIGHTH if it is determined (in the manner described in Section 6 of this Article EIGHTH) that (i) Indemnitee did not act 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, or (ii) with respect to any criminal action or proceeding, Indemnitee had reasonable cause to believe his or her conduct was unlawful. Such undertaking shall be accepted without reference to the financial ability of Indemnitee to make such repayment.

6. Procedure for Indemnification and Advancement of Expenses. In order to obtain indemnification or advancement of expenses pursuant to Section 1, 2, 3 or 5 of this Article EIGHTH, an Indemnitee shall submit to the Corporation a written request. Any such advancement of expenses shall be made promptly, and in any event within 60 days after receipt by the Corporation of the written request of Indemnitee, unless (i) the Corporation has assumed

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the defense pursuant to Section 4 of this Article EIGHTH (and none of the circumstances described in Section 4 of this Article EIGHTH that would nonetheless entitle the Indemnitee to indemnification for the fees and expenses of separate counsel have occurred) or (ii) the Corporation determines within such 60-day period that Indemnitee did not meet the applicable standard of conduct set forth in Section 1, 2 or 5 of this Article EIGHTH, as the case may be. Any such indemnification, unless ordered by a court, shall be made with respect to requests under Section 1 or 2 only as authorized in the specific case upon a determination by the Corporation that the indemnification of Indemnitee is proper because Indemnitee has met the applicable standard of conduct set forth in Section 1 or 2 of this Article EIGHTH, as the case may be. Such determination shall be made in each instance (a) by a majority vote of the directors of the Corporation consisting of persons who are not at that time parties to the action, suit or proceeding in question ("disinterested directors"), whether or not a quorum, (b) by a committee of disinterested directors designated by majority vote of disinterested directors, whether or not a quorum, (c) if there are no disinterested directors, or if the disinterested directors so direct, by independent legal counsel (who may, to the extent permitted by law, be regular legal counsel to the Corporation) in a written opinion, or (d) by the stockholders of the Corporation.

7. Remedies. The right to indemnification or advancement of expenses as granted by this Article EIGHTH shall be enforceable by Indemnitee in any court of competent jurisdiction. Neither the failure of the Corporation to have made a determination prior to the commencement of such action that indemnification is proper in the circumstances because Indemnitee has met the applicable standard of conduct, nor an actual determination by the Corporation pursuant to Section 6 of this Article EIGHTH that Indemnitee has not met such applicable standard of conduct, shall be a defense to the action or create a presumption that Indemnitee has not met the applicable standard of conduct. In any suit brought by Indemnitee to enforce a right to indemnification, or brought by the Corporation to recover an advancement of expenses pursuant to the terms of an undertaking, the Corporation shall have the burden of proving that Indemnitee is not entitled to be indemnified, or to such advancement of expenses, under this Article EIGHTH. Indemnitee's expenses (including attorneys' fees) reasonably incurred in connection with successfully establishing Indemnitee's right to indemnification, in whole or in part, in any such proceeding shall also be indemnified by the Corporation. Notwithstanding the foregoing, in any suit brought by Indemnitee to enforce a right to indemnification hereunder it shall be a defense that the Indemnitee has not met any applicable standard for indemnification set forth in the General Corporation Law of the State of Delaware.

8. Limitations. Notwithstanding anything to the contrary in this Article EIGHTH, except as set forth in Section 7 of this Article EIGHTH, the Corporation shall not indemnify an Indemnitee pursuant to this Article EIGHTH in connection with a proceeding (or part thereof) initiated by such Indemnitee unless the initiation thereof was approved by the Board of Directors of the Corporation. Notwithstanding anything to the contrary in this Article EIGHTH, the Corporation shall not indemnify an Indemnitee to the extent such Indemnitee is reimbursed from the proceeds of insurance, and in the event the Corporation makes any indemnification payments to an Indemnitee and such Indemnitee is subsequently reimbursed from the proceeds of insurance, such Indemnitee shall promptly refund indemnification payments to the Corporation to the extent of such insurance reimbursement.

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9. Subsequent Amendment. No amendment, termination or repeal of this Article EIGHTH or of the relevant provisions of the General Corporation Law of the State of Delaware or any other applicable laws shall adversely affect or diminish in any way the rights of any Indemnitee to indemnification under the provisions hereof with respect to any action, suit, proceeding or investigation arising out of or relating to any actions, transactions or facts occurring prior to the final adoption of such amendment, termination or repeal.

10. Other Rights. The indemnification and advancement of expenses provided by this Article EIGHTH shall not be deemed exclusive of any other rights to which an Indemnitee seeking indemnification or advancement of expenses may be entitled under any law (common or statutory), agreement or vote of stockholders or disinterested directors or otherwise, both as to action in Indemnitee's official capacity and as to action in any other capacity while holding office for the Corporation, and shall continue as to an Indemnitee who has ceased to be a director or officer, and shall inure to the benefit of the estate, heirs, executors and administrators of Indemnitee. Nothing contained in this Article EIGHTH shall be deemed to prohibit, and the Corporation is specifically authorized to enter into, agreements with officers and directors providing indemnification rights and procedures different from those set forth in this Article EIGHTH. In addition, the Corporation may, to the extent authorized from time to time by its Board of Directors, grant indemnification rights to other employees or agents of the Corporation or other persons serving the Corporation and such rights may be equivalent to, or greater or less than, those set forth in this Article EIGHTH.

11. Partial Indemnification. If an Indemnitee is entitled under any provision of this Article EIGHTH to indemnification by the Corporation for some or a portion of the expenses (including attorneys' fees), liabilities, losses, judgments, fines (including excise taxes and penalties arising under the Employee Retirement Income Security Act of 1974) or amounts paid in settlement actually and reasonably incurred by or on behalf of Indemnitee in connection with any action, suit, proceeding or investigation and any appeal therefrom but not, however, for the total amount thereof, the Corporation shall nevertheless indemnify Indemnitee for the portion of such expenses (including attorneys' fees), liabilities, losses, judgments, fines (including excise taxes and penalties arising under the Employee Retirement Income Security Act of 1974) or amounts paid in settlement to which Indemnitee is entitled.

12. Insurance. The Corporation may purchase and maintain insurance, at its expense, to protect itself and any director, officer, employee or agent of the Corporation or another corporation, partnership, joint venture, trust or other enterprise (including any employee benefit plan) against any expense, liability or loss incurred by him or her in any such capacity, or arising out of his or her status as such, whether or not the Corporation would have the power to indemnify such person against such expense, liability or loss under the General Corporation Law of the State of Delaware.

13. Savings Clause. If this Article EIGHTH or any portion hereof shall be invalidated on any ground by any court of competent jurisdiction, then the Corporation shall nevertheless indemnify each Indemnitee as to any expenses (including attorneys' fees), liabilities, losses, judgments, fines (including excise taxes and penalties arising under the Employee Retirement Income Security Act of 1974) and amounts paid in settlement in connection with any action, suit, proceeding or investigation, whether civil, criminal or administrative, including an action by or

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in the right of the Corporation, to the fullest extent permitted by any applicable portion of this Article EIGHTH that shall not have been invalidated and to the fullest extent permitted by applicable law.

14. Definitions. Terms used herein and defined in Section 145(h) and Section 145(i) of the General Corporation Law of the State of Delaware shall have the respective meanings assigned to such terms in such Section 145(h) and Section 145(i).

NINTH: This Article NINTH is inserted for the management of the business and for the conduct of the affairs of the Corporation.

1. General Powers. The business and affairs of the Corporation shall be managed by or under the direction of the Board of Directors.
2. Number of Directors; Election of Directors. Subject to the rights of holders of any series of Preferred Stock to elect directors, the number of directors of the Corporation shall be established by the Board of Directors. Election of directors need not be by written ballot, except as and to the extent provided in the By-laws of the Corporation.
3. Classes of Directors. Subject to the rights of holders of any series of Preferred Stock to elect directors, the Board of Directors shall be and is divided into three classes, designated Class I, Class II and Class III. Each class shall consist, as nearly as may be possible, of one-third of the total number of directors constituting the entire Board of Directors. The Board of Directors is authorized to assign members of the Board of Directors already in office to Class I, Class II or Class III at the time such classification becomes effective.
4. Terms of Office. Subject to the rights of holders of any series of Preferred Stock to elect directors, each director shall serve for a term ending on the date of the third annual meeting of stockholders following the annual meeting of stockholders at which such director was elected; provided that each director initially assigned to Class I shall serve for a term expiring at the Corporation's first annual meeting of stockholders held after the effectiveness of this Restated Certificate of Incorporation; each director initially assigned to Class II shall serve for a term expiring at the Corporation's second annual meeting of stockholders held after the effectiveness of this Restated Certificate of Incorporation; and each director initially assigned to Class III shall serve for a term expiring at the Corporation's third annual meeting of stockholders held after the effectiveness of this Restated Certificate of Incorporation; provided further, that the term of each director shall continue until the election and qualification of his or her successor and be subject to his or her earlier death, resignation or removal.
5. Quorum. The greater of (a) a majority of the directors at any time in office and (b) one-third of the number of directors fixed pursuant to Section 2 of this Article NINTH shall constitute a quorum of the Board of Directors. If at any meeting of the Board of Directors there shall be less than such a quorum, a majority of the directors present may adjourn the meeting from time to time without further notice other than announcement at the meeting, until a quorum shall be present.
6. Action at Meeting. Every act or decision done or made by a majority of the directors present at a meeting duly held at which a quorum is present shall be regarded as the act

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of the Board of Directors unless a greater number is required by law or by this Certificate of Incorporation.

7. Removal. Subject to the rights of holders of any series of Preferred Stock, directors of the Corporation may be removed only for cause and only by the affirmative vote of the holders of at least seventy-five percent (75%) of the votes which all the stockholders would be entitled to cast in any annual election of directors or class of directors.
8. Vacancies. Subject to the rights of holders of any series of Preferred Stock, any vacancy or newly created directorship in the Board of Directors, however occurring, shall be filled only by vote of a majority of the directors then in office, although less than a quorum, or by a sole remaining director and shall not be filled by the stockholders. A director elected to fill a vacancy shall hold office until the next election of the class for which such director shall have been chosen, subject to the election and qualification of a successor and to such director's earlier death, resignation or removal.
9. Stockholder Nominations and Introduction of Business, Etc. Advance notice of stockholder nominations for election of directors and other business to be brought by stockholders before a meeting of stockholders shall be given in the manner provided by the By-laws of the Corporation.
10. Amendments to Article. Notwithstanding any other provisions of law, this Certificate of Incorporation or the By-laws of the Corporation, and notwithstanding the fact that a lesser percentage may be specified by law, the affirmative vote of the holders of at least seventy-five percent (75%) of the votes which all the stockholders would be entitled to cast in any annual election of directors or class of directors shall be required to amend or repeal, or to adopt any provision inconsistent with, this Article NINTH.

TENTH: Stockholders of the Corporation may not take any action by written consent in lieu of a meeting. Notwithstanding any other provisions of law, this Certificate of Incorporation or the By-laws of the Corporation, and notwithstanding the fact that a lesser percentage may be specified by law, the affirmative vote of the holders of at least seventy-five percent (75%) of the votes which all the stockholders would be entitled to cast in any annual election of directors or class of directors shall be required to amend or repeal, or to adopt any provision inconsistent with, this Article TENTH.

ELEVENTH: Special meetings of stockholders for any purpose or purposes may be called at any time by only the Board of Directors, the Chairman of the Board or the Chief Executive Officer, and may not be called by any other person or persons. Business transacted at any special meeting of stockholders shall be limited to matters relating to the purpose or purposes stated in the notice of meeting. Notwithstanding any other provisions of law, this Certificate of Incorporation or the By-laws of the Corporation, and notwithstanding the fact that a lesser percentage may be specified by law, the affirmative vote of the holders of at least seventy-five percent (75%) of the votes which all the stockholders would be entitled to cast in any annual election of directors or class of directors shall be required to amend or repeal, or to adopt any provision inconsistent with, this Article ELEVENTH.

IN WITNESS WHEREOF, this Restated Certificate of Incorporation, which restates, integrates and amends the certificate of incorporation of the Corporation, and which has been duly adopted in accordance with Sections 228, 242 and 245 of the General Corporation Law of the State of Delaware, has been executed by its duly authorized officer this [] day of [], 201[].

SYROS PHARMACEUTICALS, INC.

By: _____

Name: Nancy Simonian, M.D.

Title: President and Chief Executive Officer

AMENDED AND RESTATED BY-LAWS
OF
SYROS PHARMACEUTICALS, INC.

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ARTICLE I
STOCKHOLDERS

1.1 Place of Meetings. All meetings of stockholders shall be held at such place as may be designated from time to time by the Board of Directors, the Chairman of the Board, the Chief Executive Officer or the President or, if not so designated, at the principal office of the corporation.

1.2 Annual Meeting. The annual meeting of stockholders for the election of directors to succeed those whose terms expire and for the transaction of such other business as may properly be brought before the meeting shall be held on a date and at a time designated by the Board of Directors, the Chairman of the Board, the Chief Executive Officer or the President. The corporation may postpone, reschedule or cancel any previously scheduled annual meeting of stockholders.

1.3 Special Meetings. Special meetings of stockholders for any purpose or purposes may be called at any time by only the Board of Directors, the Chairman of the Board or the Chief Executive Officer, and may not be called by any other person or persons. Business transacted at any special meeting of stockholders shall be limited to matters relating to the purpose or purposes stated in the notice of meeting. The corporation may postpone, reschedule or cancel any previously scheduled special meeting of stockholders.

1.4 Notice of Meetings. Except as otherwise provided by law, the Certificate of Incorporation or these By-laws, notice of each meeting of stockholders, whether annual or special, shall be given not less than 10 nor more than 60 days before the date of the meeting to each stockholder entitled to vote at such meeting. Without limiting the manner by which notice otherwise may be given to stockholders, any notice shall be effective if given by a form of electronic transmission consented to (in a manner consistent with the General Corporation Law of the State of Delaware) by the stockholder to whom the notice is given. The notices of all meetings shall state the place, date and time of the meeting and the means of remote communications, if any, by which stockholders and proxyholders may be deemed to be present in person and vote at such meeting. The notice of a special meeting shall state, in addition, the

purpose or purposes for which the meeting is called. If notice is given by mail, such notice shall be deemed given when deposited in the United States mail, postage prepaid, directed to the stockholder at such stockholder's address as it appears on the records of the corporation. If notice is given by electronic transmission, such notice shall be deemed given at the time specified in Section 232 of the General Corporation Law of the State of Delaware.

1.5 Voting List. The Secretary shall prepare, at least 10 days before every meeting of stockholders, a complete list of the stockholders entitled to vote at the meeting, arranged in alphabetical order, and showing the address of each stockholder and the number of shares registered in the name of each stockholder. Such list shall be open to the examination of any stockholder, for any purpose germane to the meeting, for a period of at least 10 days prior to the meeting: (a) on a reasonably accessible electronic network, provided that the information required to gain access to such list is provided with the notice of the meeting, or (b) during ordinary business hours, at the principal place of business of the corporation. The list shall also be produced and kept at the time and place of the meeting during the whole time thereof, and may be examined by any stockholder who is present. Except as otherwise provided by law, the stock ledger shall be the only evidence as to who are the stockholders entitled to examine the list of stockholders required by this Section 1.5 or to vote in person or by proxy at any meeting of stockholders.

1.6 Quorum. Except as otherwise provided by law, the Certificate of Incorporation or these By-laws, the holders of a majority in voting power of the shares of the capital stock of the corporation issued and outstanding and entitled to vote at the meeting, present in person, present by means of remote communication in a manner, if any, authorized by the Board of Directors in its sole discretion, or represented by proxy, shall constitute a quorum for the transaction of business; provided, however, that where a separate vote by a class or classes or series of capital stock is required by law or the Certificate of Incorporation, the holders of a majority in voting power of the shares of such class or classes or series of the capital stock of the corporation issued and outstanding and entitled to vote on such matter, present in person, present by means of remote communication in a manner, if any, authorized by the Board of Directors in its sole discretion, or represented by proxy, shall constitute a quorum entitled to take action with respect

to the vote on such matter. A quorum, once established at a meeting, shall not be broken by the withdrawal of enough votes to leave less than a quorum.

1.7 Adjournments. Any meeting of stockholders may be adjourned from time to time to any other time and to any other place at which a meeting of stockholders may be held under these By-laws by the chairman of the meeting or by the stockholders present

or represented at the meeting and entitled to vote, although less than a quorum. It shall not be necessary to notify any stockholder of any adjournment of less than 30 days if the time and place of the adjourned meeting, and the means of remote communication, if any, by which stockholders and proxyholders may be deemed to be present in person and vote at such adjourned meeting, are announced at the meeting at which adjournment is taken, unless after the adjournment a new record date is fixed for the adjourned meeting. At the adjourned meeting, the corporation may transact any business which might have been transacted at the original meeting.

1.8 Voting and Proxies. Each stockholder shall have one vote for each share of stock entitled to vote held of record by such stockholder and a proportionate vote for each fractional share so held, unless otherwise provided by law or the Certificate of Incorporation. Each stockholder of record entitled to vote at a meeting of stockholders may vote in person (including by means of remote communications, if any, by which stockholders may be deemed to be present in person and vote at such meeting) or may authorize another person or persons to vote for such stockholder by a proxy executed or transmitted in a manner permitted by the General Corporation Law of the State of Delaware by the stockholder or such stockholder's authorized agent and delivered (including by electronic transmission) to the Secretary of the corporation. No such proxy shall be voted upon after three years from the date of its execution, unless the proxy expressly provides for a longer period.

1.9 Action at Meeting. When a quorum is present at any meeting, any matter other than the election of directors to be voted upon by the stockholders at such meeting shall be decided by the vote of the holders of shares of stock having a majority in voting power of the votes cast by the holders of all of the shares of stock present or represented at the meeting and voting affirmatively or negatively on such matter (or if there are two or more classes or series of stock entitled to vote as separate classes, then in the case of each such class or series, the holders

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of a majority in voting power of the shares of stock of that class or series present or represented at the meeting and voting affirmatively or negatively on such matter), except when a different vote is required by law, the Certificate of Incorporation or these By-laws. When a quorum is present at any meeting, any election by stockholders of directors shall be determined by a plurality of the votes cast by the stockholders entitled to vote on the election.

1.10 Nomination of Directors.

(a) Except for (1) any directors entitled to be elected by the holders of preferred stock, (2) any directors elected in accordance with Section 2.9 hereof by the Board of Directors to fill a vacancy or newly-created directorship or (3) as otherwise required by applicable law or stock exchange regulation, at any meeting of stockholders, only persons who are nominated in accordance with the procedures in this Section 1.10 shall be eligible for election as directors. Nomination for election to the Board of Directors at a meeting of stockholders may be made (i) by or at the direction of the Board of Directors or (ii) by any stockholder of the corporation who (x) timely complies with the notice procedures in Section 1.10(b), (y) is a stockholder of record on the date of the giving of such notice and on the record date for the determination of stockholders entitled to vote at such meeting and (z) is entitled to vote at such meeting.

(b) To be timely, a stockholder's notice must be received in writing by the Secretary at the principal executive offices of the corporation as follows: (i) in the case of an election of directors at an annual meeting of stockholders, not less than 90 days nor more than 120 days prior to the first anniversary of the preceding year's annual meeting; provided, however, that (x) in the case of the annual meeting of stockholders of the corporation to be held in 2017 or (y) in the event that the date of the annual meeting in any other year is advanced by more than 30 days, or delayed by more than 60 days, from the first anniversary of the preceding year's annual meeting, a stockholder's notice must be so received not earlier than the 120th day prior to such annual meeting and not later than the close of business on the later of (A) the 90th day prior to such annual meeting and (B) the tenth day following the day on which notice of the date of such annual meeting was mailed or public disclosure of the date of such annual meeting was made, whichever first occurs; or (ii) in the case of an election of directors at a special

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meeting of stockholders, provided that the Board of Directors, the Chairman of the Board or the Chief Executive Officer has determined, in accordance with Section 1.3, that directors shall be elected at such special meeting and provided further that the nomination made by the stockholder is for one of the director positions that the Board of Directors, the Chairman of the Board or the Chief Executive Officer, as the case may be, has determined will be filled at such special meeting, not earlier than the 120th day prior to such special meeting and not later than the close of business on the later of (x) the 90th day prior to such special meeting and (y) the tenth day following the day on which notice of the date of such special meeting was mailed or public disclosure of the date of such special meeting was made, whichever first occurs. In no event shall the adjournment or postponement of a meeting (or the public disclosure thereof) commence a new time period (or extend any time period) for the giving of a stockholder's notice.

The stockholder's notice to the Secretary shall set forth: (A) as to each proposed nominee (1) such person's name, age, business address and, if known, residence address, (2) such person's principal occupation or employment, (3) the class and series and number of shares of stock of the corporation that are, directly or indirectly, owned, beneficially or of record, by such person, (4) a description of all direct and indirect compensation and other material monetary agreements, arrangements and understandings during the past three years, and any other material relationships, between or among (x) the stockholder, the beneficial owner, if any, on whose behalf the nomination is being made and the respective affiliates and associates of, or others acting in concert with, such stockholder and such beneficial owner, on the one hand, and (y) each proposed nominee, and his or her respective affiliates and associates, or others acting in concert with such nominee(s), on the other hand, including all information that would be required to be disclosed pursuant to Item 404 of Regulation S-K if the stockholder making the nomination and any beneficial owner on whose behalf the nomination is made or any affiliate or associate

thereof or person acting in concert therewith were the “registrant” for purposes of such Item and the proposed nominee were a director or executive officer of such registrant, and (5) any other information concerning such person that must be disclosed as to nominees in proxy solicitations pursuant to Regulation 14A under the Securities Exchange Act of 1934, as amended (the “Exchange Act”); and (B) as to the stockholder giving the notice and the beneficial owner, if any, on whose behalf the nomination is being made (1) the name and address of such

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stockholder, as they appear on the corporation’s books, and of such beneficial owner, (2) the class and series and number of shares of stock of the corporation that are, directly or indirectly, owned, beneficially or of record, by such stockholder and such beneficial owner, (3) a description of any agreement, arrangement or understanding between or among such stockholder and/or such beneficial owner and each proposed nominee and any other person or persons (including their names) pursuant to which the nomination(s) are being made or who may participate in the solicitation of proxies in favor of electing such nominee(s), (4) a description of any agreement, arrangement or understanding (including any derivative or short positions, swaps, profit interests, options, warrants, convertible securities, stock appreciation or similar rights, hedging transactions, and borrowed or loaned shares) that has been entered into by, or on behalf of, such stockholder or such beneficial owner, the effect or intent of which is to mitigate loss to, manage risk or benefit of share price changes for, or increase or decrease the voting power of, such stockholder or such beneficial owner with respect to shares of stock of the corporation, (5) any other information relating to such stockholder and such beneficial owner that would be required to be disclosed in a proxy statement or other filings required to be made in connection with solicitations of proxies for the election of directors in a contested election pursuant to Section 14 of the Exchange Act and the rules and regulations promulgated thereunder, (6) a representation that such stockholder intends to appear in person or by proxy at the meeting to nominate the person(s) named in its notice and (7) a representation whether such stockholder and/or such beneficial owner intends or is part of a group which intends (x) to deliver a proxy statement and/or form of proxy to holders of at least the percentage of the corporation’s outstanding capital stock reasonably believed by such stockholder or such beneficial owner to be sufficient to elect the nominee (and such representation shall be included in any such proxy statement and form of proxy) and/or (y) otherwise to solicit proxies or votes from stockholders in support of such nomination (and such representation shall be included in any such solicitation materials). Not later than 10 days after the record date for the meeting, the information required by Items (A)(1)-(5) and (B)(1)-(5) of the prior sentence shall be supplemented by the stockholder giving the notice to provide updated information as of the record date. In addition, to be effective, the stockholder’s notice must be accompanied by the written consent of the proposed nominee to serve as a director if elected. The corporation may require any proposed nominee to furnish such other information as the corporation may

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reasonably require to determine the eligibility of such proposed nominee to serve as a director of the corporation or whether such nominee would be independent under applicable Securities and Exchange Commission and stock exchange rules and the corporation’s publicly disclosed corporate governance guidelines. A stockholder shall not have complied with this Section 1.10(b) if the stockholder (or beneficial owner, if any, on whose behalf the nomination is made) solicits or does not solicit, as the case may be, proxies or votes in support of such stockholder’s nominee in contravention of the representations with respect thereto required by this Section 1.10.

(c) The chairman of any meeting shall have the power and duty to determine whether a nomination was made in accordance with the provisions of this Section 1.10 (including whether the stockholder or beneficial owner, if any, on whose behalf the nomination is made solicited (or is part of a group which solicited) or did not so solicit, as the case may be, proxies in support of such stockholder’s nominee in compliance with the representations with respect thereto required by this Section 1.10), and if the chairman should determine that a nomination was not made in accordance with the provisions of this Section 1.10, the chairman shall so declare to the meeting and such nomination shall not be brought before the meeting.

(d) Except as otherwise required by law, nothing in this Section 1.10 shall obligate the corporation or the Board of Directors to include in any proxy statement or other stockholder communication distributed on behalf of the corporation or the Board of Directors information with respect to any nominee for director submitted by a stockholder.

(e) Notwithstanding the foregoing provisions of this Section 1.10, unless otherwise required by law, if the stockholder (or a qualified representative of the stockholder) does not appear at the meeting to present a nomination, such nomination shall not be brought before the meeting, notwithstanding that proxies in respect of such nominee may have been received by the corporation. For purposes of this Section 1.10, to be considered a “qualified representative of the stockholder”, a person must be authorized by a written instrument executed by such stockholder or an electronic transmission delivered by such stockholder to act for such stockholder as proxy at the meeting of stockholders and such person must produce

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such written instrument or electronic transmission, or a reliable reproduction of the written instrument or electronic transmission, at the meeting of stockholders.

(f) For purposes of this Section 1.10, “public disclosure” shall include disclosure in a press release reported by the Dow Jones News Service, Associated Press or comparable national news service or in a document publicly filed by the corporation with the Securities and Exchange Commission pursuant to Section 13, 14 or 15(d) of the Exchange Act.

1.11 Notice of Business at Annual Meetings.

(a) At any annual meeting of the stockholders, only such business shall be conducted as shall have been properly brought before the meeting. To be properly brought before an annual meeting, business must be (1) specified in the notice of meeting (or any supplement thereto) given by or at the direction of the Board of Directors, (2) otherwise properly brought before the meeting by or at the direction of the Board of Directors, or (3) properly brought before the meeting by a stockholder. For business to be properly brought before an annual meeting by a stockholder, (i) if such business relates to the nomination of a person for election as a director of the corporation, the procedures in Section 1.10 must be complied with and (ii) if such business relates to any other matter, the business must constitute a proper matter under Delaware law for stockholder action and the stockholder must (x) have given timely notice thereof in writing to the Secretary in accordance with the procedures in Section 1.11(b), (y) be a stockholder of record on the date of the giving of such notice and on the record date for the determination of stockholders entitled to vote at such annual meeting and (z) be entitled to vote at such annual meeting.

(b) To be timely, a stockholder's notice must be received in writing by the Secretary at the principal executive offices of the corporation not less than 90 days nor more than 120 days prior to the first anniversary of the preceding year's annual meeting; provided, however, that (x) in the case of the annual meeting of stockholders of the corporation to be held in 2017 or (y) in the event that the date of the annual meeting in any other year is advanced by more than 30 days, or delayed by more than 60 days, from the first anniversary of the preceding year's annual meeting, a stockholder's notice must be so received not earlier than the 120th day prior to such annual meeting and not later than the close of business on the later of (A) the 90th

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day prior to such annual meeting and (B) the tenth day following the day on which notice of the date of such annual meeting was mailed or public disclosure of the date of such annual meeting was made, whichever first occurs. In no event shall the adjournment or postponement of an annual meeting (or the public disclosure thereof) commence a new time period (or extend any time period) for the giving of a stockholder's notice.

The stockholder's notice to the Secretary shall set forth: (A) as to each matter the stockholder proposes to bring before the annual meeting (1) a brief description of the business desired to be brought before the annual meeting, (2) the text of the proposal (including the exact text of any resolutions proposed for consideration and, in the event that such business includes a proposal to amend the By-laws, the exact text of the proposed amendment), and (3) the reasons for conducting such business at the annual meeting, and (B) as to the stockholder giving the notice and the beneficial owner, if any, on whose behalf the proposal is being made (1) the name and address of such stockholder, as they appear on the corporation's books, and of such beneficial owner, (2) the class and series and number of shares of stock of the corporation that are, directly or indirectly, owned, beneficially or of record, by such stockholder and such beneficial owner, (3) a description of any material interest of such stockholder or such beneficial owner and the respective affiliates and associates of, or others acting in concert with, such stockholder or such beneficial owner in such business, (4) a description of any agreement, arrangement or understanding between or among such stockholder and/or such beneficial owner and any other person or persons (including their names) in connection with the proposal of such business or who may participate in the solicitation of proxies in favor of such proposal, (5) a description of any agreement, arrangement or understanding (including any derivative or short positions, swaps, profit interests, options, warrants, convertible securities, stock appreciation or similar rights, hedging transactions, and borrowed or loaned shares) that has been entered into by, or on behalf of, such stockholder or such beneficial owner, the effect or intent of which is to mitigate loss to, manage risk or benefit of share price changes for, or increase or decrease the voting power of, such stockholder or such beneficial owner with respect to shares of stock of the corporation, (6) any other information relating to such stockholder and such beneficial owner that would be required to be disclosed in a proxy statement or other filings required to be made in connection with solicitations of proxies for the business proposed pursuant to Section 14 of the Exchange Act and the rules and regulations promulgated thereunder, (7) a representation that

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such stockholder intends to appear in person or by proxy at the annual meeting to bring such business before the meeting and (8) a representation whether such stockholder and/or such beneficial owner intends or is part of a group which intends (x) to deliver a proxy statement and/or form of proxy to holders of at least the percentage of the corporation's outstanding capital stock required to approve or adopt the proposal (and such representation shall be included in any such proxy statement and form of proxy) and/or (y) otherwise to solicit proxies or votes from stockholders in support of such proposal (and such representation shall be included in any such solicitation materials). Not later than 10 days after the record date for the meeting, the information required by Items (A)(3) and (B)(1)-(6) of the prior sentence shall be supplemented by the stockholder giving the notice to provide updated information as of the record date. Notwithstanding anything in these By-laws to the contrary, no business shall be conducted at any annual meeting of stockholders except in accordance with the procedures in this Section 1.11; provided that any stockholder proposal which complies with Rule 14a-8 of the proxy rules (or any successor provision) promulgated under the Exchange Act and is to be included in the corporation's proxy statement for an annual meeting of stockholders shall be deemed to comply with the notice requirements of this Section 1.11. A stockholder shall not have complied with this Section 1.11(b) if the stockholder (or beneficial owner, if any, on whose behalf the proposal is made) solicits or does not solicit, as the case may be, proxies in support of such stockholder's proposal in contravention of the representations with respect thereto required by this Section 1.11.

(c) The chairman of any annual meeting shall have the power and duty to determine whether business was properly brought before the annual meeting in accordance with the provisions of this Section 1.11 (including whether the stockholder or beneficial owner, if any, on whose behalf the proposal is made solicited (or is part of a group which solicited) or did not so solicit, as the case may be, proxies or votes in support of such stockholder's proposal in compliance with the representation with respect thereto required by this

Section 1.11), and if the chairman should determine that business was not properly brought before the annual meeting in accordance with the provisions of this Section 1.11, the chairman shall so declare to the meeting and such business shall not be brought before the annual meeting.

(d) Except as otherwise required by law, nothing in this Section 1.11 shall obligate the corporation or the Board of Directors to include in any proxy statement or other stockholder communication distributed on behalf of the corporation or the Board of Directors information with respect to any proposal submitted by a stockholder.

(e) Notwithstanding the foregoing provisions of this Section 1.11, unless otherwise required by law, if the stockholder (or a qualified representative of the stockholder) does not appear at the annual meeting to present business, such business shall not be considered, notwithstanding that proxies in respect of such business may have been received by the corporation.

(f) For purposes of this Section 1.11, the terms “qualified representative of the stockholder” and “public disclosure” shall have the same meaning as in Section 1.10.

1.12 Conduct of Meetings.

(a) Meetings of stockholders shall be presided over by the Chairman of the Board, if any, or in the Chairman’s absence by the Vice Chairman of the Board, if any, or in the Vice Chairman’s absence by the Chief Executive Officer, or in the Chief Executive Officer’s absence, by the President, or in the President’s absence by a Vice President, or in the absence of all of the foregoing persons by a chairman designated by the Board of Directors. The Secretary shall act as secretary of the meeting, but in the Secretary’s absence the chairman of the meeting may appoint any person to act as secretary of the meeting.

(b) The Board of Directors may adopt by resolution such rules, regulations and procedures for the conduct of any meeting of stockholders of the corporation as it shall deem appropriate including, without limitation, such guidelines and procedures as it may deem appropriate regarding the participation by means of remote communication of stockholders and proxyholders not physically present at a meeting. Except to the extent inconsistent with such rules, regulations and procedures as adopted by the Board of Directors, the chairman of any meeting of stockholders shall have the right and authority to convene and (for any or no reason) to recess and/or adjourn the meeting and prescribe such rules, regulations and procedures and to do all such acts as, in the judgment of such chairman, are appropriate for the proper conduct of

the meeting. Such rules, regulations or procedures, whether adopted by the Board of Directors or prescribed by the chairman of the meeting, may include, without limitation, the following: (i) the establishment of an agenda or order of business for the meeting; (ii) rules and procedures for maintaining order at the meeting and the safety of those present; (iii) limitations on attendance at or participation in the meeting to stockholders entitled to vote at the meeting, their duly authorized and constituted proxies or such other persons as shall be determined; (iv) restrictions on entry to the meeting after the time fixed for the commencement thereof; and (v) limitations on the time allotted to questions or comments by participants. Unless and to the extent determined by the Board of Directors or the chairman of the meeting, meetings of stockholders shall not be required to be held in accordance with the rules of parliamentary procedure.

(c) The chairman of the meeting shall announce at the meeting when the polls for each matter to be voted upon at the meeting will be opened and closed. After the polls close, no ballots, proxies or votes or any revocations or changes thereto may be accepted.

(d) In advance of any meeting of stockholders, the Board of Directors, the Chairman of the Board, the Chief Executive Officer or the President shall appoint one or more inspectors of election to act at the meeting and make a written report thereof. One or more other persons may be designated as alternate inspectors to replace any inspector who fails to act. If no inspector or alternate is present, ready and willing to act at a meeting of stockholders, the chairman of the meeting shall appoint one or more inspectors to act at the meeting. Unless otherwise required by law, inspectors may be officers, employees or agents of the corporation. Each inspector, before entering upon the discharge of such inspector’s duties, shall take and sign an oath faithfully to execute the duties of inspector with strict impartiality and according to the best of such inspector’s ability. The inspector shall have the duties prescribed by law and shall take charge of the polls and, when the vote is completed, shall make a certificate of the result of the vote taken and of such other facts as may be required by law. Every vote taken by ballots shall be counted by a duly appointed inspector or duly appointed inspectors.

1.13 No Action by Consent in Lieu of a Meeting. Stockholders of the corporation may not take any action by written consent in lieu of a meeting.

DIRECTORS

2.1 General Powers. The business and affairs of the corporation shall be managed by or under the direction of a Board of Directors, who may exercise all of the powers of the corporation except as otherwise provided by law or the Certificate of Incorporation.

2.2 Number, Election and Qualification. Subject to the rights of holders of any series of Preferred Stock to elect directors, the number of directors of the corporation shall be established by the Board of Directors. Election of directors need not be by written ballot. Directors need not be stockholders of the corporation.

2.3 Chairman of the Board; Vice Chairman of the Board. The Board of Directors may appoint from its members a Chairman of the Board and a Vice Chairman of the Board, neither of whom need be an employee or officer of the corporation. If the Board of Directors appoints a Chairman of the Board, such Chairman shall perform such duties and possess such powers as are assigned by the Board of Directors and, if the Chairman of the Board is also designated as the corporation's Chief Executive Officer, shall have the powers and duties of the Chief Executive Officer prescribed in Section 3.7 of these By-laws. If the Board of Directors appoints a Vice Chairman of the Board, such Vice Chairman shall perform such duties and possess such powers as are assigned by the Board of Directors. Unless otherwise provided by the Board of Directors, the Chairman of the Board or, in the Chairman's absence, the Vice Chairman of the Board, if any, shall preside at all meetings of the Board of Directors.

2.4 Classes of Directors. Subject to the rights of holders of any series of Preferred Stock to elect directors, the Board of Directors shall be and is divided into three classes: Class I, Class II and Class III. Each class shall consist, as nearly as may be possible, of one-third of the total number of directors constituting the entire Board of Directors. The allocation of directors among classes shall be determined by resolution of the Board of Directors.

2.5 Terms of Office. Subject to the rights of holders of any series of Preferred Stock to elect directors, each director shall serve for a term ending on the date of the third annual

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meeting of stockholders following the annual meeting of stockholders at which such director was elected; provided that each director initially assigned to Class I shall serve for a term expiring at the corporation's first annual meeting of stockholders held after the effectiveness of these Amended and Restated By-laws; each director initially assigned to Class II shall serve for a term expiring at the corporation's second annual meeting of stockholders held after the effectiveness of these Amended and Restated By-laws; and each director initially assigned to Class III shall serve for a term expiring at the corporation's third annual meeting of stockholders held after the effectiveness of these Amended and Restated By-laws; provided further, that the term of each director shall continue until the election and qualification of his or her successor and be subject to his or her earlier death, resignation or removal.

2.6 Quorum. The greater of (a) a majority of the directors at any time in office and (b) one-third of the number of directors established by the Board of Directors pursuant to Section 2.2 of these By-laws shall constitute a quorum of the Board of Directors. If at any meeting of the Board of Directors there shall be less than such a quorum, a majority of the directors present may adjourn the meeting from time to time without further notice other than announcement at the meeting, until a quorum shall be present.

2.7 Action at Meeting. Every act or decision done or made by a majority of the directors present at a meeting duly held at which a quorum is present shall be regarded as the act of the Board of Directors, unless a greater number is required by law or by the Certificate of Incorporation.

2.8 Removal. Subject to the rights of holders of any series of Preferred Stock, directors of the corporation may be removed only for cause and only by the affirmative vote of the holders of at least 75% of the votes which all the stockholders would be entitled to cast in any annual election of directors or class of directors.

2.9 Vacancies. Subject to the rights of holders of any series of Preferred Stock, any vacancy or newly-created directorship on the Board of Directors, however occurring, shall be filled only by vote of a majority of the directors then in office, although less than a quorum, or by a sole remaining director and shall not be filled by the stockholders. A director elected to fill a vacancy shall hold office until the next election of the class for which such director shall have

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been chosen, subject to the election and qualification of a successor or until such director's earlier death, resignation or removal.

2.10 Resignation. Any director may resign by delivering a resignation in writing or by electronic transmission to the corporation at its principal office or to the Chairman of the Board, the Chief Executive Officer, the President or the Secretary. Such resignation shall be effective upon receipt unless it is specified to be effective at some later time or upon the happening of some later event.

2.11 Regular Meetings. Regular meetings of the Board of Directors may be held without notice at such time and place as shall be determined from time to time by the Board of Directors; provided that any director who is absent when such a determination is made shall be given notice of the determination. A regular meeting of the Board of Directors may be held without notice immediately after and at the same place as the annual meeting of stockholders.

2.12 Special Meetings. Special meetings of the Board of Directors may be held at any time and place designated in a call by the Chairman of the Board, the Chief Executive Officer, the President, two or more directors, or by one director in the event that there is only a single director in office.

2.13 Notice of Special Meetings. Notice of the date, place and time of any special meeting of directors shall be given to each director by the Secretary or by the officer or one of the directors calling the meeting. Notice shall be duly given to each director (a) in person or by telephone at least 24 hours in advance of the meeting, (b) by sending an electronic transmission, or delivering written notice by hand, to such director's last known business, home or electronic transmission address at least 48 hours in advance of the meeting, or (c) by sending written notice by first-class mail to such director's last known business or home address at least 72 hours in advance of the meeting. A notice or waiver of notice of a meeting of the Board of Directors need not specify the purposes of the meeting.

2.14 Meetings by Conference Communications Equipment. Directors may participate in meetings of the Board of Directors or any committee thereof by means of conference telephone or other communications equipment by means of which all persons participating in the

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meeting can hear each other, and participation by such means shall constitute presence in person at such meeting.

2.15 Action by Consent. Any action required or permitted to be taken at any meeting of the Board of Directors or of any committee thereof may be taken without a meeting, if all members of the Board of Directors or committee, as the case may be, consent to the action in writing or by electronic transmission, and the written consents or electronic transmissions are filed with the minutes of proceedings of the Board of Directors or committee. Such filing shall be in paper form if the minutes are maintained in paper form and shall be in electronic form if the minutes are maintained in electronic form.

2.16 Committees. The Board of Directors may designate one or more committees, each committee to consist of one or more of the directors of the corporation with such lawfully delegable powers and duties as the Board of Directors thereby confers, to serve at the pleasure of the Board of Directors. The Board of Directors may designate one or more directors as alternate members of any committee, who may replace any absent or disqualified member at any meeting of the committee. In the absence or disqualification of a member of a committee, the member or members of the committee present at any meeting and not disqualified from voting, whether or not such member or members constitute a quorum, may unanimously appoint another member of the Board of Directors to act at the meeting in the place of any such absent or disqualified member. Any such committee, to the extent provided in the resolution of the Board of Directors and subject to the provisions of law, shall have and may exercise all the powers and authority of the Board of Directors in the management of the business and affairs of the corporation and may authorize the seal of the corporation to be affixed to all papers which may require it. Each such committee shall keep minutes and make such reports as the Board of Directors may from time to time request. Except as the Board of Directors may otherwise determine, any committee may make rules for the conduct of its business, but unless otherwise provided by the directors or in such rules, its business shall be conducted as nearly as possible in the same manner as is provided in these By-laws for the Board of Directors. Except as otherwise provided in the Certificate of Incorporation, these By-laws, or the resolution of the Board of Directors designating the committee, a committee may create one or more subcommittees, each

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subcommittee to consist of one or more members of the committee, and delegate to a subcommittee any or all of the powers and authority of the committee.

2.17 Compensation of Directors. Directors may be paid such compensation for their services and such reimbursement for expenses of attendance at meetings as the Board of Directors may from time to time determine. No such payment shall preclude any director from serving the corporation or any of its parent or subsidiary entities in any other capacity and receiving compensation for such service.

ARTICLE III

OFFICERS

3.1 Titles. The officers of the corporation shall consist of a Chief Executive Officer, a President, a Secretary, a Treasurer and such other officers with such other titles as the Board of Directors shall determine, including one or more Vice Presidents, Assistant Treasurers and Assistant Secretaries. The Board of Directors may appoint such other officers as it may deem appropriate.

3.2 Election. The Chief Executive Officer, President, Treasurer and Secretary shall be elected annually by the Board of Directors at its first meeting following the annual meeting of stockholders. Other officers may be appointed by the Board of Directors at such meeting or at any other meeting.

3.3 Qualification. No officer need be a stockholder. Any two or more offices may be held by the same person.

3.4 Tenure. Except as otherwise provided by law, by the Certificate of Incorporation or by these By-laws, each officer shall hold office until such officer's successor is elected and qualified, unless a different term is specified in the resolution electing or appointing such officer, or until such officer's earlier death, resignation or removal.

3.5 Resignation and Removal. Any officer may resign by delivering a resignation in writing or by electronic transmission

Executive Officer, the President or the Secretary. Such resignation shall be effective upon receipt unless it is specified to be effective at some later time or upon the happening of some later event. Any officer may be removed at any time, with or without cause, by vote of a majority of the directors then in office. Except as the Board of Directors may otherwise determine, no officer who resigns or is removed shall have any right to any compensation as an officer for any period following such officer's resignation or removal, or any right to damages on account of such removal, whether such officer's compensation be by the month or by the year or otherwise, unless such compensation is expressly provided for in a duly authorized written agreement with the corporation.

3.6 Vacancies. The Board of Directors may fill any vacancy occurring in any office for any reason and may, in its discretion, leave unfilled for such period as it may determine any offices other than those of Chief Executive Officer, President, Treasurer and Secretary. Each such successor shall hold office for the unexpired term of such officer's predecessor and until a successor is elected and qualified, or until such officer's earlier death, resignation or removal.

3.7 President: Chief Executive Officer. Unless the Board of Directors has designated another person as the corporation's Chief Executive Officer, the President shall be the Chief Executive Officer of the corporation. The Chief Executive Officer shall have general charge and supervision of the business of the corporation subject to the direction of the Board of Directors, and shall perform all duties and have all powers that are commonly incident to the office of chief executive or that are delegated to such officer by the Board of Directors. The President shall perform such other duties and shall have such other powers as the Board of Directors or the Chief Executive Officer (if the President is not the Chief Executive Officer) may from time to time prescribe. In the event of the absence, inability or refusal to act of the Chief Executive Officer or the President (if the President is not the Chief Executive Officer), the Vice President (or if there shall be more than one, the Vice Presidents in the order determined by the Board of Directors) shall perform the duties of the Chief Executive Officer and when so performing such duties shall have all the powers of and be subject to all the restrictions upon the Chief Executive Officer.

3.8 Vice Presidents. Each Vice President shall perform such duties and possess such powers as the Board of Directors or the Chief Executive Officer may from time to time prescribe. The Board of Directors may assign to any Vice President the title of Executive Vice President, Senior Vice President or any other title selected by the Board of Directors.

3.9 Secretary and Assistant Secretaries. The Secretary shall perform such duties and shall have such powers as the Board of Directors or the Chief Executive Officer may from time to time prescribe. In addition, the Secretary shall perform such duties and have such powers as are incident to the office of the secretary, including without limitation the duty and power to give notices of all meetings of stockholders and special meetings of the Board of Directors, to attend all meetings of stockholders and the Board of Directors and keep a record of the proceedings, to maintain a stock ledger and prepare lists of stockholders and their addresses as required, to be custodian of corporate records and the corporate seal and to affix and attest to the same on documents.

Any Assistant Secretary shall perform such duties and possess such powers as the Board of Directors, the Chief Executive Officer or the Secretary may from time to time prescribe. In the event of the absence, inability or refusal to act of the Secretary, the Assistant Secretary (or if there shall be more than one, the Assistant Secretaries in the order determined by the Board of Directors) shall perform the duties and exercise the powers of the Secretary.

In the absence of the Secretary or any Assistant Secretary at any meeting of stockholders or directors, the chairman of the meeting shall designate a temporary secretary to keep a record of the meeting.

3.10 Treasurer and Assistant Treasurers. The Treasurer shall perform such duties and shall have such powers as may from time to time be assigned by the Board of Directors or the Chief Executive Officer. In addition, the Treasurer shall perform such duties and have such powers as are incident to the office of treasurer, including without limitation the duty and power to keep and be responsible for all funds and securities of the corporation, to deposit funds of the corporation in depositories selected in accordance with these By-laws, to disburse such funds as ordered by the Board of Directors, to make proper accounts of such funds, and to render as

required by the Board of Directors statements of all such transactions and of the financial condition of the corporation.

The Assistant Treasurers shall perform such duties and possess such powers as the Board of Directors, the Chief Executive Officer or the Treasurer may from time to time prescribe. In the event of the absence, inability or refusal to act of the Treasurer, the Assistant Treasurer (or if there shall be more than one, the Assistant Treasurers in the order determined by the Board of Directors) shall perform the duties and exercise the powers of the Treasurer.

3.11 Salaries. Officers of the corporation shall be entitled to such salaries, compensation or reimbursement as shall be fixed or allowed from time to time by the Board of Directors.

3.12 Delegation of Authority. The Board of Directors may from time to time delegate the powers or duties of any officer to any other officer or agent, notwithstanding any provision hereof.

ARTICLE IV

CAPITAL STOCK

4.1 Issuance of Stock. Subject to the provisions of the Certificate of Incorporation, the whole or any part of any unissued balance of the authorized capital stock of the corporation or the whole or any part of any shares of the authorized capital stock of the corporation held in the corporation's treasury may be issued, sold, transferred or otherwise disposed of by vote of the Board of Directors in such manner, for such lawful consideration and on such terms as the Board of Directors may determine.

4.2 Stock Certificates; Uncertificated Shares. The shares of the corporation shall be represented by certificates, provided that the Board of Directors may provide by resolution or resolutions that some or all of any or all classes or series of the corporation's stock shall be uncertificated shares. Any such resolution shall not apply to shares represented by a certificate until such certificate is surrendered to the corporation. Every holder of stock of the corporation represented by certificates shall be entitled to have a certificate, in such form as may be

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prescribed by law and by the Board of Directors, representing the number of shares held by such holder registered in certificate form. Each such certificate shall be signed in a manner that complies with Section 158 of the General Corporation Law of the State of Delaware.

Each certificate for shares of stock which are subject to any restriction on transfer pursuant to the Certificate of Incorporation, these By-laws, applicable securities laws or any agreement among any number of stockholders or among such holders and the corporation shall have conspicuously noted on the face or back of the certificate either the full text of the restriction or a statement of the existence of such restriction.

If the corporation shall be authorized to issue more than one class of stock or more than one series of any class, the powers, designations, preferences and relative participating, optional or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights shall be set forth in full or summarized on the face or back of each certificate representing shares of such class or series of stock, provided that in lieu of the foregoing requirements there may be set forth on the face or back of each certificate representing shares of such class or series of stock a statement that the corporation will furnish without charge to each stockholder who so requests a copy of the full text of the powers, designations, preferences and relative, participating, optional or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights.

Within a reasonable time after the issuance or transfer of uncertificated shares, the corporation shall send to the registered owner thereof a written notice containing the information required to be set forth or stated on certificates pursuant to Sections 151, 202(a) or 218(a) of the General Corporation Law of the State of Delaware or, with respect to Section 151 of General Corporation Law of the State of Delaware, a statement that the corporation will furnish without charge to each stockholder who so requests the powers, designations, preferences and relative participating, optional or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights.

4.3 Transfers. Shares of stock of the corporation shall be transferable in the manner prescribed by law and in these By-laws. Transfers of shares of stock of the corporation shall be

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made only on the books of the corporation or by transfer agents designated to transfer shares of stock of the corporation. Subject to applicable law, shares of stock represented by certificates shall be transferred only on the books of the corporation by the surrender to the corporation or its transfer agent of the certificate representing such shares properly endorsed or accompanied by a written assignment or power of attorney properly executed, and with such proof of authority or the authenticity of signature as the corporation or its transfer agent may reasonably require. Uncertificated shares may be transferred by delivery of a written assignment or power of attorney properly executed, and with such proof of authority or the authenticity of signature as the corporation or its transfer agent may reasonably require. Except as may be otherwise required by law, by the Certificate of Incorporation or by these By-laws, the corporation shall be entitled to treat the record holder of stock as shown on its books as the owner of such stock for all purposes, including the payment of dividends and the right to vote with respect to such stock, regardless of any transfer, pledge or other disposition of such stock until the shares have been transferred on the books of the corporation in accordance with the requirements of these By-laws.

4.4 Lost, Stolen or Destroyed Certificates. The corporation may issue a new certificate of stock in place of any previously issued certificate alleged to have been lost, stolen or destroyed, upon such terms and conditions as the corporation may prescribe, including the presentation of reasonable evidence of such loss, theft or destruction and the giving of such indemnity and posting of such bond as the corporation may require for the protection of the corporation or any transfer agent or registrar.

4.5 Record Date. The Board of Directors may fix in advance a date as a record date for the determination of the stockholders entitled to notice of or to vote at any meeting of stockholders, or entitled to receive payment of any dividend or other

distribution or allotment of any rights in respect of any change, conversion or exchange of stock, or for the purpose of any other lawful action. Such record date shall not precede the date on which the resolution fixing the record date is adopted, and such record date shall not be more than 60 nor less than 10 days before the date of such meeting, nor more than 60 days prior to any other action to which such record date relates.

If no record date is fixed, the record date for determining stockholders entitled to notice of or to vote at a meeting of stockholders shall be at the close of business on the day before the day on which notice is given, or, if notice is waived, at the close of business on the day before the day on which the meeting is held. If no record date is fixed, the record date for determining stockholders for any other purpose shall be at the close of business on the day on which the Board of Directors adopts the resolution relating to such purpose.

A determination of stockholders of record entitled to notice of or to vote at a meeting of stockholders shall apply to any adjournment of the meeting; provided, however, that the Board of Directors may fix a new record date for the adjourned meeting.

4.6 Regulations. The issue, transfer, conversion and registration of shares of stock of the corporation shall be governed by such other regulations as the Board of Directors may establish.

ARTICLE V

GENERAL PROVISIONS

5.1 Fiscal Year. Except as from time to time otherwise designated by the Board of Directors, the fiscal year of the corporation shall begin on the first day of January of each year and end on the last day of December in each year.

5.2 Corporate Seal. The corporate seal shall be in such form as shall be approved by the Board of Directors.

5.3 Waiver of Notice. Whenever notice is required to be given by law, by the Certificate of Incorporation or by these By-laws, a written waiver signed by the person entitled to notice, or a waiver by electronic transmission by the person entitled to notice, whether before, at or after the time of the event for which notice is to be given, shall be deemed equivalent to notice required to be given to such person. Neither the business nor the purpose of any meeting need be specified in any such waiver. Attendance of a person at a meeting shall constitute a waiver of notice of such meeting, except when the person attends a meeting for the express purpose of

objecting at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened.

5.4 Voting of Securities. Except as the Board of Directors may otherwise designate, the Chief Executive Officer, the President or the Treasurer may waive notice of, vote, or appoint any person or persons to vote, on behalf of the corporation at, and act as, or appoint any person or persons to act as, proxy or attorney-in-fact for this corporation (with or without power of substitution) at, any meeting of stockholders or securityholders of any other entity, the securities of which may be held by this corporation.

5.5 Evidence of Authority. A certificate by the Secretary, or an Assistant Secretary, or a temporary Secretary, as to any action taken by the stockholders, directors, a committee or any officer or representative of the corporation shall as to all persons who rely on the certificate in good faith be conclusive evidence of such action.

5.6 Certificate of Incorporation. All references in these By-laws to the Certificate of Incorporation shall be deemed to refer to the Certificate of Incorporation of the corporation, as amended and/or restated and in effect from time to time.

5.7 Severability. Any determination that any provision of these By-laws is for any reason inapplicable, illegal or ineffective shall not affect or invalidate any other provision of these By-laws.

5.8 Pronouns. All pronouns used in these By-laws shall be deemed to refer to the masculine, feminine or neuter, singular or plural, as the identity of the person or persons may require.

ARTICLE VI

AMENDMENTS

These By-laws may be altered, amended or repealed, in whole or in part, or new By-laws may be adopted by the Board of Directors or by the stockholders as provided in the Certificate of Incorporation.

SYROS PHARMACEUTICALS, INC.

THE COMPANY WILL FURNISH WITHOUT CHARGE TO EACH SHAREHOLDER WHO SO REQUESTS A COPY OF THE CERTIFICATE OF INCORPORATION OF THE COMPANY, AS AMENDED. SUCH REQUEST MAY BE MADE TO THE OFFICE OF THE SECRETARY OF THE COMPANY OR TO THE TRANSFER AGENT. THE BOARD OF DIRECTORS MAY REQUIRE THE OWNER OF A LOST OR DESTROYED STOCK CERTIFICATE, OR HIS LEGAL REPRESENTATIVES, TO GIVE THE COMPANY A BOND TO INDEMNIFY IT AND ITS TRANSFER AGENTS AND REGISTRARS AGAINST ANY CLAIM THAT MAY BE MADE AGAINST THEM ON ACCOUNT OF THE ALLEGED LOSS OR DESTRUCTION OF ANY SUCH CERTIFICATE.

The following abbreviations, when used in the inscription on the face of this certificate, shall be construed as though they were written out in full according to applicable laws or regulations:	
TEN COM - as tenants in common	UNIF GIFT MIN ACT *Custodian (Cust) (Minor)
TEN ENT - as tenants by the entireties	under Uniform Gifts to Minors Act..... (State)
JT TEN - as joint tenants with right of survivorship and not as tenants in common	UNIF TRF MIN ACT *Custodian (until age) (Cust) (State)
under Uniform Transfers to Minors Act (Minor) (State)
Additional abbreviations may also be used though not in the above list.	

For value received, _____ hereby sell, assign and transfer unto _____ PLEASE INSERT SOCIAL SECURITY OR OTHER IDENTIFYING NUMBER OF ASSIGNEE

(PLEASE PRINT OR TYPEWRITE NAME AND ADDRESS, INCLUDING POSTAL ZIP CODE, OF ASSIGNEE)

_____ Shares
 of the common stock represented by the within Certificate, and do hereby irrevocably constitute and appoint _____ Attorney
 to transfer the said stock on the books of the within-named Company with full power of substitution in the premises.

Dated: _____ 20 _____
 Signature: _____
 Signature: _____

Notice: The signature to this assignment must correspond with the name as written upon the face of the certificate, in every particular, without alteration or enlargement, or any change whatever.

Signature(s) Guaranteed: Medallion Guarantee Stamp

THE SIGNATURE(S) SHOULD BE GUARANTEED BY AN ELIGIBLE GUARANTOR INSTITUTION (Banks, Stockbrokers, Savings and Loan Associations and Credit Unions) WITH MEMBERSHIP IN AN APPROVED SIGNATURE GUARANTEE MEDALLION PROGRAM, PURSUANT TO S.E.C. RULE 17AD-15.



The IRS requires that the named transfer agent ("we") report the cost basis of certain shares or units acquired after January 1, 2011. If your shares or units are covered by the legislation, and you requested to sell or transfer the shares or units using a specific cost basis calculation method, then we have processed as you requested. If you did not specify a cost basis calculation method, then we have defaulted to the first in, first out (FIFO) method. Please consult your tax advisor if you need additional information about cost basis.

If you do not keep in contact with the issuer or do not have any activity in your account for the time period specified by state law, your property may become subject to state unclaimed property laws and transferred to the appropriate state.

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SYROS PHARMACEUTICALS, INC.

2012 EQUITY INCENTIVE PLAN1. Purpose

The purpose of this 2012 Equity Incentive Plan (the “*Plan*”) of Syros Pharmaceuticals, Inc., a Delaware corporation (the “*Company*”), is to advance the interests of the Company’s stockholders by enhancing the Company’s ability to attract, retain and motivate persons who are expected to make important contributions to the Company and by providing such persons with equity ownership opportunities and performance-based incentives that are intended to better align the interests of such persons with those of the Company’s stockholders. Except where the context otherwise requires, the term “*Company*” shall include any of the Company’s present or future parent or subsidiary corporations as defined in Sections 424(e) or (f) of the Internal Revenue Code of 1986, as amended, and any regulations thereunder (the “*Code*”) and any other business venture (including, without limitation, joint venture or limited liability company) in which the Company has a controlling interest, as determined by the Board of Directors of the Company (the “*Board*”); *provided, however*, that such other business ventures shall be limited to entities that, where required by Section 409A of the Code, are eligible issuers of service recipient stock (as defined in Treas. Reg. Section 1.409A-1(b)(5)(iii)(E), or applicable successor regulation).

2. Eligibility

All of the Company’s employees, officers and directors, as well as consultants and advisors to the Company (as such terms are defined and interpreted for purposes of Rule 701 under the Securities Act of 1933, as amended (the “*Securities Act*”) (or any successor rule)) are eligible to be granted Awards under the Plan. Each person who is granted an Award under the Plan is deemed a “*Participant*.” “*Award*” means Options (as defined in Section 5), SARs (as defined in Section 6), Restricted Stock (as defined in Section 7), Restricted Stock Units (as defined in Section 7) and Other Stock-Based Awards (as defined in Section 8) and Cash-Based Awards (as defined in Section 8).

3. Administration and Delegation

(a) Administration by Board of Directors. The Plan will be administered by the Board. The Board shall have authority to grant Awards and to adopt, amend and repeal such administrative rules, guidelines and practices relating to the Plan as it shall deem advisable. The Board may construe and interpret the terms of the Plan and any Award agreements entered into under the Plan. The Board may correct any defect, supply any omission or reconcile any inconsistency in the Plan or any Award in the manner and to the extent it shall deem expedient to carry the Plan into effect and it shall be the sole and final judge of such expediency. All decisions by the Board shall be made in the Board’s sole discretion and shall be final and binding on all persons having or claiming any interest in the Plan or in any Award.

(b) Appointment of Committees. To the extent permitted by applicable law, the Board may delegate any or all of its powers under the Plan to one or more committees or subcommittees of the Board (a “*Committee*”). All references in the Plan to the “*Board*” shall

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mean the Board or a Committee of the Board or the officers referred to in Section 3(c) to the extent that the Board’s powers or authority under the Plan have been delegated to such Committee or officers.

(c) Delegation to Officers. To the extent permitted by applicable law, the Board may delegate to one or more officers of the Company the power to grant Options and other Awards that constitute rights under Delaware law (subject to any limitations under the Plan) to employees or officers of the Company and to exercise such other powers under the Plan as the Board may determine, *provided* that the Board shall fix the terms of such Awards to be granted by such officers (including the exercise price of such Awards, which may include a formula by which the exercise price will be determined) and the maximum number of shares subject to such Awards that the officers may grant; *provided* further, however, that no officer shall be authorized to grant such Awards to any “executive officer” of the Company (as defined by Rule 3b-7 under the Securities Exchange Act of 1934, as amended (the “*Exchange Act*”)) or to any “officer” of the Company (as defined by Rule 16a-1 under the Exchange Act). The Board may not delegate authority under this Section 3(c) to grant Restricted Stock, unless Delaware law then permits such delegation.]

4. Stock Available for Awards

(a) Number of Shares. Subject to adjustment under Section 9, Awards may be made under the Plan for up to 5,500,000 shares of common stock, \$0.001 par value per share, of the Company (the “*Common Stock*”), any or all of which Awards may be in the form of Incentive Stock Options (as defined in Section 5(b)). If any Award expires or is terminated, surrendered or canceled without having been fully exercised, is forfeited in whole or in part (including as the result of shares of Common Stock subject to such Award being repurchased by the Company at the original issuance price pursuant to a contractual repurchase right), or results in any Common Stock not being issued, the unused Common Stock covered by such Award shall again be available for the grant of Awards under the Plan. Further, shares of Common Stock tendered to the Company by a Participant to exercise an Award shall be added to the number of shares of Common Stock available for the grant of Awards under the Plan. However, in the case of Incentive Stock Options, the two immediately preceding sentences shall be subject to any limitations under the Code. Shares issued under the Plan may consist in whole or in part of authorized but unissued shares or treasury shares.

(b) Substitute Awards. In connection with a merger or consolidation of an entity with the Company or the acquisition by the Company of property or stock of an entity, the Board may grant Awards in substitution for any options or other stock or stock-based awards granted by such entity or an affiliate thereof. Substitute Awards may be granted on such terms as the Board deems appropriate in the circumstances, notwithstanding any limitations on Awards contained in the Plan. Substitute Awards shall not count against the overall share limit set forth in Section 4(a), except as may be required by reason of Section 422 and related provisions of the Code.

5. Stock Options

(a) General. The Board may grant options to purchase Common Stock (each, an “*Option*”) and determine the number of shares of Common Stock to be covered by each Option,

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the exercise price of each Option and the conditions and limitations applicable to the exercise of each Option, including conditions relating to applicable federal or state securities laws, as it considers necessary or advisable.

(b) Incentive Stock Options. An Option that the Board intends to be an “incentive stock option” as defined in Section 422 of the Code (an “*Incentive Stock Option*”) shall only be granted to employees of Syros Pharmaceuticals, Inc., any of Syros Pharmaceuticals, Inc.’s present or future parent or subsidiary corporations as defined in Sections 424(e) or (f) of the Code, and any other entities the employees of which are eligible to receive Incentive Stock Options under the Code, and shall be subject to and shall be construed consistently with the requirements of Section 422 of the Code. An Option that is not intended to be an Incentive Stock Option shall be designated a “*Nonstatutory Stock Option.*” The Company shall have no liability to a Participant, or any other party, if an Option (or any part thereof) that is intended to be an Incentive Stock Option is not an Incentive Stock Option or if the Company converts an Incentive Stock Option to a Nonstatutory Stock Option.

(c) Exercise Price. The Board shall establish the exercise price of each Option and specify the exercise price in the applicable Option agreement. The exercise price shall be not less than 100% of the fair market value per share of Common Stock, as determined by (or in a manner approved by) the Board (“*Fair Market Value*”), on the date the Option is granted.

(d) Duration of Options. Each Option shall be exercisable at such times and subject to such terms and conditions as the Board may specify in the applicable option agreement; *provided, however,* that no Option will be granted with a term in excess of 10 years.

(e) Exercise of Options. Options may be exercised by delivery to the Company of a notice of exercise in a form of notice (which may be electronic) approved by the Company, together with payment in full (in a manner specified in Section 5(f)) of the exercise price for the number of shares for which the Option is exercised. Shares of Common Stock subject to the Option will be delivered by the Company as soon as practicable following exercise.

(f) Payment Upon Exercise. Common Stock purchased upon the exercise of an Option granted under the Plan shall be paid for as follows:

(1) in cash or by check, payable to the order of the Company;

(2) when the Common Stock is registered under the Exchange Act, except as may otherwise be provided in the applicable Option agreement or approved by the Board, in its sole discretion, by (i) delivery of an irrevocable and unconditional undertaking by a creditworthy broker to deliver promptly to the Company sufficient funds to pay the exercise price and any required tax withholding or (ii) delivery by the Participant to the Company of a copy of irrevocable and unconditional instructions to a creditworthy broker to deliver promptly to the Company cash or a check sufficient to pay the exercise price and any required tax withholding;

(3) when the Common Stock is registered under the Exchange Act and to the extent provided for in the applicable Option agreement or approved by the Board, in its sole discretion, by delivery (either by actual delivery or attestation) of shares of Common Stock owned by the Participant valued at their Fair Market Value, *provided* (i) such method of payment

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is then permitted under applicable law, (ii) such Common Stock, if acquired directly from the Company, was owned by the Participant for such minimum period of time, if any, as may be established by the Board in its discretion and (iii) such Common Stock is not subject to any repurchase, forfeiture, unfulfilled vesting or other similar requirements;

(4) to the extent provided for in the applicable Nonstatutory Stock Option agreement or approved by the Board in its sole discretion, by delivery of a notice of “net exercise” to the Company, as a result of which the Participant would pay the exercise price for the portion of the Option being exercised by cancelling a portion of the Option for such number of shares as is equal to the exercise price divided by the excess of the Fair Market Value on the date of exercise over the Option exercise price per share.

(5) to the extent permitted by applicable law and provided for in the applicable Option agreement or approved by the Board, in its sole discretion, by (i) delivery of a promissory note of the Participant to the Company on terms determined by the Board, or (ii) payment of such other lawful consideration as the Board may determine; or

(6) by any combination of the above permitted forms of payment.

6. Stock Appreciation Rights

(a) General. The Board may grant Awards consisting of stock appreciation rights (“**SARs**”) entitling the holder, upon exercise, to receive an amount of Common Stock or cash or a combination thereof (such form to be determined by the Board) determined by reference to appreciation, from and after the date of grant, in the Fair Market Value of a share of Common Stock over the measurement price established pursuant to Section 6(b). The date as of which such appreciation is determined shall be the exercise date.

(b) Measurement Price. The Board shall establish the measurement price of each SAR and specify it in the applicable SAR agreement. The measurement price shall not be less than 100% of the Fair Market Value on the date the SAR is granted.

(c) Duration of SARs. Each SAR shall be exercisable at such times and subject to such terms and conditions as the Board may specify in the applicable SAR agreement; *provided, however*, that no SAR will be granted with a term in excess of 10 years.

(d) Exercise of SARs. SARs may be exercised by delivery to the Company of a notice of exercise in a form (which may be electronic) approved by the Company, together with any other documents required by the Board.

7. Restricted Stock; Restricted Stock Units

(a) General. The Board may grant Awards entitling recipients to acquire shares of Common Stock (“**Restricted Stock**”), subject to the right of the Company to repurchase all or part of such shares at their issue price or other stated or formula price (or to require forfeiture of such shares if issued at no cost) from the recipient in the event that conditions specified by the Board in the applicable Award are not satisfied prior to the end of the applicable restriction period or periods established by the Board for such Award. The Board may also grant Awards

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entitling the recipient to receive shares of Common Stock or cash to be delivered at the time such Award vests (“**Restricted Stock Units**”) (Restricted Stock and Restricted Stock Units are each referred to herein as a “**Restricted Stock Award**”).

(b) Terms and Conditions for All Restricted Stock Awards. The Board shall determine the terms and conditions of a Restricted Stock Award, including the conditions for vesting and repurchase (or forfeiture) and the issue price, if any.

(c) Additional Provisions Relating to Restricted Stock.

(1) Dividends. Unless otherwise provided in the applicable Award agreement, any dividends (whether paid in cash, stock or property) declared and paid by the Company with respect to shares of Restricted Stock (“**Accrued Dividends**”) shall be paid to the Participant only if and when such shares become free from the restrictions on transferability and forfeitability that apply to such shares. Each payment of Accrued Dividends will be made no later than the end of the calendar year in which the dividends are paid to stockholders of that class of stock or, if later, the 15th day of the third month following the lapsing of the restrictions on transferability and the forfeitability provisions applicable to the underlying shares of Restricted Stock.

(2) Stock Certificates. The Company may require that any stock certificates issued in respect of shares of Restricted Stock, as well as dividends or distributions paid on such Restricted Stock, shall be deposited in escrow by the Participant, together with a stock power endorsed in blank, with the Company (or its designee). At the expiration of the applicable restriction periods, the Company (or such designee) shall deliver the certificates no longer subject to such restrictions to the Participant or if the Participant has died, to his or her Designated Beneficiary. “**Designated Beneficiary**” means (i) the beneficiary designated, in a manner determined by the Board, by a Participant to receive amounts due or exercise rights of the Participant in the event of the Participant’s death or (ii) in the absence of an effective designation by a Participant, “**Designated Beneficiary**” the Participant’s estate.

(d) Additional Provisions Relating to Restricted Stock Units.

(1) Settlement. Upon the vesting of and/or lapsing of any other restrictions (i.e., settlement) with respect to each Restricted Stock Unit, the Participant shall be entitled to receive from the Company one share of Common Stock or (if so provided in the applicable Award agreement) an amount of cash equal to the Fair Market Value of one share of Common Stock. The Board may, in its discretion, provide that settlement of Restricted Stock Units shall be deferred, on a mandatory basis or at the election of the Participant in a manner that complies with Section 409A of the Code.

(2) Voting Rights. A Participant shall have no voting rights with respect to any Restricted Stock Units.

(3) Dividend Equivalents. The Award agreement for Restricted Stock Units may provide Participants with the right to receive an amount equal to any dividends or other distributions declared and paid on an equal number of outstanding shares of Common Stock (“**Dividend Equivalents**”). Dividend Equivalents may be paid currently or credited to an account

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for the Participants, may be settled in cash and/or shares of Common Stock and may be subject to the same restrictions on transfer and forfeitability as the Restricted Stock Units with respect to which paid, in each case to the extent provided in the applicable Award agreement.

8. Other Stock-Based and Cash-Based Awards

(a) General. Other Awards of shares of Common Stock, and other Awards that are valued in whole or in part by reference to, or are otherwise based on, shares of Common Stock or other property, may be granted hereunder to Participants (“**Other Stock-Based Awards**”). Such Other Stock-Based Awards shall also be available as a form of payment in the settlement of other Awards granted under the Plan or as payment in lieu of compensation to which a Participant is otherwise entitled. Other Stock-Based Awards may be paid in shares of Common Stock or cash, as the Board shall determine. The Company may also grant Performance Awards or other Awards denominated in cash rather than shares of Common Stock (“**Cash-Based Awards**”).

(b) Terms and Conditions. Subject to the provisions of the Plan, the Board shall determine the terms and conditions of each Other Stock-Based Award or Cash-Based Award, including any purchase price applicable thereto.

9. Adjustments for Changes in Common Stock and Certain Other Events

(a) Changes in Capitalization. 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 Common Stock other than an ordinary cash dividend, (i) the number and class of securities available under the Plan, (ii) the number and class of securities and exercise price per share of each outstanding Option, (iii) the share and per-share provisions and the measurement price of each outstanding SAR, (iv) the number of shares subject to and the repurchase price per share subject to each outstanding Restricted Stock Award and (v) the share and per-share-related provisions and the purchase price, if any, of each outstanding Other Stock-Based Award, shall be equitably adjusted by the Company (or substituted Awards may be made, if applicable) in the manner determined by the Board. Without limiting the generality of the foregoing, in the event the Company effects a split of the Common Stock by means of a stock dividend and the exercise price of and the number of shares subject to an outstanding Option are adjusted as of the date of the distribution of the dividend (rather than as of the record date for such dividend), then an optionee who exercises an Option between the record date and the distribution date for such stock dividend shall be entitled to receive, on the distribution date, the stock dividend with respect to the shares of Common Stock acquired upon such Option exercise, notwithstanding the fact that such shares were not outstanding as of the close of business on the record date for such stock dividend.

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(b) Reorganization Events.(1)

(1) Definition. A “**Reorganization Event**” shall mean: (a) any merger or consolidation of the Company with or into another entity as a result of which all of the Common Stock of the Company is converted into or exchanged for the right to receive cash, securities or other property or is cancelled, (b) any transfer or disposition of all of the Common Stock of the Company for cash, securities or other property pursuant to a share exchange or other transaction or (c) any liquidation or dissolution of the Company.

(2) Consequences of a Reorganization Event on Awards Other than Restricted Stock.

(i) In connection with a Reorganization Event, the Board may take any one or more of the following actions as to all or any (or any portion of) outstanding Awards other than Restricted Stock on such terms as the Board determines (except to the extent specifically provided otherwise in an applicable Award agreement or another agreement between the Company and the Participant): (i) provide that such Awards shall be assumed, or substantially equivalent Awards shall be substituted, by the acquiring or succeeding corporation (or an affiliate thereof), (ii) upon written notice to a Participant, provide that all of the Participant’s unexercised Awards will terminate immediately prior to the consummation of such Reorganization Event unless exercised by the Participant (to the extent then exercisable) within a specified period following the date of such notice, (iii) 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 Reorganization Event, (iv) in the event of a Reorganization Event under the terms of which holders of Common Stock will receive upon consummation thereof a cash payment for each share surrendered in the Reorganization Event (the “**Acquisition Price**”), make or provide for a cash payment to Participants with respect to each Award held by a Participant equal to (A) the number of shares of 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 (B) the excess, if any, of (I) the Acquisition Price over (II) the exercise, measurement or purchase price of such Award and any applicable tax withholdings, in exchange for the termination of such Award, (v) provide that, in connection with a liquidation or dissolution of the Company, Awards shall convert into the right to receive liquidation proceeds (if applicable, net of the exercise, measurement or purchase price thereof and any applicable tax withholdings) and (vi) any combination of the foregoing. In taking any of the actions permitted under this Section 9(b)(2), the Board shall not

(1) If the Company desires to include acceleration of vesting provisions upon an acquisition or change in control, they should be dealt with in a separate section of the Plan, or in the forms of agreement for granting Awards under the Plan. Private companies might also consider imposing a requirement that the acceleration receive shareholder approval at the time of a change in control, if such approval would prevent the participants from being subject to the parachute taxes under 280G. The additional language would be something like “The Participant must agree, as a condition to receipt of the Award, that this provision will only accelerate exercisability or vesting if and to the extent that such acceleration does not create or increase an excess parachute payment under Section 280G of the Code, unless the Board provides otherwise. The Company will use good faith efforts to obtain stockholder approval of any such acceleration if such stockholder vote would exempt the acceleration from the effects of Section 280G.”

be obligated by the Plan to treat all Awards, all Awards held by a Participant, or all Awards of the same type, identically.

(ii) Notwithstanding the terms of Section 9(b)(2)(A), in the case of outstanding Restricted Stock Units that are subject to Section 409A of the Code: (i) if the applicable Restricted Stock Unit agreement provides that the Restricted Stock Units shall be settled upon a “change in control event” within the meaning of Treasury Regulation Section 1.409A-3(i)(5)(i), and the Reorganization Event constitutes such a “change in control event”, then no assumption or substitution shall be permitted pursuant to Section 9(b)(2)(A)(i) and the Restricted Stock Units shall instead be settled in accordance with the terms of the applicable Restricted Stock Unit agreement; and (ii) the Board may only undertake the actions set forth in clauses (iii), (iv) or (v) of Section 9(b)(2)(A) if the Reorganization Event constitutes a “change in control event” as defined under Treasury Regulation Section 1.409A-3(i)(5)(i) and such action is permitted or required by Section 409A of the Code; if the Reorganization Event is not a “change in control event” as so defined or such action is not permitted or required by Section 409A of the Code, and the acquiring or succeeding corporation does not assume or substitute the Restricted Stock Units pursuant to clause (i) of Section 9(b)(2)(A), then the unvested Restricted Stock Units shall terminate immediately prior to the consummation of the Reorganization Event without any payment in exchange therefor.

(iii) For purposes of Section 9(b)(2)(A)(i), an Award (other than Restricted Stock) shall be considered assumed if, following consummation of the Reorganization Event, such Award confers the right to purchase or receive pursuant to the terms of such Award, for each share of Common Stock subject to the Award immediately prior to the consummation of the Reorganization Event, the consideration (whether cash, securities or other property) received as a result of the Reorganization Event by holders of Common Stock for each share of Common Stock held immediately prior to the consummation of the Reorganization Event (and if holders were offered a choice of consideration, the type of consideration chosen by the holders of a majority of the outstanding shares of Common Stock); *provided, however*, that if the consideration received as a result of the Reorganization Event is not solely common stock of the acquiring or succeeding corporation (or an affiliate thereof), the Company may, with the consent of the acquiring or succeeding corporation, provide for the consideration to be received upon the exercise or settlement of the Award to consist solely of such number of shares of common stock of the acquiring or succeeding corporation (or an affiliate thereof) that the Board determined to be equivalent in value (as of the date of such determination or another date specified by the Board) to the per share consideration received by holders of outstanding shares of Common Stock as a result of the Reorganization Event.

(3) Consequences of a Reorganization Event on Restricted Stock. Upon the occurrence of a Reorganization Event other than a liquidation or dissolution of the Company, the repurchase and other rights of the Company with respect to outstanding Restricted Stock shall inure to the benefit of the Company’s successor and shall, unless the Board determines otherwise, apply to the cash, securities or other property which the Common Stock was converted into or exchanged for pursuant to such Reorganization Event in the same manner and to the same extent as they applied to such Restricted Stock; *provided, however*, that the Board may provide for termination or deemed satisfaction of such repurchase or other rights under the instrument evidencing any Restricted Stock or any other agreement between a Participant and the

Company, either initially or by amendment. Upon the occurrence of a Reorganization Event involving the liquidation or dissolution of the Company, except to the extent specifically provided to the contrary in the instrument evidencing any Restricted Stock or any other agreement between a Participant and the Company, all restrictions and conditions on all Restricted Stock then outstanding shall automatically be deemed terminated or satisfied.

10. General Provisions Applicable to Awards

(a) Transferability of Awards. Awards (or any interest in an Award, including, prior to exercise, any interest in shares of Common Stock issuable upon exercise of an Option or SAR) shall not be sold, assigned, transferred (including by establishing any short position, put equivalent position (as defined in Rule 16a-1 issued under the Exchange Act) or call equivalent position (as defined in Rule 16a-1 issued under the Exchange Act)), pledged, hypothecated or otherwise encumbered by the person to whom they are granted, either voluntarily or by operation of law, and, during the life of the Participant, shall be exercisable only by the Participant; except that Awards may be transferred to family members (as defined in Rule 701(c)(3) under the Securities Act) through gifts or (other than Incentive Stock Options) domestic relations orders or to an executor or guardian upon the death or disability of the Participant. The Company shall not be required to recognize any such permitted transfer until such time as such permitted transferee shall deliver to the Company a written instrument, as a condition to such transfer, in form and substance satisfactory to the Company confirming that such transferee shall be bound by all of the terms and conditions of the Award. References to a Participant, to the extent relevant in the context, shall include references to authorized transferees. For the avoidance of doubt, nothing contained in this Section 10(a) shall be deemed to restrict a transfer to the Company.

(b) Documentation. Each Award shall be evidenced in such form (written, electronic or otherwise) as the Board shall determine. Each Award may contain terms and conditions in addition to those set forth in the Plan.

(c) Board Discretion. Except as otherwise provided by the Plan, each Award may be made alone or in addition or in relation to any other Award. The terms of each Award need not be identical, and the Board need not treat Participants uniformly.

(d) Termination of Status. The Board shall determine the effect on an Award of the disability, death, termination or other cessation of employment, authorized leave of absence or other change in the employment or other status of a Participant and the extent to which, and the period during which, the Participant, or the Participant’s legal representative, conservator, guardian or Designated

Beneficiary, may exercise rights under the Award.

(e) Withholding. The Participant must satisfy all applicable federal, state, and local or other income and employment tax withholding obligations before the Company will deliver stock certificates or otherwise recognize ownership of Common Stock under an Award. The Company may decide to satisfy the withholding obligations through additional withholding on salary or wages. If the Company elects not to or cannot withhold from other compensation, the Participant must pay the Company the full amount, if any, required for withholding or have a broker tender to the Company cash equal to the withholding obligations. Payment of withholding obligations is due before the Company will issue any shares on exercise, vesting or

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release from forfeiture of an Award or at the same time as payment of the exercise or purchase price unless the Company determines otherwise. If provided for in an Award or approved by the Board in its sole discretion, a Participant may satisfy such tax obligations in whole or in part by delivery (either by actual delivery or attestation) of shares of Common Stock, including shares retained from the Award creating the tax obligation, valued at their Fair Market Value; *provided, however*, except as otherwise provided by the Board, that the total tax withholding where stock is being used to satisfy such tax obligations cannot exceed the Company's minimum statutory withholding obligations (based on minimum statutory withholding rates for federal and state tax purposes, including payroll taxes, that are applicable to such supplemental taxable income). Shares used to satisfy tax withholding requirements cannot be subject to any repurchase, forfeiture, unfulfilled vesting or other similar requirements.

(f) Amendment of Award.

(1) The Board may amend, modify or terminate any outstanding Award, 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 to a Nonstatutory Stock Option. The Participant's consent to such action shall be required unless (i) the Board determines that the action, taking into account any related action, does not materially and adversely affect the Participant's rights under the Plan or (ii) the change is permitted under Section 9.

(2) The Board may, without stockholder approval, amend any outstanding Award granted under the Plan to provide an exercise price per share that is lower than the then-current exercise price per share of such outstanding Award. The Board may also, without stockholder approval, cancel any outstanding award (whether or not granted under the Plan) and grant in substitution therefor new Awards under the Plan covering the same or a different number of shares of Common Stock and having an exercise price per share lower than the then-current exercise price per share of the cancelled award.

(g) Conditions on Delivery of Stock. The Company will not be obligated to deliver any shares of Common Stock pursuant to the Plan or to remove restrictions from shares previously issued or delivered under the Plan until (i) all conditions of the Award have been met or removed to the satisfaction of the Company, (ii) in the opinion of the Company's counsel, all other legal matters in connection with the issuance and delivery of such shares have been satisfied, including any applicable securities laws and regulations and any applicable stock exchange or stock market rules and regulations, and (iii) the Participant has executed and delivered to the Company such representations or agreements as the Company may consider appropriate to satisfy the requirements of any applicable laws, rules or regulations.

(h) Acceleration. The Board may at any time provide that any Award 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.

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11. Miscellaneous

(a) No Right To Employment or Other Status. No person shall have any claim or right to be granted an Award by virtue of the adoption of the Plan, and the grant of an Award shall not be construed as giving a Participant the right to continued employment or any other relationship with the Company. The Company expressly reserves the right at any time to dismiss or otherwise terminate its relationship with a Participant free from any liability or claim under the Plan, except as expressly provided in the applicable Award.

(b) No Rights As Stockholder. Subject to the provisions of the applicable Award, no Participant or Designated Beneficiary shall have any rights as a stockholder with respect to any shares of Common Stock to be distributed with respect to an Award until becoming the record holder of such shares.

(c) Effective Date and Term of Plan. The Plan shall become effective on the date on which it is adopted by the Board. No Awards shall be granted under the Plan after the expiration of 10 years from the earlier of (i) the date on which the Plan was adopted by the Board or (ii) the date the Plan was approved by the Company's stockholders, but Awards previously granted may extend beyond that date.

(d) Amendment of Plan. The Board may amend, suspend or terminate the Plan or any portion thereof at any time; *provided* that if at any time the approval of the Company's stockholders is required as to any modification or amendment under Section 422 of the Code or any successor provision with respect to Incentive Stock Options, the Board may not effect such modification or amendment without such approval. Unless otherwise specified in the amendment, any amendment to the Plan adopted in accordance with this Section 11(d) shall apply to, and be binding on the holders of, all Awards outstanding under the Plan at the time the amendment is

adopted, provided the Board determines that such amendment, taking into account any related action, does not materially and adversely affect the rights of Participants under the Plan.

(e) Authorization of Sub-Plans (including Grants to non-U.S. Employees). The Board may from time to time establish one or more sub-plans under the Plan for purposes of satisfying applicable securities, tax or other laws of various jurisdictions. The Board shall establish such sub-plans by adopting supplements to the Plan containing (i) such limitations on the Board's discretion under the Plan as the Board deems necessary or desirable or (ii) such additional terms and conditions not otherwise inconsistent with the Plan as the Board shall deem necessary or desirable. All supplements adopted by the Board shall be deemed to be part of the Plan, but each supplement shall apply only to Participants within the affected jurisdiction and the Company shall not be required to provide copies of any supplement to Participants in any jurisdiction which is not the subject of such supplement.

(f) Compliance with Section 409A of the Code. Except as provided in individual Award agreements initially or by amendment, if and to the extent (i) any portion of any payment, compensation or other benefit provided to a Participant pursuant to the Plan in connection with his or her employment termination constitutes "nonqualified deferred compensation" within the meaning of Section 409A of the Code and (ii) the Participant is a specified employee as defined

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in Section 409A(a)(2)(B)(i) of the Code, in each case as determined by the Company in accordance with its procedures, by which determinations the Participant (through accepting the Award) agrees that he or she is bound, such portion of the payment, compensation or other benefit shall not be paid before the day that is six months plus one day after the date of "separation from service" (as determined under Section 409A of the Code) (the "**New Payment Date**"), except as Section 409A of the Code may then permit. The aggregate of any payments that otherwise would have been paid to the Participant during the period between the date of separation from service and the New Payment Date shall be paid to the Participant in a lump sum on such New Payment Date, and any remaining payments will be paid on their original schedule.

The Company makes no representations or warranty and shall have no liability to the Participant or any other person if any provisions of or payments, compensation or other benefits under the Plan are determined to constitute nonqualified deferred compensation subject to Section 409A of the Code but do not to satisfy the conditions of that section.

(g) Limitations on Liability. Notwithstanding any other provisions of the Plan, no individual acting as a director, officer, other employee, or agent of the Company will be liable to any Participant, former Participant, spouse, beneficiary, or any other person for any claim, loss, liability, or expense incurred in connection with the Plan, nor will such individual be personally liable with respect to the Plan because of any contract or other instrument he or she executes in his or her capacity as a director, officer, other employee, or agent of the Company. The Company will indemnify and hold harmless each director, officer, other employee, or agent of the Company to whom any duty or power relating to the administration or interpretation of the Plan has been or will be delegated, against any cost or expense (including attorneys' fees) or liability (including any sum paid in settlement of a claim with the Board's approval) arising out of any act or omission to act concerning the Plan unless arising out of such person's own fraud or bad faith.

(h) Governing Law. The provisions of the Plan and all Awards made hereunder shall be governed by and interpreted in accordance with the laws of the State of Delaware, excluding choice-of-law principles of the law of such state that would require the application of the laws of a jurisdiction other than the State of Delaware.

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**SYROS PHARMACEUTICALS, INC.
2012 EQUITY INCENTIVE PLAN**

CALIFORNIA SUPPLEMENT

Pursuant to Section 11(e) of the Plan, the Board has adopted this supplement for purposes of satisfying the requirements of Section 25102(o) of the California Law:

Any Awards granted under the Plan to a Participant who is a resident of the State of California on the date of grant (a "**California Participant**") shall be subject to the following additional limitations, terms and conditions:

1. Additional Limitations on Options.

(a) Maximum Duration of Options. No Options granted to California Participants shall have a term in excess of 10 years measured from the Option grant date.

(b) Minimum Exercise Period Following Termination. Unless a California Participant's employment is terminated for cause (as defined by applicable law, the terms of the Plan or option grant or a contract of employment), in the event of termination of employment of such Participant, such Participant shall have the right to exercise an Option, to the extent that such Participant is entitled to exercise such Option on the date employment terminated, until the earlier of: (i) at least six months from the date of termination, if termination was caused by such Participant's death or disability, (ii) at least 30 days from the date of termination, if termination was caused other than by such Participant's death or disability and (iii) the Option expiration date.

2. Additional Limitations for Other Stock-Based Awards. The terms of all Awards granted to a California Participant under Section 8 of the Plan shall comply, to the extent applicable, with Sections 260.140.42, 260.140.45 and 260.140.46 of the California Code of Regulations.

3. Additional Limitations on Timing of Awards. No Award granted to a California Participant shall become exercisable, vested or realizable, as applicable to such Award, unless the Plan has been approved by the holders of a majority of the Company's outstanding voting securities by the later of (i) within 12 months before or after the date the Plan was adopted by the Board, or (ii) prior to or within 12 months of the granting of any Award to a California Participant.

4. Additional Restriction Regarding Recapitalizations, Stock Splits, Etc. For purposes of Section 9 of the Plan, in the event of a stock split, reverse stock split, stock dividend, recapitalization, combination, reclassification or other distribution of the Company's securities underlying the Award without the receipt of consideration by the Company, the number of securities purchasable, and in the case of Options, the exercise price of such Options, must be proportionately adjusted.

5. Additional Limitations on Transferability of Awards. Notwithstanding the provisions of Section 10(a) of the Plan, an Award granted to a California Participant may not be transferred to an executor or guardian upon the disability of the Participant.

SYROS PHARMACEUTICALS, INC.

**AMENDMENT NO. 1 TO
2012 EQUITY INCENTIVE PLAN**

Pursuant to Section 11(d) of the 2012 Equity Incentive Plan (the "Plan") of Syros Pharmaceuticals, Inc., a Delaware corporation (the "Company"), the Plan be, and hereby is, amended as set forth below. Capitalized terms used and not otherwise defined herein shall have the meanings ascribed to them in the Plan.

1. Section 4(a) of the Plan is hereby deleted in its entirety and the following is substituted in its place:

(a) Number of Shares. Subject to adjustment under Section 9, Awards may be made under the Plan for up to 3,661,000 shares of common stock, \$0.001 par value per share, of the Company (the "**Common Stock**"), any or all of which Awards may be in the form of Incentive Stock Options (as defined in Section 5(b)). If any Award expires or is terminated, surrendered or canceled without having been fully exercised, is forfeited in whole or in part (including as the result of shares of Common Stock subject to such Award being repurchased by the Company at the original issuance price pursuant to a contractual repurchase right), or results in any Common Stock not being issued, the unused Common Stock covered by such Award shall again be available for the grant of Awards under the Plan. Further, shares of Common Stock tendered to the Company by a Participant to exercise an Award shall be added to the number of shares of Common Stock available for the grant of Awards under the Plan. However, in the case of Incentive Stock Options, the two immediately preceding sentences shall be subject to any limitations under the Code. Shares issued under the Plan may consist in whole or in part of authorized but unissued shares or treasury shares.

Adopted by the Board of Directors on March 22, 2013
Approved by Stockholders on March 22, 2013

SYROS PHARMACEUTICALS, INC.

**AMENDMENT NO. 2 TO
2012 EQUITY INCENTIVE PLAN**

Pursuant to Section 11(d) of the 2012 Equity Incentive Plan (the "Plan") of Syros Pharmaceuticals, Inc., a Delaware corporation (the "Company"), the Plan be, and hereby is, amended as set forth below. Capitalized terms used and not otherwise defined herein shall have the meanings ascribed to them in the Plan.

1. Section 4(a) of the Plan is hereby deleted in its entirety and the following is substituted in its place:

(a) Number of Shares. Subject to adjustment under Section 9, Awards may be made under the Plan for up to 5,161,000 shares of common stock, \$0.001 par value per share, of the Company (the "**Common Stock**"), any or all of which Awards may be in the form of Incentive Stock Options (as defined in Section 5(b)). If any Award expires or is terminated, surrendered or canceled without having been fully exercised, is forfeited in whole or in part (including as the result of shares of Common Stock subject to such Award being repurchased by the Company at the original issuance price pursuant to a contractual repurchase right), or results in any Common Stock not being issued, the unused Common Stock covered by such Award shall again be available for the grant of Awards under the Plan. Further, shares of Common Stock tendered to the Company by a Participant to exercise an Award shall be added to the number of shares of Common Stock available for the grant of Awards under the Plan. However, in the case of Incentive Stock Options, the two immediately preceding sentences shall be subject to any limitations under the Code. Shares issued under the Plan may consist in whole or in part of authorized but unissued shares or treasury shares.

Adopted by the Board of Directors on April 10, 2013

SYROS PHARMACEUTICALS, INC.

**AMENDMENT NO. 3 TO
2012 EQUITY INCENTIVE PLAN**

Pursuant to Section 11(d) of the 2012 Equity Incentive Plan (the "Plan") of Syros Pharmaceuticals, Inc., a Delaware corporation (the "Company"), the Plan be, and hereby is, amended as set forth below. Capitalized terms used and not otherwise defined herein shall have the meanings ascribed to them in the Plan.

1. Section 4(a) of the Plan is hereby deleted in its entirety and the following is substituted in its place:

(a) Number of Shares. Subject to adjustment under Section 9, Awards may be made under the Plan for up to 6,900,000 shares of common stock, \$0.001 par value per share, of the Company (the "**Common Stock**"), any or all of which Awards may be in the form of Incentive Stock Options (as defined in Section 5(b)). If any Award expires or is terminated, surrendered or canceled without having been fully exercised, is forfeited in whole or in part (including as the result of shares of Common Stock subject to such Award being repurchased by the Company at the original issuance price pursuant to a contractual repurchase right), or results in any Common Stock not being issued, the unused Common Stock covered by such Award shall again be available for the grant of Awards under the Plan. Further, shares of Common Stock tendered to the Company by a Participant to exercise an Award shall be added to the number of shares of Common Stock available for the grant of Awards under the Plan. However, in the case of Incentive Stock Options, the two immediately preceding sentences shall be subject to any limitations under the Code. Shares issued under the Plan may consist in whole or in part of authorized but unissued shares or treasury shares.

Adopted by the Board of Directors on June 3, 2014
Approved by Stockholders on August 26, 2014

SYROS PHARMACEUTICALS, INC.

**AMENDMENT NO. 4 TO
2012 EQUITY INCENTIVE PLAN**

Pursuant to Section 11(d) of the 2012 Equity Incentive Plan (the "Plan") of Syros Pharmaceuticals, Inc., a Delaware corporation (the "Company"), the Plan be, and hereby is, amended as set forth below. Capitalized terms used and not otherwise defined herein shall have the meanings ascribed to them in the Plan.

1. Section 4(a) of the Plan is hereby deleted in its entirety and the following is substituted in its place:

(a) Number of Shares. Subject to adjustment under Section 9, Awards may be made under the Plan for up to 8,711,306 shares of common stock, \$0.001 par value per share, of the Company (the "**Common Stock**"), any or all of which Awards may be in the form of Incentive Stock Options (as defined in Section 5(b)). If any Award expires or is terminated, surrendered or canceled without having been fully exercised, is forfeited in whole or in part (including as the result of shares of Common Stock subject to such Award being repurchased by the Company at the original issuance price pursuant to a contractual repurchase right), or results in any Common Stock not being issued, the unused Common Stock covered by such Award shall again be available for the grant of Awards under the Plan. Further, shares of Common Stock tendered to the Company by a Participant to exercise an Award shall be added to the number of shares of Common Stock available for the grant of Awards under the Plan. However, in the case of Incentive Stock Options, the two immediately preceding sentences shall be subject to any limitations under the Code. Shares issued under the Plan may consist in whole or in part of authorized but unissued shares or treasury shares.

Adopted by the Board of Directors on October 8, 2014
Approved by Stockholders on October 8, 2014

SYROS PHARMACEUTICALS, INC.

**AMENDMENT NO. 5 TO
2012 EQUITY INCENTIVE PLAN**

Pursuant to Section 11(d) of the 2012 Equity Incentive Plan (the "Plan") of Syros Pharmaceuticals, Inc., a Delaware corporation (the "Company"), the Plan be, and hereby is, amended as set forth below. Capitalized terms used and not otherwise defined herein shall have the meanings ascribed to them in the Plan.

1. Section 4(a) of the Plan is hereby deleted in its entirety and the following is substituted in its place:

(a) Number of Shares. Subject to adjustment under Section 9, Awards may be made under the Plan for up to 10,311,306 shares of common stock, \$0.001 par value per share, of the Company (the “*Common Stock*”), any or all of which Awards may be in the form of Incentive Stock Options (as defined in Section 5(b)). If any Award expires or is terminated, surrendered or canceled without having been fully exercised, is forfeited in whole or in part (including as the result of shares of Common Stock subject to such Award being repurchased by the Company at the original issuance price pursuant to a contractual repurchase right), or results in any Common Stock not being issued, the unused Common Stock covered by such Award shall again be available for the grant of Awards under the Plan. Further, shares of Common Stock tendered to the Company by a Participant to exercise an Award shall be added to the number of shares of Common Stock available for the grant of Awards under the Plan. However, in the case of Incentive Stock Options, the two immediately preceding sentences shall be subject to any limitations under the Code. Shares issued under the Plan may consist in whole or in part of authorized but unissued shares or treasury shares.

Adopted by the Board of Directors on December 15, 2015
Approved by Stockholders on December 23, 2015

SYROS PHARMACEUTICALS, INC.

2016 STOCK INCENTIVE PLAN1. Purpose

The purpose of this 2016 Stock Incentive Plan (the “*Plan*”) of Syros Pharmaceuticals, Inc., a Delaware corporation (the “*Company*”), is to advance the interests of the Company’s stockholders by enhancing the Company’s ability to attract, retain and motivate persons who are expected to make important contributions to the Company and by providing such persons with equity ownership opportunities and performance-based incentives that are intended to better align the interests of such persons with those of the Company’s stockholders. Except where the context otherwise requires, the term “*Company*” shall include any of the Company’s present or future parent or subsidiary corporations as defined in Sections 424(e) or (f) of the Internal Revenue Code of 1986, as amended, and any regulations thereunder (the “*Code*”) and any other business venture (including, without limitation, joint venture or limited liability company) in which the Company has a controlling interest, as determined by the Board of Directors of the Company (the “*Board*”).

2. Eligibility

All of the Company’s employees, officers and directors, as well as consultants and advisors to the Company (as such terms are defined and interpreted for purposes of Form S-8 under the Securities Act of 1933, as amended (the “*Securities Act*”), or any successor form) are eligible to be granted Awards under the Plan. Each person who is granted an Award under the Plan is deemed a “*Participant*.” “*Award*” means Options (as defined in Section 5), SARs (as defined in Section 6), Restricted Stock (as defined in Section 7), Restricted Stock Units (as defined in Section 7) and Other Stock-Based Awards (as defined in Section 8).

3. Administration and Delegation

(a) Administration by Board of Directors. The Plan will be administered by the Board. The Board shall have authority to grant Awards and to adopt, amend and repeal such administrative rules, guidelines and practices relating to the Plan as it shall deem advisable. The Board may construe and interpret the terms of the Plan and any Award agreements entered into under the Plan. The Board may correct any defect, supply any omission or reconcile any inconsistency in the Plan or any Award in the manner and to the extent it shall deem expedient and it shall be the sole and final judge of such expediency. All decisions by the Board shall be made in the Board’s sole discretion and shall be final and binding on all persons having or claiming any interest in the Plan or in any Award.

(b) Appointment of Committees. To the extent permitted by applicable law, the Board may delegate any or all of its powers under the Plan to one or more committees or subcommittees of the Board (a “*Committee*”). All references in the Plan to the “*Board*” shall mean the Board or a Committee of the Board or the officers referred to in Section 3(c) to the extent that the Board’s powers or authority under the Plan have been delegated to such Committee or officers.

(c) Delegation to Officers. To the extent permitted by applicable law, the Board may delegate to one or more officers of the Company the power to grant Options, Restricted Stock, and other Awards that constitute rights under Delaware law (subject to any limitations under the Plan) to employees or officers of the Company and to exercise such other powers under the Plan as the Board may determine, *provided* that the Board shall fix the terms of such Awards to be granted by such officers (including the exercise price of such Awards, which may include a formula by which the exercise price will be determined) and the maximum number of shares subject to such Awards that the officers may grant; *provided further*, however, that no officer shall be authorized to grant such Awards to any “executive officer” of the Company (as defined by Rule 3b-7 under the Securities Exchange Act of 1934, as amended (the “*Exchange Act*”)) or to any “officer” of the Company (as defined by Rule 16a-1 under the Exchange Act).

4. Stock Available for Awards(a) Number of Shares; Share Counting.

(1) Authorized Number of Shares. Subject to adjustment under Section 9, Awards may be made under the Plan (any or all of which Awards may be in the form of Incentive Stock Options, as defined in Section 5(b)) for up to such number of shares of common stock, \$0.001 par value per share, of the Company (the “*Common Stock*”) as is equal to the sum of:

(A) 11,700,000 shares of Common Stock; plus

(B) such additional number of shares of Common Stock (up to 8,815,298 shares) as is equal to the sum of (x) the number of shares of Common Stock reserved for issuance under the Company’s 2012 Equity Incentive Plan (the “*Existing Plan*”) that remain available for grant under the Existing Plan immediately prior to the effectiveness of the registration statement for the Company’s initial public offering and (y) the number of shares of Common Stock subject to awards granted under the Existing Plan which awards expire, terminate or are otherwise surrendered, canceled, forfeited or repurchased by the Company 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 Code); plus

(C) an annual increase to be added on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2017 and continuing for each fiscal year until, and including, the fiscal year ending December 31, 2025, equal to the least of (i) 6,000,000 shares of Common Stock, (ii) 4.0% of the outstanding shares on such date and (iii) an amount determined by the

Board.

Shares issued under the Plan may consist in whole or in part of authorized but unissued shares or treasury shares.

(2) Share Counting. For purposes of counting the number of shares available for the grant of Awards under the Plan:

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(A) all shares of Common Stock covered by SARs shall be counted against the number of shares available for the grant of Awards under the Plan; *provided, however*, that (i) SARs that may be settled only in cash shall not be so counted and (ii) if the Company grants an SAR in tandem with an Option for the same number of shares of Common Stock and provides that only one such Award may be exercised (a “**Tandem SAR**”), only the shares covered by the Option, and not the shares covered by the Tandem SAR, shall be so counted, and the expiration of one in connection with the other’s exercise will not restore shares to the Plan;

(B) if any Award (i) expires or is terminated, surrendered or canceled without having been fully exercised or is forfeited in whole or in part (including as the result of shares of Common Stock subject to such Award being repurchased by the Company at the original issuance price pursuant to a contractual repurchase right) or (ii) results in any Common Stock not being issued (including as a result of an SAR that was settleable either in cash or in stock actually being settled in cash), the unused Common Stock covered by such Award shall again be available for the grant of Awards; *provided, however*, that (1) in the case of Incentive Stock Options, the foregoing shall be subject to any limitations under the Code, (2) in the case of the exercise of an SAR, the number of shares counted against the shares available under the Plan shall be the full number of shares subject to the SAR multiplied by the percentage of the SAR actually exercised, regardless of the number of shares actually used to settle such SAR upon exercise and (3) the shares covered by a Tandem SAR shall not again become available for grant upon the expiration or termination of such Tandem SAR; and

(C) shares of Common Stock delivered (by actual delivery, attestation, or net exercise) to the Company by a Participant to (i) purchase shares of Common Stock upon the exercise of an Award or (ii) satisfy tax withholding obligations (including shares retained from the Award creating the tax obligation) shall be added back to the number of shares available for the future grant of Awards.

(b) Substitute Awards. In connection with a merger or consolidation of an entity with the Company or the acquisition by the Company of property or stock of an entity, the Board may grant Awards in substitution for any options or other stock or stock-based awards granted by such entity or an affiliate thereof. Substitute Awards may be granted on such terms as the Board deems appropriate in the circumstances, notwithstanding any limitations on Awards contained in the Plan. Substitute Awards shall not count against the overall share limit set forth in Section 4(a)(1), except as may be required by reason of Section 422 and related provisions of the Code.

5. Stock Options

(a) General. The Board may grant options to purchase Common Stock (each, an “**Option**”) and determine the number of shares of Common Stock to be covered by each Option, the exercise price of each Option and the conditions and limitations applicable to the exercise of each Option, including conditions relating to applicable federal or state securities laws, as it considers necessary or advisable.

(b) Incentive Stock Options. An Option that the Board intends to be an “incentive stock option” as defined in Section 422 of the Code (an “**Incentive Stock Option**”) shall only be

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granted to employees of Syros Pharmaceuticals, Inc., any of Syros Pharmaceuticals, Inc.’s present or future parent or subsidiary corporations as defined in Sections 424(e) or (f) of the Code, and any other entities the employees of which are eligible to receive Incentive Stock Options under the Code, and shall be subject to and shall be construed consistently with the requirements of Section 422 of the Code. An Option that is not intended to be an Incentive Stock Option shall be designated a “**Nonstatutory Stock Option**.” The Company shall have no liability to a Participant, or any other party, if an Option (or any part thereof) that is intended to be an Incentive Stock Option is not an Incentive Stock Option or if the Company converts an Incentive Stock Option to a Nonstatutory Stock Option.

(c) Exercise Price. The Board shall establish the exercise price of each Option and specify the exercise price in the applicable Option agreement. The exercise price shall be not less than 100% of the fair market value per share of Common Stock as determined by (or in a manner approved by) the Board (“**Fair Market Value**”) on the date the Option is granted; *provided* that if the Board approves the grant of an Option with an exercise price to be determined on a future date, the exercise price shall be not less than 100% of the Fair Market Value on such future date.

(d) Duration of Options. Each Option shall be exercisable at such times and subject to such terms and conditions as the Board may specify in the applicable option agreement; *provided, however*, that no Option will be granted with a term in excess of 10 years.

(e) Exercise of Options. Options may be exercised by delivery to the Company of a notice of exercise in a form (which may be electronic) approved by the Company, together with payment in full (in the manner specified in Section 5(f)) of the exercise price for the number of shares for which the Option is exercised. Shares of Common Stock subject to the Option will be delivered by the

Company as soon as practicable following exercise.

(f) Payment Upon Exercise. Common Stock purchased upon the exercise of an Option granted under the Plan shall be paid for as follows:

- (1) in cash or by check, payable to the order of the Company;
- (2) except as may otherwise be provided in the applicable Option agreement or approved by the Board, in its sole discretion, by (i) delivery of an irrevocable and unconditional undertaking by a creditworthy broker to deliver promptly to the Company sufficient funds to pay the exercise price and any required tax withholding or (ii) delivery by the Participant to the Company of a copy of irrevocable and unconditional instructions to a creditworthy broker to deliver promptly to the Company cash or a check sufficient to pay the exercise price and any required tax withholding;
- (3) to the extent provided for in the applicable Option agreement or approved by the Board, in its sole discretion, by delivery (either by actual delivery or attestation) of shares of Common Stock owned by the Participant valued at their Fair Market Value, provided (i) such method of payment is then permitted under applicable law, (ii) such Common Stock, if acquired directly from the Company, was owned by the Participant for such minimum period of time, if any, as may be established by the Board in its sole discretion and (iii) such Common Stock is not subject to any repurchase, forfeiture, unfulfilled vesting or other similar requirements;

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(4) to the extent provided for in the applicable Nonstatutory Stock Option agreement or approved by the Board in its sole discretion, by delivery of a notice of “net exercise” to the Company, as a result of which the Participant would receive (i) the number of shares underlying the portion of the Option being exercised, less (ii) such number of shares as is equal to (A) the aggregate exercise price for the portion of the Option being exercised divided by (B) the Fair Market Value on the date of exercise;

(5) to the extent permitted by applicable law and provided for in the applicable Option agreement or approved by the Board, in its sole discretion, by payment of such other lawful consideration as the Board may determine; or

(6) by any combination of the above permitted forms of payment.

(g) Limitation on Repricing. Unless such action is approved by the Company’s stockholders, the Company may not (except as provided for under Section 9): (1) amend any outstanding Option granted under the Plan to provide an exercise price per share that is lower than the then-current exercise price per share of such outstanding Option, (2) cancel any outstanding option (whether or not granted under the Plan) and grant in substitution therefor new Awards under the Plan (other than Awards granted pursuant to Section 4(b)) covering the same or a different number of shares of Common Stock and having an exercise price per share lower than the then-current exercise price per share of the cancelled option, (3) cancel in exchange for a cash payment any outstanding Option with an exercise price per share above the then-current Fair Market Value or (4) take any other action under the Plan that constitutes a “repricing” within the meaning of the rules of the NASDAQ Stock Market (“*NASDAQ*”).

6. Stock Appreciation Rights

(a) General. The Board may grant Awards consisting of stock appreciation rights (“*SARs*”) entitling the holder, upon exercise, to receive an amount of Common Stock or cash or a combination thereof (such form to be determined by the Board) determined by reference to appreciation, from and after the date of grant, in the Fair Market Value of a share of Common Stock over the measurement price established pursuant to Section 6(b). The date as of which such appreciation is determined shall be the exercise date.

(b) Measurement Price. The Board shall establish the measurement price of each SAR and specify it in the applicable SAR agreement. The measurement price shall not be less than 100% of the Fair Market Value on the date the SAR is granted; *provided* that if the Board approves the grant of an SAR effective as of a future date, the measurement price shall be not less than 100% of the Fair Market Value on such future date.

(c) Duration of SARs. Each SAR shall be exercisable at such times and subject to such terms and conditions as the Board may specify in the applicable SAR agreement; *provided, however*, that no SAR will be granted with a term in excess of 10 years.

(d) Exercise of SARs. SARs may be exercised by delivery to the Company of a notice of exercise in a form (which may be electronic) approved by the Company, together with any other documents required by the Board.

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(e) Limitation on Repricing. Unless such action is approved by the Company’s stockholders, the Company may not (except as provided for under Section 9): (1) amend any outstanding SAR granted under the Plan to provide a measurement price per share that is lower than the then-current measurement price per share of such outstanding SAR, (2) cancel any outstanding SAR (whether or not granted under the Plan) and grant in substitution therefor new Awards under the Plan (other than Awards granted pursuant to Section 4(b)) covering the same or a different number of shares of Common Stock and having an exercise or measurement price per share lower than the then-current measurement price per share of the cancelled SAR, (3) cancel in exchange for a cash payment any outstanding SAR with a measurement price per share above the then-current Fair Market Value or (4) take any other action under the Plan that constitutes a “repricing” within the meaning of the rules of NASDAQ.

7. Restricted Stock; Restricted Stock Units

(a) General. The Board may grant Awards entitling recipients to acquire shares of Common Stock (“**Restricted Stock**”), subject to the right of the Company to repurchase all or part of such shares at their issue price or other stated or formula price (or to require forfeiture of such shares if issued at no cost) from the recipient in the event that conditions specified by the Board in the applicable Award are not satisfied prior to the end of the applicable restriction period or periods established by the Board for such Award. The Board may also grant Awards entitling the recipient to receive shares of Common Stock or cash to be delivered at the time such Award vests (“**Restricted Stock Units**”) (Restricted Stock and Restricted Stock Units are each referred to herein as a “**Restricted Stock Award**”).

(b) Terms and Conditions for All Restricted Stock Awards. The Board shall determine the terms and conditions of a Restricted Stock Award, including the conditions for vesting and repurchase (or forfeiture) and the issue price, if any.

(c) Additional Provisions Relating to Restricted Stock.

(1) Dividends. Unless otherwise provided in the applicable Award agreement, any dividends (whether paid in cash, stock or property) declared and paid by the Company with respect to shares of Restricted Stock (“**Accrued Dividends**”) shall be paid to the Participant only if and when such shares become free from the restrictions on transferability and forfeitability that apply to such shares. Each payment of Accrued Dividends will be made no later than the end of the calendar year in which the dividends are paid to stockholders of that class of stock or, if later, the 15th day of the third month following the lapsing of the restrictions on transferability and the forfeitability provisions applicable to the underlying shares of Restricted Stock.

(2) Stock Certificates. The Company may require that any stock certificates issued in respect of shares of Restricted Stock, as well as dividends or distributions paid on such Restricted Stock, shall be deposited in escrow by the Participant, together with a stock power endorsed in blank, with the Company (or its designee). At the expiration of the applicable restriction periods, the Company (or such designee) shall deliver the certificates no longer subject to such restrictions to the Participant or if the Participant has died, to his or her Designated Beneficiary. “**Designated Beneficiary**” means (i) the beneficiary designated, in a

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manner determined by the Board, by a Participant to receive amounts due or exercise rights of the Participant in the event of the Participant’s death or (ii) in the absence of an effective designation by a Participant, the Participant’s estate.

(d) Additional Provisions Relating to Restricted Stock Units.

(1) Settlement. Upon the vesting of and/or lapsing of any other restrictions (i.e., settlement) with respect to each Restricted Stock Unit, the Participant shall be entitled to receive from the Company such number of shares of Common Stock or (if so provided in the applicable Award agreement) an amount of cash equal to the Fair Market Value of such number of shares of Common Stock as are set forth in the applicable Restricted Stock Unit agreement. The Board may, in its discretion, provide that settlement of Restricted Stock Units shall be deferred, on a mandatory basis or at the election of the Participant in a manner that complies with Section 409A of the Code.

(2) Voting Rights. A Participant shall have no voting rights with respect to any Restricted Stock Units.

(3) Dividend Equivalents. The Award agreement for Restricted Stock Units may provide Participants with the right to receive an amount equal to any dividends or other distributions declared and paid on an equal number of outstanding shares of Common Stock (“**Dividend Equivalents**”). Dividend Equivalents may be settled in cash and/or shares of Common Stock and shall be subject to the same restrictions on transfer and forfeitability as the Restricted Stock Units with respect to which paid, in each case to the extent provided in the Award agreement.

8. Other Stock-Based Awards

(a) General. Other Awards of shares of Common Stock, and other Awards that are valued in whole or in part by reference to, or are otherwise based on, shares of Common Stock or other property, may be granted hereunder to Participants (“**Other Stock-Based Awards**”). Such Other Stock-Based Awards shall also be available as a form of payment in the settlement of other Awards granted under the Plan or as payment in lieu of compensation to which a Participant is otherwise entitled. Other Stock-Based Awards may be paid in shares of Common Stock or cash, as the Board shall determine.

(b) Terms and Conditions. Subject to the provisions of the Plan, the Board shall determine the terms and conditions of each Other Stock-Based Award, including any purchase price applicable thereto.

9. Adjustments for Changes in Common Stock and Certain Other Events

(a) Changes in Capitalization. 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 Common Stock other than an ordinary cash dividend, (i) the number and class of securities available under the Plan, (ii) the share counting rules set forth in Section 4(a), (iii) the number

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and class of securities and exercise price per share of each outstanding Option, (iv) the share and per-share provisions and the measurement price of each outstanding SAR, (v) the number of shares subject to and the repurchase price per share subject to each outstanding Restricted Stock Award and (vi) the share and per-share-related provisions and the purchase price, if any, of each outstanding Other Stock-Based Award, shall be equitably adjusted by the Company (or substituted Awards may be made, if applicable) in the manner determined by the Board. Without limiting the generality of the foregoing, in the event the Company effects a split of the Common Stock by means of a stock dividend and the exercise price of and the number of shares subject to an outstanding Option are adjusted as of the date of the distribution of the dividend (rather than as of the record date for such dividend), then an optionee who exercises an Option between the record date and the distribution date for such stock dividend shall be entitled to receive, on the distribution date, the stock dividend with respect to the shares of Common Stock acquired upon such Option exercise, notwithstanding the fact that such shares were not outstanding as of the close of business on the record date for such stock dividend.

(b) Reorganization Events.

(1) Definition. A “**Reorganization Event**” shall mean: (a) any merger or consolidation of the Company with or into another entity as a result of which all of the Common Stock of the Company is converted into or exchanged for the right to receive cash, securities or other property or is cancelled, (b) any transfer or disposition of all of the Common Stock of the Company for cash, securities or other property pursuant to a share exchange or other transaction or (c) any liquidation or dissolution of the Company.

(2) Consequences of a Reorganization Event on Awards Other than Restricted Stock.

(A) In connection with a Reorganization Event, the Board may take any one or more of the following actions as to all or any (or any portion of) outstanding Awards other than Restricted Stock on such terms as the Board determines (except to the extent specifically provided otherwise in an applicable Award agreement or another agreement between the Company and the Participant): (i) provide that such Awards shall be assumed, or substantially equivalent Awards shall be substituted, by the acquiring or succeeding corporation (or an affiliate thereof), (ii) upon written notice to a Participant, provide that all of the Participant’s unvested and/or unexercised Awards will terminate immediately prior to the consummation of such Reorganization Event unless exercised by the Participant (to the extent then exercisable) within a specified period following the date of such notice, (iii) 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 Reorganization Event, (iv) in the event of a Reorganization Event under the terms of which holders of Common Stock will receive upon consummation thereof a cash payment for each share surrendered in the Reorganization Event (the “**Acquisition Price**”), make or provide for a cash payment to Participants with respect to each Award held by a Participant equal to (A) the number of shares of 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 (B) the excess, if any, of (I) the Acquisition Price over (II) the exercise, measurement or purchase price of such Award and any applicable tax withholdings, in exchange

for the termination of such Award, (v) provide that, in connection with a liquidation or dissolution of the Company, Awards shall convert into the right to receive liquidation proceeds (if applicable, net of the exercise, measurement or purchase price thereof and any applicable tax withholdings) and (vi) any combination of the foregoing. In taking any of the actions permitted under this Section 9(b)(2), the Board shall not be obligated by the Plan to treat all Awards, all Awards held by a Participant, or all Awards of the same type, identically.

(B) Notwithstanding the terms of Section 9(b)(2)(A), in the case of outstanding Restricted Stock Units that are subject to Section 409A of the Code: (i) if the applicable Restricted Stock Unit agreement provides that the Restricted Stock Units shall be settled upon a “change in control event” within the meaning of Treasury Regulation Section 1.409A-3(i)(5)(i), and the Reorganization Event constitutes such a “change in control event”, then no assumption or substitution shall be permitted pursuant to Section 9(b)(2)(A)(i) and the Restricted Stock Units shall instead be settled in accordance with the terms of the applicable Restricted Stock Unit agreement; and (ii) the Board may only undertake the actions set forth in clauses (iii), (iv) or (v) of Section 9(b)(2)(A) if the Reorganization Event constitutes a “change in control event” as defined under Treasury Regulation Section 1.409A-3(i)(5)(i) and such action is permitted or required by Section 409A of the Code; if the Reorganization Event is not a “change in control event” as so defined or such action is not permitted or required by Section 409A of the Code, and the acquiring or succeeding corporation does not assume or substitute the Restricted Stock Units pursuant to clause (i) of Section 9(b)(2)(A), then the unvested Restricted Stock Units shall terminate immediately prior to the consummation of the Reorganization Event without any payment in exchange therefor.

(C) For purposes of Section 9(b)(2)(A)(i), an Award (other than Restricted Stock) shall be considered assumed if, following consummation of the Reorganization Event, such Award confers the right to purchase or receive pursuant to the terms of such Award, for each share of Common Stock subject to the Award immediately prior to the consummation of the Reorganization Event, the consideration (whether cash, securities or other property) received as a result of the Reorganization Event by holders of Common Stock for each share of Common Stock held immediately prior to the consummation of the Reorganization Event (and if holders were offered a choice of consideration, the type of consideration chosen by the holders of a majority of the outstanding shares of Common Stock); *provided, however*, that if the consideration received as a result of the Reorganization Event is not solely common stock of the acquiring or succeeding corporation (or an affiliate thereof), the Company may, with the consent of the acquiring or succeeding corporation, provide for the consideration to be received upon the exercise or settlement of the Award to consist solely of such number of shares of common stock of the acquiring or succeeding corporation (or an affiliate thereof) that the Board determines to be equivalent in value (as of the date of such determination or another date specified by the Board) to the per share consideration received by holders of outstanding shares of Common Stock as a result of the Reorganization Event.

(3) Consequences of a Reorganization Event on Restricted Stock. Upon the occurrence of a Reorganization Event other than a liquidation or dissolution of the Company, the repurchase and other rights of the Company with respect to outstanding

Restricted Stock shall inure to the benefit of the Company's successor and shall, unless the Board determines otherwise, apply to the cash, securities or other property which the Common Stock was

converted into or exchanged for pursuant to such Reorganization Event in the same manner and to the same extent as they applied to such Restricted Stock; *provided, however*, that the Board may provide for termination or deemed satisfaction of such repurchase or other rights under the instrument evidencing any Restricted Stock or any other agreement between a Participant and the Company, either initially or by amendment. Upon the occurrence of a Reorganization Event involving the liquidation or dissolution of the Company, except to the extent specifically provided to the contrary in the instrument evidencing any Restricted Stock or any other agreement between a Participant and the Company, all restrictions and conditions on all Restricted Stock then outstanding shall automatically be deemed terminated or satisfied.

10. General Provisions Applicable to Awards

(a) Transferability of Awards. Awards shall not be sold, assigned, transferred, pledged or otherwise encumbered by the person to whom they are granted, either voluntarily or by operation of law, except by will or the laws of descent and distribution or, other than in the case of an Incentive Stock Option, pursuant to a qualified domestic relations order, and, during the life of the Participant, shall be exercisable only by the Participant; *provided, however*, that the Board may permit or provide in an Award for the gratuitous transfer of the Award by the Participant to or for the benefit of any immediate family member, family trust or other entity established for the benefit of the Participant and/or an immediate family member thereof if the Company would be eligible to use a Form S-8 under the Securities Act for the registration of the sale of the Common Stock subject to such Award to such proposed transferee; *provided further*, that the Company shall not be required to recognize any such permitted transfer until such time as such permitted transferee shall, as a condition to such transfer, deliver to the Company a written instrument in form and substance satisfactory to the Company confirming that such transferee shall be bound by all of the terms and conditions of the Award. References to a Participant, to the extent relevant in the context, shall include references to authorized transferees. For the avoidance of doubt, nothing contained in this Section 10(a) shall be deemed to restrict a transfer to the Company.

(b) Documentation. Each Award shall be evidenced in such form (written, electronic or otherwise) as the Board shall determine. Each Award may contain terms and conditions in addition to those set forth in the Plan.

(c) Board Discretion. Except as otherwise provided by the Plan, each Award may be made alone or in addition or in relation to any other Award. The terms of each Award need not be identical, and the Board need not treat Participants uniformly.

(d) Termination or Change of Status. The Board shall determine, either at the time an Award is granted or thereafter, the effect on an Award of the disability, death, termination or other cessation of employment, authorized leave of absence or other change in the employment or other status of a Participant and the extent to which, and the period during which, the Participant, or the Participant's legal representative, conservator, guardian or Designated Beneficiary, may exercise rights under the Award.

(e) Withholding. The Participant must satisfy all applicable federal, state, and local or other income and employment tax withholding obligations before the Company will deliver

stock certificates or otherwise recognize ownership of Common Stock under an Award. The Company may decide to satisfy the withholding obligations through additional withholding on salary or wages. If the Company elects not to or cannot withhold from other compensation, the Participant must pay the Company the full amount, if any, required for withholding or have a broker tender to the Company cash equal to the withholding obligations. Payment of withholding obligations is due before the Company will issue any shares on exercise, vesting or release from forfeiture of an Award or at the same time as payment of the exercise or purchase price, unless the Company determines otherwise. If provided for in an Award or approved by the Board in its sole discretion, a Participant may satisfy such tax obligations in whole or in part by delivery (either by actual delivery or attestation) of shares of Common Stock, including shares retained from the Award creating the tax obligation, valued at their Fair Market Value; *provided, however*, except as otherwise provided by the Board, that the total tax withholding where stock is being used to satisfy such tax obligations cannot exceed the Company's minimum statutory withholding obligations (based on minimum statutory withholding rates for federal and state tax purposes, including payroll taxes, that are applicable to such supplemental taxable income). Shares used to satisfy tax withholding requirements cannot be subject to any repurchase, forfeiture, unfulfilled vesting or other similar requirements.

(f) Amendment of Award. Except as otherwise provided in Sections 5(g) and 6(e) with respect to repricings and Section 11(d) with respect to actions requiring stockholder approval, the Board may amend, modify or terminate any outstanding Award, 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 to a Nonstatutory Stock Option. The Participant's consent to such action shall be required unless (i) the Board determines that the action, taking into account any related action, does not materially and adversely affect the Participant's rights under the Plan or (ii) the change is permitted under Section 9.

(g) Conditions on Delivery of Stock. The Company will not be obligated to deliver any shares of Common Stock pursuant to the Plan or to remove restrictions from shares previously issued or delivered under the Plan until (i) all conditions of the Award have been met or removed to the satisfaction of the Company, (ii) in the opinion of the Company's counsel, all other legal matters in connection with the issuance and delivery of such shares have been satisfied, including any applicable securities laws and regulations and

any applicable stock exchange or stock market rules and regulations and (iii) the Participant has executed and delivered to the Company such representations or agreements as the Company may consider appropriate to satisfy the requirements of any applicable laws, rules or regulations.

(h) Acceleration. The Board may at any time provide that any Award 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.

11. Miscellaneous

(a) No Right To Employment or Other Status. No person shall have any claim or right to be granted an Award by virtue of the adoption of the Plan, and the grant of an Award shall not be construed as giving a Participant the right to continued employment or any other

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relationship with the Company. The Company expressly reserves the right at any time to dismiss or otherwise terminate its relationship with a Participant free from any liability or claim under the Plan, except as expressly provided in the applicable Award.

(b) No Rights As Stockholder; Clawback Policy. Subject to the provisions of the applicable Award, no Participant or Designated Beneficiary shall have any rights as a stockholder with respect to any shares of Common Stock to be distributed with respect to an Award until becoming the record holder of such shares. In accepting an award under the Plan, a Participant shall agree to be bound by any clawback policy the Company may adopt in future.

(c) Effective Date and Term of Plan. The Plan shall become effective immediately prior to the effectiveness of the Company's registration statement for its initial public offering (the "**Effective Date**"). No Awards shall be granted under the Plan after the expiration of 10 years from the Effective Date, but Awards previously granted may extend beyond that date.

(d) Amendment of Plan. The Board may amend, suspend or terminate the Plan or any portion thereof at any time provided that no amendment that would require stockholder approval under the rules of NASDAQ may be made effective unless and until the Company's stockholders approve such amendment. In addition, if at any time the approval of the Company's stockholders is required as to any other modification or amendment under Section 422 of the Code or any successor provision with respect to Incentive Stock Options, the Board may not effect such modification or amendment without such approval. Unless otherwise specified in the amendment, any amendment to the Plan adopted in accordance with this Section 11(d) shall apply to, and be binding on the holders of, all Awards outstanding under the Plan at the time the amendment is adopted, provided the Board determines that such amendment, taking into account any related action, does not materially and adversely affect the rights of Participants under the Plan. No Award shall be made that is conditioned upon stockholder approval of any amendment to the Plan unless the Award provides that (i) it will terminate or be forfeited if stockholder approval of such amendment is not obtained within no more than 12 months from the date of grant and (2) it may not be exercised or settled (or otherwise result in the issuance of Common Stock) prior to such stockholder approval.

(e) Authorization of Sub-Plans (including for Grants to non-U.S. Employees). The Board may from time to time establish one or more sub-plans under the Plan for purposes of satisfying applicable securities, tax or other laws of various jurisdictions. The Board shall establish such sub-plans by adopting supplements to the Plan containing (i) such limitations on the Board's discretion under the Plan as the Board deems necessary or desirable or (ii) such additional terms and conditions not otherwise inconsistent with the Plan as the Board shall deem necessary or desirable. All supplements adopted by the Board shall be deemed to be part of the Plan, but each supplement shall apply only to Participants within the affected jurisdiction and the Company shall not be required to provide copies of any supplement to Participants in any jurisdiction which is not the subject of such supplement.

(f) Compliance with Section 409A of the Code. Except as provided in individual Award agreements initially or by amendment, if and to the extent (i) any portion of any payment, compensation or other benefit provided to a Participant pursuant to the Plan in connection with his or her employment termination constitutes "nonqualified deferred compensation" within the

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meaning of Section 409A of the Code and (ii) the Participant is a specified employee as defined in Section 409A(a)(2)(B)(i) of the Code, in each case as determined by the Company in accordance with its procedures, by which determinations the Participant (through accepting the Award) agrees that he or she is bound, such portion of the payment, compensation or other benefit shall not be paid before the day that is six months plus one day after the date of "separation from service" (as determined under Section 409A of the Code) (the "**New Payment Date**"), except as Section 409A of the Code may then permit. The aggregate of any payments that otherwise would have been paid to the Participant during the period between the date of separation from service and the New Payment Date shall be paid to the Participant in a lump sum on such New Payment Date, and any remaining payments will be paid on their original schedule.

The Company makes no representations or warranty and shall have no liability to the Participant or any other person if any provisions of or payments, compensation or other benefits under the Plan are determined to constitute nonqualified deferred compensation subject to Section 409A of the Code but do not to satisfy the conditions of that section.

(g) Effect on Other Employee Benefit Plans. The value of any Award issued to a Participant and the Shares issuable or amounts payable thereunder shall not be included as compensation, earnings, salaries or other similar terms used when calculating benefits under any employee benefit plan (other than the Plan) sponsored by the Company, except as such plans otherwise expressly

provide.

(h) Limitations on Liability. Notwithstanding any other provisions of the Plan, no individual acting as a director, officer, employee or agent of the Company will be liable to any Participant, former Participant, spouse, beneficiary, or any other person for any claim, loss, liability, or expense incurred in connection with the Plan, nor will such individual be personally liable with respect to the Plan because of any contract or other instrument he or she executes in his or her capacity as a director, officer, employee or agent of the Company. The Company will indemnify and hold harmless each director, officer, employee or agent of the Company to whom any duty or power relating to the administration or interpretation of the Plan has been or will be delegated, against any cost or expense (including attorneys' fees) or liability (including any sum paid in settlement of a claim with the Board's approval) arising out of any act or omission to act concerning the Plan unless arising out of such person's own fraud or bad faith.

(i) Governing Law. The provisions of the Plan and all Awards made hereunder shall be governed by and interpreted in accordance with the laws of the State of Delaware, excluding choice-of-law principles of the law of such state that would require the application of the laws of a jurisdiction other than the State of Delaware.

SYROS PHARMACEUTICALS, INC.
INCENTIVE STOCK OPTION AGREEMENT

Syros Pharmaceuticals, Inc. (the “Company”) hereby grants the following stock option pursuant to its 2016 Stock Incentive Plan. The terms and conditions attached hereto are also a part hereof.

Notice of Grant

Name of optionee (the “Participant”):
 Grant Date:
 Number of shares of the Company’s Common Stock subject to this option (“Shares”):
 Option exercise price per Share:(1)
 Number, if any, of Shares that vest immediately on the grant date:
 Shares that are subject to vesting schedule:
 Vesting Start Date:
 Final Exercise Date: (2)

Vesting Schedule:

All vesting is dependent on the Participant remaining an Eligible Participant, as provided herein.

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

SYROS PHARMACEUTICALS, INC.

 Signature of Participant

 Street Address

 City/State/Zip Code

By: _____
 Name of Officer
 Title:

- (1) This must be at least 100% of the fair market value of the Common Stock on the date of grant (or 110% in the case of a Participant that owns more than 10% of the total combined voting power of all classes of stock of the Company or its parent or subsidiary (a “10% Shareholder”)) for the option to qualify as an incentive stock option (an “ISO”) under Section 422 of the Code.
- (2) The Final Exercise Date must be no more than 10 years (5 years in the case of a 10% shareholder) from the date of grant for the option to qualify as an ISO. The correct approach to calculate the final exercise date is to use the day immediately prior to the date ten years out from the date of the stock option award grant (5 years in the case of a 10% stockholder). For example, an award granted to someone on July 1, 2015 would expire on June 30, 2025 (not on July 1, 2025).

SYROS PHARMACEUTICALS, INC.

Incentive Stock Option Agreement
Incorporated Terms and Conditions

1. Grant of Option.

This agreement evidences the grant by the Company, on the grant date (the “Grant Date”) set forth in the Notice of Grant that forms part of this agreement (the “Notice of Grant”), to the Participant of an option to purchase, in whole or in part, on the terms provided herein and in the Company’s 2016 Stock Incentive Plan (the “Plan”), the number of Shares set forth in the Notice of Grant of common stock, \$0.001 par value per share, of the Company (“Common Stock”), at the exercise price per Share set forth in the Notice of Grant. Unless earlier terminated, this option shall expire at 5:00 p.m., Eastern time, on the Final Exercise Date set forth in the Notice of Grant (the “Final Exercise Date”).

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

2. Vesting Schedule.

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

The right of exercise shall be cumulative so that to the extent the option is not exercised in any period to the maximum extent

permissible it shall continue to be exercisable, in whole or in part, with respect to all Shares for which it is vested until the earlier of the Final Exercise Date or the termination of this option under Section 3 hereof or the Plan.

3. Exercise of Option.

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

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

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(c) Termination of Relationship with the Company. If the Participant ceases to be an Eligible Participant for any reason, then, except as provided in paragraphs (d) and (e) below, the right to exercise this option shall terminate three months after such cessation (but in no event after the Final Exercise Date), provided that this option shall be exercisable only to the extent that the Participant was entitled to exercise this option on the date of such cessation. Notwithstanding the foregoing, if the Participant, prior to the Final Exercise Date, violates the non-competition or confidentiality provisions of any employment contract, confidentiality and nondisclosure agreement or other agreement between the Participant and the Company, the right to exercise this option shall terminate immediately upon such violation.

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

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

4. Tax Matters.

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

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

5. Transfer Restrictions; Clawback.

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

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

future.

6. Provisions of the Plan.

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

ANNEX A

SYROS PHARMACEUTICALS, INC.

Stock Option Exercise Notice

Syros Pharmaceuticals, Inc.
480 Arsenal Street, Suite 130
Watertown, MA 02472

Dear Sir or Madam:

I, _____ (the "Participant"), hereby irrevocably exercise the right to purchase _____ shares of the Common Stock, \$0.001 par value per share (the "Shares"), of Syros Pharmaceuticals, Inc. (the "Company") at \$ _____ per share pursuant to the Company's 2016 Stock Incentive Plan and a stock option agreement with the Company dated _____ (the "Option Agreement"). Enclosed herewith is a payment of \$ _____, the aggregate purchase price for the Shares. The certificate for the Shares should be registered in my name as it appears below or, if so indicated below, jointly in my name and the name of the person designated below, with right of survivorship.

Dated: _____

Signature

Print Name:

Address:

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

SYROS PHARMACEUTICALS, INC.
NONSTATUTORY STOCK OPTION AGREEMENT

Syros Pharmaceuticals, Inc. (the “Company”) hereby grants the following stock option pursuant to its 2016 Stock Incentive Plan. The terms and conditions attached hereto are also a part hereof.

Notice of Grant

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

Vesting Schedule:

All vesting is dependent on the Participant remaining an Eligible Participant, as provided herein.

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

SYROS PHARMACEUTICALS, INC.

 Signature of Participant

 Street Address

 City/State/Zip Code

By: _____
 Name of Officer
 Title:

SYROS PHARMACEUTICALS, INC.

Nonstatutory Stock Option Agreement
Incorporated Terms and Conditions

1. Grant of Option.

This agreement evidences the grant by the Company, on the grant date (the “Grant Date”) set forth in the Notice of Grant that forms part of this agreement (the “Notice of Grant”), to the Participant of an option to purchase, in whole or in part, on the terms provided herein and in the Company’s 2016 Stock Incentive Plan (the “Plan”), the number of Shares set forth in the Notice of Grant of common stock, \$0.001 par value per share, of the Company (“Common Stock”), at the exercise price per Share set forth in the Notice of Grant. Unless earlier terminated, this option shall expire at 5:00 p.m., Eastern time, on the Final Exercise Date set forth in the Notice of Grant (the “Final Exercise Date”).

It is intended that the option evidenced by this agreement shall not be an incentive stock option as defined in Section 422 of the Internal Revenue Code of 1986, as amended, and any regulations promulgated thereunder (the “Code”). Except as otherwise indicated by the context, the term “Participant”, as used in this option, shall be deemed to include any person who acquires the right to exercise this option validly under its terms.

2. Vesting Schedule.

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

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

3. Exercise of Option.

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

this option may be for any fractional share.

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

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(c) Termination of Relationship with the Company. If the Participant ceases to be an Eligible Participant for any reason, then, except as provided in paragraphs (d) and (e) below, the right to exercise this option shall terminate three months after such cessation (but in no event after the Final Exercise Date), provided that this option shall be exercisable only to the extent that the Participant was entitled to exercise this option on the date of such cessation. Notwithstanding the foregoing, if the Participant, prior to the Final Exercise Date, violates the non-competition or confidentiality provisions of any employment contract, confidentiality and nondisclosure agreement or other agreement between the Participant and the Company, the right to exercise this option shall terminate immediately upon such violation.

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

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

4. Withholding.

No Shares will be issued pursuant to the exercise of this option unless and until the Participant pays to the Company, or makes provision satisfactory to the Company for payment

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of, any federal, state or local withholding taxes required by law to be withheld in respect of this option.

5. Transfer Restrictions: Clawback.

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

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

6. Provisions of the Plan.

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

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SYROS PHARMACEUTICALS, INC.

Stock Option Exercise Notice

Syros Pharmaceuticals, Inc.
480 Arsenal Street, Suite 130
Watertown, MA 02472

Dear Sir or Madam:

I, _____ (the "Participant"), hereby irrevocably exercise the right to purchase _____ shares of the Common Stock, \$0.001 par value per share (the "Shares"), of Syros Pharmaceuticals, Inc. (the "Company") at \$ _____ per share pursuant to the Company's 2016 Stock Incentive Plan and a stock option agreement with the Company dated _____ (the "Option Agreement"). Enclosed herewith is a payment of \$ _____, the aggregate purchase price for the Shares. The certificate for the Shares should be registered in my name as it appears below or, if so indicated below, jointly in my name and the name of the person designated below, with right of survivorship.

Dated: _____

Signature
Print Name:

Address:

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

SYROS PHARMACEUTICALS, INC.

2016 EMPLOYEE STOCK PURCHASE PLAN

The purpose of this 2016 Employee Stock Purchase Plan (this “Plan”) is to provide eligible employees of Syros Pharmaceuticals, Inc. (the “Company”) and certain of its subsidiaries with opportunities to purchase shares of the Company’s common stock, \$0.001 par value per share (the “Common Stock”), commencing at such time and on such dates as the Board of Directors of the Company (the “Board”) shall determine. Subject to adjustment under Section 15 hereof, the number of shares of Common Stock that have been approved for this purpose is the sum of:

- (a) 2,200,000 shares of Common Stock; plus
- (b) an annual increase to be added on the first day of each fiscal year, beginning with the fiscal year ended December 31, 2017 and ending on December 31, 2025, equal to the lowest of (i) 4,400,000 shares of Common Stock, (ii) 1.0% of the outstanding shares on such date or (iii) an amount determined by the Board.

This Plan is intended to qualify as an “employee stock purchase plan” as defined in Section 423 of the Internal Revenue Code of 1986, as amended (the “Code”), and the regulations issued thereunder, and shall be interpreted consistent therewith.

1. Administration. The Plan will be administered by the Board or by a Committee appointed by the Board (the “Committee”). The Board or the Committee has authority to make rules and regulations for the administration of the Plan and its interpretation and decisions with regard thereto shall be final and conclusive.

2. Eligibility. All employees of the Company and all employees of any subsidiary of the Company (as defined in Section 424(f) of the Code) designated by the Board or the Committee from time to time (a “Designated Subsidiary”), are eligible to participate in any one or more of the offerings of Options (as defined in Section 9) to purchase Common Stock under the Plan provided that:

- (a) they are customarily employed by the Company or a Designated Subsidiary for more than twenty (20) hours a week and for more than six months in a calendar year;
- (b) they have been employed by the Company or a Designated Subsidiary for at least three (3) months prior to enrolling in the Plan; and
- (c) they are employees of the Company or a Designated Subsidiary on the first day of the applicable Plan Period (as defined below).

No employee may be granted an Option hereunder if such employee, immediately after the Option is granted, owns 5% or more of the total combined voting power or value of the stock

of the Company or any subsidiary. For purposes of the preceding sentence, the attribution rules of Section 424(d) of the Code shall apply in determining the stock ownership of an employee, and all stock that the employee has a contractual right to purchase shall be treated as stock owned by the employee.

The Company retains the discretion to determine which eligible employees may participate in an offering pursuant to and consistent with Treasury Regulation Sections 1.423-2(e) and (f).

3. Offerings. The Company will make one or more offerings (“Offerings”) to employees to purchase stock under this Plan. Offerings will begin at such time and on such dates as the Board shall determine, or the first business day thereafter (such dates, the “Offering Commencement Dates”). Each Offering Commencement Date will begin a six (6) month period (a “Plan Period”) during which payroll deductions will be made and held for the purchase of Common Stock at the end of the Plan Period. The Board or the Committee may, at its discretion, choose a different Plan Period of not more than twelve (12) months for Offerings.

4. Participation. An employee eligible on the Offering Commencement Date of any Offering may participate in such Offering by completing and forwarding either a written or electronic payroll deduction authorization form to the employee’s appropriate payroll office at least fifteen (15) days prior to the applicable Offering Commencement Date. The form will authorize a regular payroll deduction from the Compensation received by the employee during the Plan Period. Unless an employee files a new form or withdraws from the Plan, his or her deductions and purchases will continue at the same rate for future Offerings under the Plan as long as the Plan remains in effect. The term “Compensation” means the amount of money reportable on the employee’s Federal Income Tax Withholding Statement, excluding overtime, shift premium, incentive or bonus awards, allowances and reimbursements for expenses such as relocation allowances for travel expenses, income or gains associated with the grant or vesting of restricted stock, income or gains on the exercise of Company stock options or stock appreciation rights, and similar items, whether or not shown or separately identified on the employee’s Federal Income Tax Withholding Statement, but including, in the case of salespersons, sales commissions to the extent determined by the Board or the Committee.

5. Deductions. The Company will maintain payroll deduction accounts for all participating employees. With respect to

any Offering made under this Plan, an employee may authorize a payroll deduction in any percentage amount (in whole percentages) up to a maximum of fifteen percent (15%) of the Compensation he or she receives during the Plan Period or such shorter period during which deductions from payroll are made. The Board or the Committee may, at its discretion, designate a lower maximum contribution rate. The minimum payroll deduction is such percentage of Compensation as may be established from time to time by the Board or the Committee.

6. Deduction Changes. An employee may decrease or discontinue his or her payroll deduction once during any Plan Period, by filing either a written or electronic new payroll deduction authorization form. However, an employee may not increase his or her payroll deduction during a Plan Period. If an employee elects to discontinue his or her payroll deductions during a Plan Period, but does not elect to withdraw his or her funds pursuant to

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Section 8 hereof, funds deducted prior to his or her election to discontinue will be applied to the purchase of Common Stock on the Exercise Date (as defined below).

7. Interest. Interest will not be paid on any employee accounts, except to the extent that the Board or the Committee, in its sole discretion, elects to credit employee accounts with interest at such rate as it may from time to time determine.

8. Withdrawal of Funds. An employee may at any time prior to the close of business on the fifteenth business day prior to the end of a Plan Period and for any reason permanently draw out the balance accumulated in the employee's account and thereby withdraw from participation in an Offering. Partial withdrawals are not permitted. The employee may not begin participation again during the remainder of the Plan Period during which the employee withdrew his or her balance. The employee may participate in any subsequent Offering in accordance with terms and conditions established by the Board or the Committee.

9. Purchase of Shares.

(a) Number of Shares. On the Offering Commencement Date, the Company will grant to each eligible employee who is then a participant in the Plan an option (an "Option") to purchase on the last business day of such Plan Period (the "Exercise Date") at the applicable purchase price (the "Option Price") up to that number of shares of Common Stock determined by multiplying \$2,083 by the number of full months in the Plan Period and dividing the result by the closing price (as determined below) on the Offering Commencement Date; provided, however, that no employee may be granted an Option which permits his or her rights to purchase Common Stock under this Plan and any other employee stock purchase plan (as defined in Section 423(b) of the Code) of the Company and its subsidiaries, to accrue at a rate which exceeds \$25,000 of the fair market value of such Common Stock (determined at the date such Option is granted) for each calendar year in which the Option is outstanding at any time; and, provided, further, however, that the Committee may, in its discretion, set a fixed maximum number of shares of Common Stock that each eligible employee may purchase per Plan Period which number may not be greater than the number of shares of Common Stock determined by using the formula in the first clause of this Section 9(a) and which number shall be subject to the second clause of this Section 9(a).

(b) Option Price. The Board or the Committee shall determine the Option Price for each Plan Period, including whether such Option Price shall be determined based on the lesser of the closing price of the Common Stock on (i) the first business day of the Plan Period or (ii) the Exercise Date, or shall be based solely on the closing price of the Common Stock on the Exercise Date; provided, however, that such Option Price shall be at least 85% of the applicable closing price. In the absence of a determination by the Board or the Committee, the Option Price will be 85% of the lesser of the closing price of the Common Stock on (i) the first business day of the Plan Period or (ii) the Exercise Date. The closing price shall be (a) the closing price (for the primary trading session) on any national securities exchange on which the Common Stock is listed or (b) the average of the closing bid and asked prices in the over-the-counter-market, whichever is applicable, as published in The Wall Street Journal or another source selected by the Board or the Committee. If no sales of Common Stock were made on such a day, the price of

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the Common Stock shall be the reported price for the next preceding day on which sales were made.

(c) Exercise of Option. Each employee who continues to be a participant in the Plan on the Exercise Date shall be deemed to have exercised his or her Option at the Option Price on such date and shall be deemed to have purchased from the Company the number of whole shares of Common Stock reserved for the purpose of the Plan that his or her accumulated payroll deductions on such date will pay for, but not in excess of the maximum numbers determined in the manner set forth above.

(d) Return of Unused Payroll Deductions. Any balance remaining in an employee's payroll deduction account at the end of a Plan Period will be automatically refunded to the employee, except that any balance that is less than the purchase price of one share of Common Stock will be carried forward into the employee's payroll deduction account for the following Offering, unless the employee elects not to participate in the following Offering under the Plan, in which case the balance in the employee's account shall be refunded.

10. Issuance of Certificates. Certificates representing shares of Common Stock purchased under the Plan may be issued only in the name of the employee, in the name of the employee and another person of legal age as joint tenants with rights of survivorship, or (in the Company's sole discretion) in the name of a brokerage firm, bank, or other nominee holder designated by the employee. The Company may, in its sole discretion and in compliance with applicable laws, authorize the use of book entry registration of shares in lieu of issuing stock certificates.

11. Rights on Retirement, Death or Termination of Employment. If a participating employee's employment ends before the last business day of a Plan Period, no payroll deduction shall be taken from any pay then due and owing to the employee and the balance in the employee's account shall be paid to the employee. In the event of the employee's death before the last business day of a Plan Period, the Company shall, upon notification of such death, pay the balance of the employee's account (a) to the executor or administrator of the employee's estate or (b) if no such executor or administrator has been appointed to the knowledge of the Company, to such other person(s) as the Company may, in its discretion, designate. If, before the last business day of the Plan Period, the Designated Subsidiary by which an employee is employed ceases to be a subsidiary of the Company, or if the employee is transferred to a subsidiary of the Company that is not a Designated Subsidiary, the employee shall be deemed to have terminated employment for the purposes of this Plan.

12. Optionees Not Stockholders. Neither the granting of an Option to an employee nor the deductions from his or her pay shall make such employee a stockholder of the shares of Common Stock covered by an Option under this Plan until he or she has purchased and received such shares.

13. Options Not Transferable. Options under this Plan are not transferable by a participating employee other than by will or the laws of descent and distribution, and are exercisable during the employee's lifetime only by the employee.

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14. Application of Funds. All funds received or held by the Company under this Plan may be combined with other corporate funds and may be used for any corporate purpose.

15. Adjustment for Changes in Common Stock and Certain Other Events.

(a) Changes in Capitalization. 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 Common Stock other than an ordinary cash dividend, (i) the number and class of securities available under this Plan, (ii) the share limitations set forth in Section 9, and (iii) the Option Price shall be equitably adjusted to the extent determined by the Board or the Committee.

(b) Reorganization Events.

(1) Definition. A "Reorganization Event" shall mean: (a) any merger or consolidation of the Company with or into another entity as a result of which all of the Common Stock of the Company is converted into or exchanged for the right to receive cash, securities or other property or is cancelled, (b) any transfer or disposition of all of the Common Stock of the Company for cash, securities or other property pursuant to a share exchange or other transaction or (c) any liquidation or dissolution of the Company.

(2) Consequences of a Reorganization Event on Options. In connection with a Reorganization Event, the Board or the Committee may take any one or more of the following actions as to outstanding Options on such terms as the Board or the Committee determines: (i) provide that Options shall be assumed, or substantially equivalent Options shall be substituted, by the acquiring or succeeding corporation (or an affiliate thereof), (ii) 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 the Board or the Committee in such notice, which date shall not be less than ten (10) days preceding the effective date of the Reorganization Event, (iii) 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, (iv) in the event of a Reorganization Event under the terms of which holders of Common Stock will receive upon consummation thereof a cash payment for each share surrendered in the Reorganization Event (the "Acquisition Price"), change the last day of the Plan 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 (A) (1) the Acquisition Price times (2) the number of shares of Common Stock that the employee's accumulated payroll deductions as of immediately prior to the Reorganization Event could purchase at the Option Price, where the Acquisition Price is treated as the fair market value of the Common Stock on the last day of the applicable Plan Period for purposes of determining the Option Price under Section 9(b) hereof, and where the number of shares that could be purchased is subject to the limitations set forth in Section 9(a), minus (B) the result of multiplying such number of shares by such Option Price, (v) provide that, in connection with a liquidation or dissolution of the Company, Options shall convert into the right to receive liquidation proceeds (net of the Option Price thereof) and (vi) any combination of the foregoing.

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For purposes of clause (i) above, an Option shall be considered assumed if, following consummation of the Reorganization Event, the Option confers the right to purchase, for each share of Common Stock subject to the Option immediately prior to the consummation of the Reorganization Event, the consideration (whether cash, securities or other property) received as a result of the Reorganization Event by holders of Common Stock for each share of Common Stock held immediately prior to the consummation of the Reorganization Event (and if holders were offered a choice of consideration, the type of consideration chosen by the holders of a majority of the outstanding shares of Common Stock); provided, however, that if the consideration received as a result of the Reorganization Event is not solely common stock of the acquiring or succeeding corporation (or an affiliate thereof), the Company may, with the consent of the acquiring or succeeding corporation, provide for the consideration to be received upon the exercise of Options to consist solely of such number of shares of common stock of the acquiring or succeeding corporation (or an affiliate thereof) that the Board determines to be

equivalent in value (as of the date of such determination or another date specified by the Board) to the per share consideration received by holders of outstanding shares of Common Stock as a result of the Reorganization Event.

16. Amendment of the Plan. The Board may at any time, and from time to time, amend or suspend this Plan or any portion thereof, except that (a) if the approval of any such amendment by the shareholders of the Company is required by Section 423 of the Code, such amendment shall not be effected without such approval, and (b) in no event may any amendment be made that would cause the Plan to fail to comply with Section 423 of the Code.

17. Insufficient Shares. If the total number of shares of Common Stock specified in elections to be purchased under any Offering plus the number of shares purchased under previous Offerings under this Plan exceeds the maximum number of shares issuable under this Plan, the Board or the Committee will allot the shares then available on a pro-rata basis.

18. Termination of the Plan. This Plan may be terminated at any time by the Board. Upon termination of this Plan all amounts in the accounts of participating employees shall be promptly refunded.

19. Governmental Regulations. The Company's obligation to sell and deliver Common Stock under this Plan is subject to listing on a national stock exchange (to the extent the Common Stock is then so listed or quoted) and the approval of all governmental authorities required in connection with the authorization, issuance or sale of such stock.

20. Governing Law. The Plan shall be governed by Delaware law except to the extent that such law is preempted by federal law.

21. Issuance of Shares. Shares may be issued upon exercise of an Option from authorized but unissued Common Stock, from shares held in the treasury of the Company, or from any other proper source.

22. Notification upon Sale of Shares. Each employee agrees, by entering the Plan, to promptly give the Company notice of any disposition of shares purchased under the Plan where

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such disposition occurs within two years after the date of grant of the Option pursuant to which such shares were purchased.

23. Grants to Employees in Foreign Jurisdictions. The Company may, to comply with the laws of a foreign jurisdiction, grant Options to employees of the Company or a Designated Subsidiary who are citizens or residents of such foreign jurisdiction (without regard to whether they are also citizens of the United States or resident aliens (within the meaning of Section 7701(b)(1)(A) of the Code)) with terms that are less favorable (but not more favorable) than the terms of Options granted under the Plan to employees of the Company or a Designated Subsidiary who are resident in the United States. Notwithstanding the preceding provisions of this Plan, employees of the Company or a Designated Subsidiary who are citizens or residents of a foreign jurisdiction (without regard to whether they are also citizens of the United States or resident aliens (within the meaning of Section 7701(b)(1)(A) of the Code)) may be excluded from eligibility under the Plan if (a) the grant of an Option under the Plan to a citizen or resident of the foreign jurisdiction is prohibited under the laws of such jurisdiction or (b) compliance with the laws of the foreign jurisdiction would cause the Plan to violate the requirements of Section 423 of the Code. The Company may add one or more appendices to this Plan describing the operation of the Plan in those foreign jurisdictions in which employees are excluded from participation or granted less favorable Options.

24. Authorization of Sub-Plans. The Board may from time to time establish one or more sub-plans under the Plan with respect to one or more Designated Subsidiaries, provided that such sub-plan complies with Section 423 of the Code.

25. Withholding. If applicable tax laws impose a tax withholding obligation, each affected employee shall, no later than the date of the event creating the tax liability, make provision satisfactory to the Board for payment of any taxes required by law to be withheld in connection with any transaction related to Options granted to or shares acquired by such employee pursuant to the Plan. The Company may, to the extent permitted by law, deduct any such taxes from any payment of any kind otherwise due to an employee.

26. Effective Date and Approval of Shareholders. The Plan shall take effect as of the closing of the Company's initial public offering, subject to approval by the shareholders of the Company as required by Section 423 of the Code, which approval must occur within twelve months of the adoption of the Plan by the Board.

Adopted by the Board of Directors on
December 15, 2015

Approved by the stockholders on
, 201

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SYROS PHARMACEUTICALS, INC.
One Memorial Drive
7th Floor
Cambridge, MA 02142

November 13, 2012 (and effective as of July 2, 2012)

Nancy Simonian, M.D.

Dear Nancy:

I am pleased to offer you the position of Chief Executive Officer with Syros Pharmaceuticals, Inc. (the "Company") working out of the Company's headquarters in Cambridge, Massachusetts. Outlined below are the terms of this Offer Letter for your review.

Effective as of July 2, 2012, you will be employed by the Company, on a full-time basis, as its Chief Executive Officer and shall have all authority commensurate with such position, subject to the supervision of, and any conditions or restrictions on such authority as determined from time to time by, the Board of Directors (the "Board").

You agree to perform the duties and responsibilities inherent in such position, and such other duties and responsibilities as shall from time to time be mutually agreed upon between you and the Board, including, but not limited to, (i) leadership regarding efforts to create value for the Company, (ii) guiding the Company's effort to identify and diligence business development opportunities that are consistent with the strategic goals of the Company, and to negotiate such opportunities as are approved by the Board, (iii) leading the effort to develop and achieve the annual financial and business plan goals for the Company, and (iv) development and ongoing maintenance of the Company's values and positive culture, reinforcing the Company's mission to be a highly productive organization that aspires to become one of the leading companies in the industry. You also agree that, while employed by the Company, you will devote your full business time and your best efforts, business judgment, skill and knowledge exclusively to the advancement of the business and interests of the Company and to the discharge of your duties and responsibilities for it. Provided, however, it is agreed that you may serve on outside boards and participate in charitable and civic organizations to the extent such activities do not interfere with your duties and responsibilities to the Company. You agree to abide by the rules, regulations, instructions, personnel practices and policies of the Company, as adopted and amended from time to time by the Company, from and after the date that they are disclosed to you.

You will receive a semi-monthly salary of \$17,708.34 which, if annualized, is equivalent to \$425,000.00. All payments will be payable in accordance with the normal payroll practices of the Company, and will be subject to legally required and otherwise authorized withholdings.

Your performance will be reviewed by the Compensation Committee of the Board on an annual basis in conjunction with an annual salary review, with your salary subject to increase but not decrease at such times.

You will be eligible to receive an annual incentive bonus commencing in calendar year 2012, equal to up to 50% of your then-current base salary. Your 2012 award, which will be prorated based upon your start date, and future bonuses, will be subject to the terms of the applicable bonus plan developed under your leadership and approved by the Board. Additional details will be determined by mutual agreement between you and the Board. Any bonus awarded will be paid, subject to required withholdings and deductions, on or before March 15 of the calendar year immediately following the year for which the bonus was awarded.

On or about the first date on which the Company receives aggregate gross proceeds equal to or exceeding \$12,500,000 from the sale to one or more third parties of shares of its capital stock, or notes or other indebtedness that is convertible into or exercisable for shares of its capital stock, in a venture capital financing (the "Qualified Financing Date"), you will, subject to approval by the Board, be awarded a stock option (the "Initial Option") to purchase that number of shares of the Company's Common Stock, \$0.001 par value per share ("Common Stock") representing 5% of the fully diluted shares of Common Stock of the Company calculated immediately following the Qualified Financing Date. The exercise price of the Initial Option will be equal to the fair market value of the Company's Common Stock on the date of grant, and will be subject to the standard terms and conditions of the Company's 2012 Stock Plan and the stock incentive agreement evidencing such award. The Initial Option will vest and become exercisable over four years at the rate of 25% of the shares underlying the award on the first anniversary of the date of your July 2, 2012 commencement of employment, and then at the rate of 1/36th of the remaining shares of Common Stock underlying the award at the end of each additional month after the first anniversary of the date of your commencement of employment until the option is fully vested and exercisable, subject to your continued service to the Company. The Initial Option shall be an incentive stock option to the extent permitted by law, and shall be subject to a right of early exercise (in which case there shall be a Company right of repurchase on any unvested shares of Common Stock issued upon such early exercise that shall lapse in accordance with the same schedule as the vesting described above).

In addition to your Initial Option, on or about the Qualified Financing Date you shall also, subject to approval by the Board, be awarded an additional stock option (the "Milestone Option") to purchase the number of shares of the Company's Common Stock representing 2% of the fully diluted shares of Common Stock of the Company calculated immediately following the Qualified Financing Date. The exercise price of the Milestone Option will be equal to the fair market value of the Company's Common Stock on the date of grant, and will be subject to the standard terms and conditions of the Company's 2012 Stock Plan and the stock incentive agreement evidencing such award. The Milestone Option will vest and become exercisable on the earlier of (1) the date on which the Performance Objective (as defined below) is achieved, and (2) six years from your July 2, 2012 commencement of employment, subject to your

continued service to the Company. The Milestone Option shall be an incentive stock option to the extent permitted by law, and shall be subject to a right of early exercise (in which case there shall be a Company right of repurchase on any unvested shares of Common Stock issued upon such early exercise that shall lapse in accordance with the same schedule as the vesting described above). The Performance Objective shall be a corporate objective that will be mutually agreed upon by you and the Company, acting in good faith, and approved by the Board, on or before the date that the Milestone Option is granted.

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This Offer Letter shall not be construed as an agreement, either express or implied, to employ you for any stated term, and shall in no way alter the Company's policy of employment at-will, under which both the Company and you remain free to end the employment relationship for any reason, at any time, with or without cause or notice. Although your job duties, title, compensation and benefits, as well as the Company's personnel policies and procedures, may change from time to time, the "at-will" nature of your employment may only be changed by a written agreement signed by you and a member of the Board which expressly states the intention to modify the at-will nature of your employment. Similarly, nothing in this offer letter shall be construed as an agreement, either express or implied, to pay you any compensation or grant you any benefit beyond the end of your employment with the Company, except as otherwise explicitly set forth herein. This offer letter supersedes all prior understandings, whether written or oral, relating to the terms of your employment. Your employment and this letter will be governed by the laws of Massachusetts.

Without otherwise limiting the "at-will" nature of your employment, in the event your employment is terminated at any time by the Company without Cause or by you for Good Reason, then: (i) you shall receive your base salary accrued through the last day of your employment with the Company, (ii) you shall continue to receive your base salary at the then-current rate per semi-monthly pay period, reduced by all applicable taxes and withholdings, for a period of twelve (12) months in accordance with the Company's then-current payroll policies and practices, and (iii) you shall receive an incentive bonus (which assumes the achievement of annual targets) pro-rated for the portion of the then-current calendar year during which you were employed by the Company. In the event of a Change in Control, 100% of all unvested stock options then held by you shall become fully vested and exercisable on the earlier to occur of (a) the date your employment is terminated by the Company without Cause or by you for Good Reason (either in contemplation of, pursuant to or following a Change in Control) or (b) the date that is twelve (12) months following the effective date of the Change in Control. Notwithstanding the foregoing, you will not be entitled to receive any severance payments unless, within sixty (60) days following the date of termination, you (i) have executed a general release in a form prescribed by the Company of all known and unknown claims that you may then have against the Company or persons affiliated with the Company, and (ii) have agreed not to prosecute any legal action or other proceeding based on those claims. The severance payments shall be paid or commence on the first payroll period following the date the release becomes effective (the "Payment Date"). Notwithstanding the foregoing, if the 60th day following the date of termination occurs in the calendar year following the calendar year of the termination, then the Payment Date shall be no earlier than January 1 of such subsequent calendar year.

For purposes of this Agreement, "Change of Control" means any transaction or series of related transactions (i) the result of which is a change in the ownership of the Company, such that more than 50% of the equity securities of the Company are acquired by any person or group (as such terms are defined for purposes of Section 13(d)(3) of the Securities Exchange Act of 1934, as amended) that does not own capital stock of the Company on the effective date of such change in control, (ii) that results in the sale of all or substantially all of the assets of the Company, or (iii) that results in the consolidation or merger of the Company with or into another corporation or corporations or other entity in which the Company is not the survivor (except any such corporation or entity controlled, directly or indirectly, by the Company).

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"Cause" means: (i) your conviction of, or plea of guilty or nolo contendere to, any crime involving dishonesty or moral turpitude or any felony; or (ii) you have (A) engaged in material dishonesty, willful misconduct or gross negligence, (B) breached or threatened to breach either or both of the Ancillary Agreements (as defined below), (C) materially violated a Company policy or procedure causing or threatening to cause substantial injury to the Company, and/or (D) willfully refused to perform your assigned duties to the Company, following written notice of such refusal by the Company and a period of fifteen (15) days to cure the same.

"Good Reason" means the occurrence of one or more of the following without your written consent: (i) a change in your principal work location resulting in a new one-way commute that is more than thirty-five (35) miles greater than your one-way commute prior to the change in your principal work location, regardless of whether you receive an offer of relocation benefits, (ii) a material reduction in your authority, duties and/or responsibilities as compared to your authority, duties and/or responsibilities in effect immediately prior to the occurrence of the event (for example, but not by way of limitation, this determination will include an analysis of whether you maintain at least the same level, scope and type of duties and responsibilities with respect to the management, strategy, operations and business of the Company), or (iii) a material reduction in your base compensation as compared to your base compensation in effect immediately prior to the occurrence of the event; provided, however, that no such occurrence shall constitute Good Reason unless (A) you give the Company a written notice of termination for Good Reason not more than ninety (90) days after the initial existence of the condition, (B) the grounds for termination (if susceptible to correction) are not corrected by the Company within fifteen (15) days of its receipt of such notice, and (C) your termination of employment occurs within one year following the Company's receipt of such notice.

Any severance payments to you under this Offer Letter shall begin only after the date of your "separation from service" (determined as set forth below), which occurs on or after date of the termination of your employment, and shall be subject to the following provisions:

(i) It is intended that each installment of the severance payments under this Offer Letter shall be treated as a separate “payment” for purposes of Section 409A of the Internal Revenue Code of 1986, as amended, and the guidance issued thereunder (“Section 409A”).

Neither the Company nor you shall have the right to accelerate or defer the delivery of any such payments except to the extent specifically permitted or required by Section 409A.

(ii) If, as of the date of your “separation from service” from the Company, you are not a “specified employee” (within the meaning of Section 409A), then each installment of the severance payments shall be made on the dates and terms set forth in this Offer Letter.

(iii) If, as of the date of your “separation from service” from the Company, you are a “specified employee” (within the meaning of Section 409A), then:

A. Each installment of the severance payments that, in accordance with the dates and terms set forth in this Offer Letter, will in all circumstances, regardless of when the “separation from service” occurs, be paid within the short-term deferral period (as defined in Section 409A) shall be treated as a “short-term deferral” within the meaning of Treasury

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Regulation Section 1.409A-1(b)(4) to the maximum extent permissible under Section 409A and shall be paid on the dates and terms set forth in this Offer Letter; and

B. Each installment of the severance payments that is not described in clause (iii)(A) above and that would, absent this clause (B), be paid within the six-month period following your “separation from service” from the Company shall not be paid until the date that is six (6) months and one (1) day after such “separation from service” (or, if earlier, your death), with any such installments that are required to be delayed being accumulated during the six-month period and paid in a lump sum on the date that is six (6) months and one (1) day following your “separation from service” and any subsequent installments, if any, being paid in accordance with the dates and terms set forth in this Offer Letter; provided, however, that the preceding provisions of this clause (B) shall not apply to any installment of severance payments if and to the maximum extent that that such installment is deemed to be paid under a separation pay plan that does not provide for a deferral of compensation by reason of the application of Treasury Regulation 1.409A-1(b)(9)(iii) (relating to separation pay upon an involuntary separation from service). Any installments that qualify for the exception under Treasury Regulation Section 1.409A-1(b)(9)(iii) must be paid no later than the last day of your second taxable year following the taxable year in which the “separation from service” occurs.

(iv) The determination of whether and when your “separation from service” from the Company has occurred shall be made in a manner consistent with, and based on the presumptions set forth in, Treasury Regulation Section 1.409A-1(h). Solely for purposes of this paragraph (iv), “Company” shall include all persons with whom the Company would be considered a single employer under Section 414(b) and 414(c) of the Code.

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

(vi) Notwithstanding any other provision of this Offer Letter, the Company makes no representation or warranty and shall have no liability to you or to any other person if any provisions of this Offer Letter are determined to constitute deferred compensation subject to Section 409A but do not satisfy an exemption from, or the conditions of, that section.

You will be eligible to participate in any and all benefit programs that the Company establishes and makes available to its employees from time to time, provided that you are eligible under (and subject to all provisions of) the plan documents that govern those programs. Benefits are subject to change at any time in the Company’s sole discretion.

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You represent that you are not bound by any employment contract, restrictive covenant or other restriction preventing you from entering into employment with or carrying out your responsibilities for the Company, or which is in any way inconsistent with the terms of this offer letter.

This offer of employment is contingent upon satisfactory reference checks, and upon your execution of the Company’s (i) Invention and Non-Disclosure Agreement and (ii) Non-Competition and Non-Solicitation Agreement (collectively, the “Ancillary Agreements”), which are attached hereto as Exhibit A and Exhibit B. You will be required to submit documentation that establishes identity and employment eligibility in accordance with the US Immigration and Naturalization requirements.

[Remainder of page intentionally left blank.]

I am very excited about having you join our team and I anticipate that you will make many important contributions to our Company and strategic mission. Please acknowledge your acceptance of this offer by returning a signed copy of this letter.

Very truly yours,

SYROS PHARMACEUTICALS, INC.

By: /s/ Robert Nelsen
Robert Nelsen
Member, Board of Directors

Agreed and acknowledged as of the date first written above.

/s/ Nancy Simonian
Nancy Simonian

Syros Pharmaceuticals, Inc.

January 29, 2016

Nancy Simonian, M.D.

Re: Amendment to Employment Offer Letter

Dear Nancy:

Reference is made to that certain Employment Offer Letter dated November 13, 2012 (and effective as of July 2, 2012) between Syros Pharmaceuticals, Inc., a Delaware corporation (the "Company"), and you regarding the terms of your employment with the Company (the "Offer Letter"). This letter (the "Amendment") confirms the agreement between the Company and you regarding an amendment to the Offer Letter.

1. The portion of the Offer Letter beginning with the second full paragraph on Page 3 (beginning with the clause, "Without otherwise limiting the 'at-will' nature of your employment") through the end of Page 5 (ending with subsection (vi)) is hereby deleted in its entirety and the following inserted in lieu thereof:

"Without otherwise limiting the "at-will" nature of your employment, in the event your employment is terminated by the Company without Cause or by you for Good Reason (each as defined below), you shall be entitled to the base salary that has accrued and to which you are entitled as of the effective date of such termination, and further, subject to the conditions set forth in the next paragraph, the Company shall: (a) for a period of twelve (12) months following your termination date: (i) continue to pay you, in accordance with the Company's regularly established payroll procedure, your base salary as severance; and (ii) provided you are eligible for and timely elect to continue receiving group medical insurance pursuant to the "COBRA" law, continue to pay the share of the premium for health coverage that is paid by the Company for active and similarly-situated employees who receive the same type of coverage, unless the Company's provision of such COBRA payments will violate the nondiscrimination requirements of applicable law, in which case this benefit will not apply; and (b) pay you a lump sum pro-rata target annual bonus in respect of the year of your termination from employment, which such bonus shall be calculated as a pro-rata portion of the current calendar year bonus based on the number of full months worked in the calendar year in which termination occurs through the date of termination. If, within the three months prior to a Change in Control or in the twelve months following a Change in Control, the Company terminates your employment without Cause or you resign for Good Reason, the Company, subject to the conditions set forth in the next paragraph, will: (a) extend the severance benefits described in (i) and (ii) above for an additional six (6) months, such that the total severance benefit period shall be eighteen (18) months; (b) in lieu of paying you a lump sum pro rata target bonus as described in (b) above, pay you a lump sum amount equal to 150% of your target bonus in effect for the fiscal year

in which your separation from employment occurs; and (c) accelerate the vesting of all unvested stock options held by you as of the date your employment is terminated such that 100% of such options shall become fully vested and

exercisable effective as of such date.

Notwithstanding the foregoing, you will not be entitled to receive any severance benefits unless, within sixty (60) days following the date of termination, you (i) have executed a severance and release of claims agreement in a form prescribed by the Company or persons affiliated with the Company (which will include, at a minimum, a release of all releasable claims and non-disparagement and cooperation obligations). Any severance payments shall be paid, or commence on the first payroll period following the date the release becomes effective (the "Payment Date"). Notwithstanding the foregoing, if the 60th day following the date of termination occurs in the calendar year following the calendar year of the termination, then the Payment Date shall be no earlier than January 1st of such subsequent calendar year. The severance payments are subject to the terms and conditions set forth on Attachment A.

For purposes of this Agreement, "Change in Control" means any transaction or series of related transactions (a) the result of which is a change in the ownership of the Company, such that more than 50% of the equity securities of the Company are acquired by any person or group (as such terms are defined for purposes of Section 13(d)(3) of the Securities Exchange Act of 1934, as amended) that does not own capital stock of the Company of the effective date of such change in control, (b) that results in the sale of all or substantially all of the assets of the Company, or (c) that results in the consolidation or merger of the Company with or into another corporation or corporations or other entity in which the Company is not the survivor (except any such corporation or entity controlled, directly or indirectly, by the Company).

"Cause" means: (a) your conviction of, or plea of guilty or nolo contendere to, any crime involving dishonesty or moral turpitude or any felony; or (b) you have (i) engaged in material dishonesty, willful misconduct or gross negligence, (ii) breached or threatened to breach either or both of the Ancillary Agreements (as defined below), (iii) materially violated a Company policy or procedure causing or threatening to cause substantial injury to the Company, and/or (iv) willfully refused to perform your assigned duties to the Company, following written notice of such refusal by the Company and a period of thirty (30) days to cure the same.

"Good Reason" means the occurrence of one or more of the following without your written consent: (a) a material reduction in your authority, duties and/or responsibilities as compared to your authority, duties and/or responsibilities in effect immediately prior to the occurrence of the event (for example, but not by way of limitation, this determination will include an analysis of whether you maintain at least the same level, scope and type of duties and responsibilities with respect to the management, strategy, operations and business of the Company), or (b) a material reduction in your base compensation as compared to your base compensation in effect immediately prior to the occurrence of the event; provided, however, that no such occurrence shall constitute Good Reason unless: (i) you

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give the Company a written notice of termination for Good Reason not more than ninety (90) days after the initial existence of the condition, (ii) the grounds for termination (if susceptible to correction) are not corrected by the Company within thirty (30) days of its receipt of such notice, and (iii) your termination of employment occurs within one (1) year following the Company's receipt of such notice."

2. The following language shall be inserted as a new paragraph subsequent to the portion referenced in Section 1 of this Amendment:

"This letter is intended to provide payments that are exempt from or compliant with 409A, and should be interpreted consistent with that intent."

3. The attached exhibit entitled "Payments Subject to Section 409A" is hereby appended to the Offer Letter as Attachment A and, if applicable, replaces any previous such attachment concerning the same subject matter.

4. Except as specifically provided herein, the Offer Letter remains in full force and effect and is not modified or amended hereby.

5. This Amendment will be construed and interpreted in accordance with the laws of the Commonwealth of Massachusetts (other than choice-of-law provisions).

6. This Amendment may be executed in counterparts, each of which will be considered an original, but all of which together will constitute one agreement. Execution of a facsimile or "pdf" copy will have the same force and effect as execution of an original, and a facsimile or "pdf" signature will be deemed an original and valid signature. From and after the date of this Amendment, all references in the Offer Letter to "this agreement" or "this Agreement" or similar terms shall be deemed to be references to the Offer Letter as amended hereby.

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Please indicate your agreement with the above terms by signing below.

Very truly yours,

By: /s/ Kyle D. Kovalanka

Name: Kyle D. Kovalanka

Title: C.O.O

Accepted and Agreed as of January 29, 2016

/s/ Nancy Simonian

Nancy Simonian

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Attachment A

Payments Subject to Section 409A

1. Subject to this Attachment A, any severance payments that may be due under the letter agreement shall begin only upon the date of your "separation from service" (determined as set forth below) which occurs on or after the termination of your employment. The following rules shall apply with respect to distribution of the severance payments, if any, to be provided to you under the letter agreement, as applicable:
- a. It is intended that each installment of the severance payments under the letter agreement provided under shall be treated as a separate "payment" for purposes of Section 409A of the Internal Revenue Code of 1986, as amended ("Section 409A"). Neither the Company nor you shall have the right to accelerate or defer the delivery of any such payments except to the extent specifically permitted or required by Section 409A.
 - b. If, as of the date of your "separation from service" from the Company, you are not a "specified employee" (within the meaning of Section 409A), then each installment of the severance payments shall be made on the dates and terms set forth in the letter agreement.
 - c. If, as of the date of your "separation from service" from the Company, you are a "specified employee" (within the meaning of Section 409A), then:
 - i. Each installment of the severance payments due under the letter agreement that, in accordance with the dates and terms set forth herein, will in all circumstances, regardless of when your separation from service occurs, be paid within the short-term deferral period (as defined under Section 409A) shall be treated as a short-term deferral within the meaning of Treasury Regulation Section 1.409A-1(b)(4) to the maximum extent permissible under Section 409A and shall be paid on the dates and terms set forth in the letter agreement; and
 - ii. Each installment of the severance payments due under the letter agreement that is not described in this Attachment A, Section 1(c)(i) and that would, absent this subsection, be paid within the six-month period following your "separation from service" from the Company shall not be paid until the date that is six months and one day after such separation from service (or, if earlier, your death), with any such installments that are required to be delayed being accumulated during the six-month period and paid in a lump sum on the date that is six months and one day following your separation from service and any subsequent installments, if any, being paid in accordance with the dates and terms set forth herein; provided, however, that the preceding provisions of this sentence shall not apply to any installment of payments if and to the maximum extent that that such installment is deemed to be paid under a separation pay plan that does not provide for a deferral of compensation by reason of

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the application of Treasury Regulation 1.409A-1(b)(9)(iii) (relating to separation pay upon an involuntary separation from service). Any installments that qualify for the exception under Treasury Regulation Section 1.409A-1(b)(9)(iii) must be paid no later than the last day of your second taxable year following the taxable year in which the separation from service occurs.

2. The determination of whether and when your separation from service from the Company has occurred shall be made and in a manner consistent with, and based on the presumptions set forth in, Treasury Regulation Section 1.409A-1(h). Solely for purposes of this Attachment A, Section 2, "Company" shall include all persons with whom the Company would be considered a single employer under Section 414(b) and 414(c) of the Internal Revenue Code of 1986, as amended.

3. The Company makes no representation or warranty and shall have no liability to you or to any other person if any of the provisions of the letter agreement (including this Attachment) are determined to constitute deferred compensation subject to Section 409A but that do not satisfy an exemption from, or the conditions of, that section.



August 25th, 2015

Kyle Kovalanka
Via e-mail

Dear Kyle:

On behalf of Syros Pharmaceuticals, Inc. (the "Company"), I am pleased to extend the following offer and set forth the terms of your employment with the Company:

1. You will be employed to serve on a FULL-TIME basis as Chief Operating Officer (COO) effective September 18th, 2015. As COO you will report to Nancy Simonian, CEO and will be responsible for general oversight of the Company's finance, corporate development and non- R and D operational activities plus such other duties as may from time to time be assigned to you by the Company.
2. Your salary will be \$380,000 per year, paid semi-monthly in arrears in accordance with the Company's normal payroll processes and subject to tax and other withholdings as required by law. Such salary may be adjusted from time to time in accordance with normal business practice and in the sole discretion of the Company.
3. You will receive a one-time bonus of \$122,500, payable upon the commencement of your employment with the Company.
4. You may participate in any and all bonus and benefit programs that the Company establishes and makes available to its employees from time to time, provided you are eligible under (and subject to all provisions of) the plan documents governing those programs. Specifically you will be eligible to receive a 35.0% bonus in your first year of employment with the Company, prorated based on your start date and approved by the Board of Directors. Future bonus eligibility will be based on the Company's annual bonus plan and approved by the Board of Directors.
5. Without otherwise limiting the "at-will" nature of your employment, in the event your employment is terminated at any time by the Company without Cause or by you for Good Reason, then: (a) you shall receive your base salary accrued through the last day of your employment with the Company, and (b) you shall receive your base salary at the then-current rate, reduced by all applicable taxes and withholdings, for a period of nine (9) months commencing on the Payment Date (as defined below), payable in accordance with the Company's then current payroll policies and practices. In the event of a Change in Control, 100% of all unvested stock options then held by you shall become fully vested and exercisable on the earlier to occur of (a) the

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date your employment is terminated by the Company without Cause or by you for Good Reason (either in contemplation of, pursuant to or following a Change in Control) or (b) the date that is twelve (12) months following the effective date of the Change in Control, provided that you remain employed by us or our successor on such date. Notwithstanding the foregoing, you will not be entitled to receive any severance payments unless, within sixty (60) days following the date of termination, you (i) have executed a general release in a form mutually agreeable by you and the Company or persons affiliated with the Company, and (ii) have agreed not to prosecute any legal action or other proceeding based on those claims. The severance payments shall be paid, or commence on the first payroll period following the date the release becomes effective (the "Payment Date"). Notwithstanding the foregoing, if the 60th day following the date of termination occurs in the calendar year following the calendar year of the termination, then the Payment Date shall be no earlier than January 1st of such subsequent calendar year. The severance payments are subject to the terms and conditions set forth on Attachment A.

For purposes of this letter agreement, "Change in Control" means any transaction or series of related transactions (a) the result of which is a change in the ownership of the Company, such that more than 50% of the equity securities of the Company are acquired by any person or group (as such terms are defined for purposes of Section 13(d)(3) of the Securities Exchange Act of 1934, as amended) that does not own capital stock of the Company of the effective date of such change in control, (b) that results in the sale of all or substantially all of the assets of the Company, or (c) that results in the consolidation or merger of the Company with or into another corporation or corporations or other entity in which the Company is not the survivor (except any such corporation or entity controlled, directly or indirectly, by the Company).

"Cause" means: (a) your conviction of, or plea of guilty or nolo contendere to, any crime involving dishonesty or moral turpitude or any felony; or (b) you have (i) engaged in material dishonesty, willful misconduct or gross negligence, (ii) breached or threatened to breach either or both of the Ancillary Agreements (as defined below), (iii) materially violated a Company policy or procedure causing or threatening to cause substantial injury to the Company, and/or (iv) willfully refused to perform your reasonable assigned duties to the

Company, following written notice of such refusal by the Company and a period of thirty (30) days to cure the same.

“Good Reason” means the occurrence of one or more of the following without your written consent: (a) a material reduction in your authority, duties and/or responsibilities as compared to your authority, duties and/or responsibilities in effect immediately prior to the occurrence of the event (for example, but not by way of limitation, this determination will include an analysis of whether you maintain at least the same level, scope and type of duties and responsibilities with respect to the management, strategy, operations and business of the Company), or (b) a material reduction in your base compensation as compared to your base compensation in effect immediately prior to the occurrence of the event; provided, however, that no such occurrence shall constitute Good Reason unless: (i) you give the Company a written notice of termination for Good Reason not more than ninety (90) days after the initial existence of the condition, (ii) the grounds for termination (if susceptible to correction) are not corrected by the Company within thirty (30) days of its receipt of such notice, and (iii) your termination of employment occurs within one (1) year following the Company’s receipt of such notice.

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6. You may be eligible for a maximum of three (3) weeks of vacation per calendar year to be taken at such times as may be approved by the Company. The number of vacation days for which you are eligible shall accrue at the rate of 1.25 days per month that you are employed during such calendar year.

7. Subject to the approval of the Board of Directors of the Company, the Company will grant to you an option (a “Time-Based Option”) under the Company’s 2012 Equity Incentive Plan (the “Plan”) for the initial purchase of a number of shares of common stock of the Company equal to 1.1% of the Company’s fully-diluted outstanding shares as of the date hereof, at a price per share equal to the fair market value at the time of Board approval, which option shall be granted within 30 days of your first day of employment. The Time-Based Option shall vest as to 25% of the shares on the one-year anniversary of grant, and shall vest in equal monthly installments for the next 36 months, becoming fully vested on the fourth anniversary of grant, in each case provided that you remain employed by us on the applicable vesting date. Subject to the approval of the Board of Directors of the Company, you shall also be granted an option (a “Performance-Based Option”) under the Plan to purchase an additional number of shares of common stock of the Company equal to 0.4% of the Company’s fully-diluted outstanding shares as of the date hereof, at a price per share equal to the fair market value at the time of Board approval, which option shall be granted within 30 days of your first day of employment and will vest six years from the date of grant, subject to accelerated vesting according to the following schedule: (i) 40% on the date of the Company’s initial public offering of common stock; (ii) 40% upon the Company’s execution of a collaboration agreement; and (iii) 20% upon achievement of clinical proof of concept, in each case based on parameters approved by the Board. Subject to the foregoing, each of the Time-Based Option and the Performance-Based Option shall be subject to all terms and other provisions set forth in the Plan and in a separate option agreement.

8. You may be eligible to receive such future stock options grants as the Board of Directors of the Company shall deem appropriate.

9. You will be required to execute an Invention and Non-Disclosure Agreement and a Non-Competition and Non-Solicitation Agreement in the forms attached as Exhibit A and Exhibit B, respectively, as a condition of employment (such agreements are referred to as “Ancillary Agreements”).

10. You represent that you are not bound by any employment contract, restrictive covenant or other restriction preventing you from entering into employment with or carrying out your responsibilities for the Company, or which is in any way inconsistent with the terms of this letter.

11. You agree to provide to the Company, within three days of your hire date, documentation of your eligibility to work in the United States, as required by the Immigration Reform and Control Act of 1986. You may need to obtain a work visa in order to be eligible to work in the United States. If that is the case, your employment with the Company will be conditioned upon your obtaining a work visa in a timely manner as determined by the Company.

12. This letter shall not be construed as an agreement, either expressed or implied, to employ you for any stated term, and shall in no way alter the Company’s policy of employment at

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will, under which both you and the Company remain free to terminate the employment relationship, with or without cause, at any time, with or without notice. Similarly, nothing in this letter shall be construed as an agreement, either express or implied, to pay you any compensation or grant you any benefit beyond the end of your employment with the Company.

THE REMAINDER OF THIS PAGE INTENTIONALLY LEFT BLANK

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If you agree with the employment provisions of this letter, please sign the letter and exhibits, scan the signature pages and email to Lisa Roberts at lroberts@syros.com. If you do not accept this offer by August 13th, 2015, this offer will be revoked.

Very Truly Yours,

By: /s/ Nancy Simonian

Name: Nancy Simonian

Title: CEO

The foregoing correctly sets forth the terms of my employment by Syros Pharmaceuticals, Inc.

/s/ Kyle Kovalanka
Kyle Kovalanka

Date: 08-25-15

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Attachment A

Payments Subject to Section 409A

1. Subject to this Attachment A, any severance payments that may be due under the letter agreement shall begin only upon the date of your "separation from service" (determined as set forth below) which occurs on or after the termination of your employment. The following rules shall apply with respect to distribution of the severance payments, if any, to be provided to you under the letter agreement, as applicable:

(a) It is intended that each installment of the severance payments under the letter agreement provided under shall be treated as a separate "payment" for purposes of Section 409A of the Internal Revenue Code of 1986, as amended ("Section 409A"). Neither the Company nor you shall have the right to accelerate or defer the delivery of any such payments except to the extent specifically permitted or required by Section 409A.

(b) If, as of the date of your "separation from service" from the Company, you are not a "specified employee" (within the meaning of Section 409A), then each installment of the severance payments shall be made on the dates and terms set forth in the letter agreement.

(c) If, as of the date of your "separation from service" from the Company, you are a "specified employee" (within the meaning of Section 409A), then:

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

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

your second taxable year following the taxable year in which the separation from service occurs.

2. The determination of whether and when your separation from service from the Company has occurred shall be made and in a manner consistent with, and based on the presumptions set forth in, Treasury Regulation Section 1.409A-1(h). Solely for purposes of this Attachment A, Section 2, "Company" shall include all persons with whom the Company would be considered a single employer under Section 414(b) and 414(c) of the Internal Revenue Code of 1986, as amended.

3. The Company makes no representation or warranty and shall have no liability to you or to any other person if any of the provisions of the letter agreement (including this Attachment) are determined to constitute deferred compensation subject to Section 409A but that do not satisfy an exemption from, or the conditions of, that section.

Exhibit B

NON-COMPETITION AND NON-SOLICITATION AGREEMENT

This Agreement is made between Syros Pharmaceuticals, Inc., a Delaware corporation (hereinafter referred to collectively with its subsidiaries as the "Company"), and Kyle Kusalanka.

For good consideration and in consideration of the employment or continued employment of the Employee by the Company, including the equity consideration in the Company, the Employee and the Company agree as follows:

1. Non-Competition and Non-Solicitation. While the Employee is employed by the Company and for a period of one year after the termination or cessation of such employment for any reason, the Employee will not directly or indirectly:

(a) Engage or assist others in engaging in any business or enterprise (whether as owner, partner, officer, director, employee, consultant, investor, lender or otherwise, except as the holder of not more than 1% of the outstanding stock of a publicly-held company) that is competitive with the Company's business, including but not limited to any business or enterprise that develops, manufactures, markets, licenses, sells or provides any product or service that competes with any product or service developed, manufactured, marketed, licensed, sold or provided, or planned to be developed, manufactured, marketed, licensed, sold or provided, by the Company while the Employee was employed by the Company; or

Notwithstanding the foregoing, Section 1(a) shall not preclude the Employee from becoming an employee of, or from otherwise providing services to, a separate division or operating unit of a multi-divisional business or enterprise (a "Division") if: (i) the Division by which the Employee is employed, or to which the Employee provides services, is not competitive with the Company's business (within the meaning of Section 1(a)), (ii) the Employee does not provide services, directly or indirectly, to any other division or operating unit of such multi-divisional business or enterprise which is competitive with the Company's business (within the meaning of Section 1(a)) (individually, a "Competitive Division" and collectively, the "Competitive Divisions") and (iii) the Competitive Divisions, in the aggregate, accounted for less than one-third of the multi-divisional business or enterprises' consolidated revenues for the fiscal year, and each subsequent quarterly period, prior to the Employee's commencement of employment with the Division.

(b) Either alone or in association with others, solicit, divert or take away, or attempt to divert or take away, the business or patronage of any of the clients, customers, or business partners of the Company which were contacted, solicited, or served by the Company during the 12-month period prior to the termination or cessation of the Employee's employment with the Company; or

(c) Either alone or in association with others: (i) solicit, induce or attempt to induce, any employee or independent contractor of the Company to terminate his or her employment or other engagement with the Company, or (ii) solicit for employment or engagement as an independent contractor any person who was employed or otherwise engaged by the Company at any time during the term of the Employee's employment with the Company;

provided, that this clause (ii) shall not apply to the solicitation of any individual whose employment or other engagement with the Company has been terminated for a period of six months or longer.

(d) Extension. If the Employee violates the provisions of any of the preceding paragraphs of this Section 1, the Employee shall continue to be bound by the restrictions set forth in such paragraph until a period of one year has expired without any violation of such provisions.

2. Miscellaneous.

(a) Equitable Remedies. The restrictions contained in this Agreement are necessary for the protection of the business and goodwill of the Company and are considered by the Employee to be reasonable for such purpose. The Employee agrees that any breach of this Agreement is likely to cause the Company substantial and irrevocable damage which is difficult to measure. Therefore, in the event of any such breach or threatened breach, the Employee agrees that the Company, in addition to such other remedies which may be available, shall have the right to obtain an injunction from a court restraining such a breach or threatened breach and the right to specific performance of the provisions of this Agreement and the Employee hereby waives the adequacy of a remedy at law as a defense to such relief.

(b) Obligations to Third Parties. The Employee acknowledges and represents that this agreement and the Employee's employment with the Company will not violate any continuing obligation the Employee has to any former employer or other third party.

(c) Disclosure of this Agreement. The Employee hereby authorizes the Company to notify others, including but not limited to customers of the Company and any of the Employee's future employers or prospective business associates, of the terms and existence of this Agreement and the Employee's continuing obligations to the Company hereunder.

(d) Not Employment Contract. The Employee acknowledges that this Agreement does not constitute a contract of employment, does not imply that the Company will continue his/her employment for any period of time and does not change the at-will nature of his/her employment.

(e) Successors and Assigns. This Agreement shall be binding upon and inure to the benefit of both parties and their respective successors and assigns, including any corporation with which, or into which, the Company may be merged or which may succeed to the Company's assets or business, provided, however, that the obligations of the Employee are personal and shall not be assigned by him or her. The Employee expressly consents to be bound by the provisions of this Agreement for the benefit of the Company or any subsidiary or affiliate thereof to whose employ the Employee may be transferred without the necessity that this Agreement be re-signed at the time of such transfer. Notwithstanding the foregoing, if the Company is merged with or into a third party which is engaged in multiple lines of business, or if a third party engaged in multiple lines of business succeeds to the Company's assets or business, then for purposes of Section 1(a), the term "Company" shall mean and refer to the business of the Company as it existed immediately prior to such event and as it subsequently develops and not to the third party's other businesses.

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(f) Interpretation. If any restriction set forth in Section 1 is found by any court of competent jurisdiction to be unenforceable because it extends for too long a period of time or over too great a range of activities or in too broad a geographic area, it shall be interpreted to extend only over the maximum period of time, range of activities or geographic area as to which it may be enforceable.

(g) Severability. In case any provision of this Agreement shall be invalid, illegal or otherwise unenforceable, the validity, legality and enforceability of the remaining provisions shall in no way be affected or impaired thereby.

(h) Waivers. No delay or omission by the Company in exercising any right under this Agreement will operate as a waiver of that or any other right. A waiver or consent given by the Company on any one occasion is effective only in that instance and will not be construed as a bar to or waiver of any right on any other occasion.

(i) Governing Law. This Agreement shall be governed by and construed in accordance with the laws of the Commonwealth of Massachusetts (without reference to the conflicts of laws provisions thereof). Any action, suit, or other legal proceeding which is commenced to resolve any matter arising under or relating to any provision of this Agreement shall be commenced only in a court of the Commonwealth of Massachusetts (or, if appropriate, a federal court located within Massachusetts), and the Company and the Employee each consents to the jurisdiction of such a court. The Company and the Employee each hereby irrevocably waive any right to a trial by jury in any action, suit or other legal proceeding arising under or relating to any provision of this Agreement.

(j) Entire Agreement; Amendment. This Agreement supersedes all prior agreements, written or oral, between the Employee and the Company relating to the subject matter of this Agreement. This Agreement may not be modified, changed or discharged in whole or in part, except by an agreement in writing signed by the Employee and the Company. The Employee agrees that any change or changes in his/her duties, salary or compensation after the signing of this Agreement shall not affect the validity or scope of this Agreement.

(k) Captions. The captions of the sections of this Agreement are for convenience of reference only and in no way define, limit or affect the scope or substance of any section of this Agreement.

[Remainder of this page intentionally left blank.]

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THE EMPLOYEE ACKNOWLEDGES THAT HE/SHE HAS CAREFULLY READ THIS AGREEMENT AND UNDERSTANDS AND AGREES TO ALL OF THE PROVISIONS IN THIS AGREEMENT.

SYROS PHARMACEUTICALS, INC.

Date: _____

By: /s/ Nancy Simonian
Name: Nancy Simonian
Title: CEO

Date: 08-25-15

/s/ Kyle Kusalanka
Kyle Kusalanka

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Syros Pharmaceuticals, Inc.

January 27, 2016

Kyle Kusalanka

Re: Amendment to Employment Offer Letter

Dear Kyle:

Reference is made to that certain Employment Offer Letter dated August 25, 2015 between Syros Pharmaceuticals, Inc., a Delaware corporation (the "Company"), and you regarding the terms of your employment with the Company (the "Offer Letter"). This letter (the "Amendment") confirms the agreement between the Company and you regarding an amendment to the Offer Letter.

1. Section 5 of the Offer Letter is hereby deleted in its entirety and the following inserted in lieu thereof:

"4. Without otherwise limiting the "at-will" nature of your employment, in the event your employment is terminated by the Company without Cause or by you for Good Reason (each as defined below), you shall be entitled to the base salary that has accrued and to which you are entitled as of the effective date of such termination, and further, subject to the conditions set forth in the second paragraph of this Section 4, the Company shall, for a period of nine (9) months following your termination date: (i) continue to pay you, in accordance with the Company's regularly established payroll procedure, your base salary as severance; and (ii) provided you are eligible for and timely elect to continue receiving group medical insurance pursuant to the "COBRA" law, continue to pay the share of the premium for health coverage that is paid by the Company for active and similarly-situated employees who receive the same type of coverage, unless the Company's provision of such COBRA payments will violate the nondiscrimination requirements of applicable law, in which case this benefit will not apply. If, within the three months prior to a Change in Control or in the twelve months following a Change in Control, the Company terminates your employment without Cause or you resign for Good Reason, the Company, subject to the conditions set forth in the second paragraph of this Section 4, will: (a) extend the severance benefits described in (i) and (ii) above for an additional three months, such that the total severance benefit period shall be one (1) year; (b) pay you a lump sum amount equal to your target bonus in effect for the fiscal year in which your separation from employment occurs; and (c) accelerate the vesting of all unvested stock options held by you as of the date your employment is terminated such that 100% of such options shall become fully vested and exercisable effective as of such date.

Notwithstanding the foregoing, you will not be entitled to receive any severance benefits unless, within sixty (60) days following the date of termination, you (i) have executed a severance and release of claims agreement in a form prescribed

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by the Company or persons affiliated with the Company (which will include, at a minimum, a release of all releasable claims and non-disparagement and cooperation obligations). Any severance payments shall be paid, or commence on the first payroll period following the date the release becomes effective (the "Payment Date"). Notwithstanding the foregoing, if the 60th day following the date of termination occurs in the calendar year following the calendar year of the termination, then the Payment Date shall be no earlier than January 1st of such subsequent calendar year.

For purposes of this Agreement, "Change in Control" means any transaction or series of related transactions (a) the result of which is a change in the ownership of the Company, such that more than 50% of the equity securities of the Company are acquired by any person or group (as such terms are defined for purposes of Section 13(d)(3) of the Securities Exchange Act of 1934, as amended) that does not own capital stock of the Company of the effective date of such change in control, (b) that results in the sale of all or substantially all of the assets of the Company, or (c) that results in the consolidation or merger of the Company with or into another corporation or corporations or other entity in which the Company is not the survivor (except any such corporation or entity controlled, directly or indirectly, by the Company).

"Cause" means: (a) your conviction of, or plea of guilty or nolo contendere to, any crime involving dishonesty or moral turpitude or any felony; or (b) you have (i) engaged in material dishonesty, willful misconduct or gross negligence, (ii) breached or threatened to breach either or both of the Ancillary Agreements (as defined below), (iii) materially violated a Company policy or procedure causing or threatening to cause substantial injury to the Company, and/or (iv) willfully refused to perform your assigned duties to the Company, following written notice of such refusal by the Company and a period of thirty (30) days to cure the same.

"Good Reason" means the occurrence of one or more of the following without your written consent: (a) a material reduction in your authority, duties and/or responsibilities as compared to your authority, duties and/or responsibilities in effect immediately prior to the occurrence of the event (for example, but not by way of limitation, this determination will include an analysis of whether you maintain at least the same level, scope and type of duties and responsibilities with respect to the management, strategy, operations and business of the Company), or (b) a material reduction in your base compensation as compared to your base compensation in effect immediately prior to the occurrence of the event; provided, however, that no such occurrence shall constitute Good Reason unless: (i) you give the Company a written notice of termination for Good Reason not more than ninety (90) days after the initial existence of the condition, (ii) the grounds for termination (if susceptible to correction) are not corrected by the Company within thirty (30) days of its receipt of such notice, and (iii) your termination of employment occurs within one (1) year following the Company's receipt of such notice.

2. The following language shall be inserted as a new paragraph following the last enumerated paragraph of the Offer Letter:

2

“This letter is intended to provide payments that are exempt from or compliant with 409A, and should be interpreted consistent with that intent.”

3. The attached exhibit entitled “Payments Subject to Section 409A” is hereby appended to the Offer Letter as Attachment A and, if applicable, replaces any previous such attachment concerning the same subject matter.

4. Except as specifically provided herein, the Offer Letter remains in full force and effect and is not modified or amended hereby.

5. This Amendment will be construed and interpreted in accordance with the laws of the Commonwealth of Massachusetts (other than choice-of-law provisions).

6. This Amendment may be executed in counterparts, each of which will be considered an original, but all of which together will constitute one agreement. Execution of a facsimile or “pdf” copy will have the same force and effect as execution of an original, and a facsimile or “pdf” signature will be deemed an original and valid signature. From and after the date of this Amendment, all references in the Offer Letter to “this agreement” or “this Agreement” or similar terms shall be deemed to be references to the Offer Letter as amended hereby.

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Please indicate your agreement with the above terms by signing below.

Very truly yours,

SYROS PHARMACEUTICALS, INC.

By: /s/ Nancy Simonian
Nancy Simonian
Chief Executive Officer

Accepted and Agreed as of January 27, 2016

/s/ Kyle Kovalanka
Kyle Kovalanka

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Attachment A

Payments Subject to Section 409A

1. Subject to this Attachment A, any severance payments that may be due under the letter agreement shall begin only upon the date of your “separation from service” (determined as set forth below) which occurs on or after the termination of your employment. The following rules shall apply with respect to distribution of the severance payments, if any, to be provided to you under the letter agreement, as applicable:

- a. It is intended that each installment of the severance payments under the letter agreement provided under shall be treated as a separate “payment” for purposes of Section 409A of the Internal Revenue Code of 1986, as amended (“Section 409A”). Neither the Company nor you shall have the right to accelerate or defer the delivery of any such payments except to the extent specifically permitted or required by Section 409A.
- b. If, as of the date of your “separation from service” from the Company, you are not a “specified employee” (within the meaning of Section 409A), then each installment of the severance payments shall be made on the dates and terms set forth in the letter agreement.
- c. If, as of the date of your “separation from service” from the Company, you are a “specified employee” (within the meaning of Section 409A), then:
 - i. Each installment of the severance payments due under the letter agreement that, in accordance with the dates and terms set forth herein, will in all circumstances, regardless of when your separation from service occurs, be paid within the short-term deferral period (as defined under Section 409A) shall be treated as a short-term deferral within the meaning of Treasury Regulation Section 1.409A-1(b)(4) to

the maximum extent permissible under Section 409A and shall be paid on the dates and terms set forth in the letter agreement; and

- ii. Each installment of the severance payments due under the letter agreement that is not described in this Attachment A, Section 1(c)(i) and that would, absent this subsection, be paid within the six-month period following your "separation from service" from the Company shall not be paid until the date that is six months and one day after such separation from service (or, if earlier, your death), with any such installments that are required to be delayed being accumulated during the six-month period and paid in a lump sum on the date that is six months and one day following your separation from service and any subsequent installments, if any, being paid in accordance with the dates and terms set forth herein; provided, however, that the preceding provisions of this sentence shall not apply to any installment of payments if and to the maximum extent that that such installment is deemed to be paid under a separation pay plan that does not provide for a deferral of compensation by reason of

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the application of Treasury Regulation 1.409A-1(b)(9)(iii) (relating to separation pay upon an involuntary separation from service). Any installments that qualify for the exception under Treasury Regulation Section 1.409A-1(b)(9)(iii) must be paid no later than the last day of your second taxable year following the taxable year in which the separation from service occurs.

2. The determination of whether and when your separation from service from the Company has occurred shall be made and in a manner consistent with, and based on the presumptions set forth in, Treasury Regulation Section 1.409A-1(h). Solely for purposes of this Attachment A, Section 2, "Company" shall include all persons with whom the Company would be considered a single employer under Section 414(b) and 414(c) of the Internal Revenue Code of 1986, as amended.

3. The Company makes no representation or warranty and shall have no liability to you or to any other person if any of the provisions of the letter agreement (including this Attachment) are determined to constitute deferred compensation subject to Section 409A but that do not satisfy an exemption from, or the conditions of, that section.

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December 2, 2015

David Roth
Via e-mail

Dear David:

On behalf of Sytros Pharmaceuticals, Inc. (the "Company"), I am pleased to extend the following offer and set forth the terms of your employment with the Company:

1. You will be employed to serve on a FULL-TIME basis as Chief Medical Officer (CMO) effective December 7, 2015. As CMO you will report to Nancy Simonian, CEO and will be responsible for developing and implementing the overall medical and clinical strategy plus such other duties as may from time to time be assigned to you by the Company.
2. Your salary will be \$380,000 per year, paid semi-monthly in arrears in accordance with the Company's normal payroll processes and subject to tax and other withholdings as required by law. Such salary may be adjusted from time to time in accordance with normal business practice and in the sole discretion of the Company.
3. You may participate in any and all bonus and benefit programs that the Company establishes and makes available to its employees from time to time, provided you are eligible under (and subject to all provisions of) the plan documents governing those programs. Specifically you will be eligible to receive a 35.0% bonus in your first year of employment with the Company, prorated based on your start date and approved by the Board of Directors. Future bonus eligibility will be based on the Company's annual bonus plan and approved by the Board of Directors.
4. Without otherwise limiting the "at-will" nature of your employment, in the event your employment is terminated at any time by the Company without Cause or by you for Good Reason, then: (a) you shall receive your base salary accrued through the last day of your employment with the Company, and (b) you shall receive your base salary at the then-current rate, reduced by all applicable taxes and withholdings, for a period of nine (9) months commencing on the Payment Date (as defined below), payable in accordance with the Company's then current payroll policies and practices. In the event of a Change in Control, 100% of all unvested stock options then held by you shall become fully vested and exercisable on the earlier to occur of (a) the date your employment is terminated by the Company without Cause or by you for Good Reason (either in contemplation of, pursuant to or following a Change in Control) or (b) the date that is twelve (12) months following the effective date of the Change in Control, provided that you remain employed by us or our successor on such date. Notwithstanding the foregoing, you will not be entitled to receive any severance

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payments unless, within sixty (60) days following the date of termination, you (i) have executed a general release in a form mutually agreeable by you and the Company or persons affiliated with the Company, and (ii) have agreed not to prosecute any legal action or other proceeding based on those claims. The severance payments shall be paid, or commence on the first payroll period following the date the release becomes effective (the "Payment Date"). Notwithstanding the foregoing, if the 60th day following the date of termination occurs in the calendar year following the calendar year of the termination, then the Payment Date shall be no earlier than January 1st of such subsequent calendar year. The severance payments are subject to the terms and conditions set forth on Attachment A.

For purposes of this letter agreement, "Change in Control" means any transaction or series of related transactions (a) the result of which is a change in the ownership of the Company, such that more than 50% of the equity securities of the Company are acquired by any person or group (as such terms are defined for purposes of Section 13(d)(3) of the Securities Exchange Act of 1934, as amended) that does not own capital stock of the Company of the effective date of such change in control, (b) that results in the sale of all or substantially all of the assets of the Company, or (c) that results in the consolidation or merger of the Company with or into another corporation or corporations or other entity in which the Company is not the survivor (except any such corporation or entity controlled, directly or indirectly, by the Company).

"Cause" means: (a) your conviction of, or plea of guilty or nolo contendere to, any crime involving dishonesty or moral turpitude or any felony; or (b) you have (i) engaged in material dishonesty, willful misconduct or gross negligence, (ii) breached or threatened to breach either or both of the Ancillary Agreements (as defined below), (iii) materially violated a Company policy or procedure causing or threatening to cause substantial injury to the Company, and/or (iv) willfully refused to perform your reasonable assigned duties to the Company, following written notice of such refusal by the Company and a period of thirty (30) days to cure the same.

"Good Reason" means the occurrence of one or more of the following without your written consent: (a) a material reduction in your authority, duties and/or responsibilities as compared to your authority, duties and/or responsibilities in effect immediately prior to the occurrence of the event (for example, but not by way of limitation, this determination will include an analysis of whether you maintain at least the same level, scope and type of duties and responsibilities with respect to the management, strategy, operations and business of the

Company), or (b) a material reduction in your base compensation as compared to your base compensation in effect immediately prior to the occurrence of the event; provided, however, that no such occurrence shall constitute Good Reason unless: (i) you give the Company a written notice of termination for Good Reason not more than ninety (90) days after the initial existence of the condition, (ii) the grounds for termination (if susceptible to correction) are not corrected by the Company within thirty (30) days of its receipt of such notice, and (iii) your termination of employment occurs within one (1) year following the Company's receipt of such notice.

5. You may be eligible for a maximum of three (3) weeks of vacation per calendar year to be taken at such times as may be approved by the Company. The number of vacation

days for which you are eligible shall accrue at the rate of 1.25 days per month that you are employed during such calendar year.

6. Subject to the approval of the Board of Directors of the Company, the Company will grant to you an option (a "Time-Based Option") under the Company's 2012 Equity Incentive Plan (the "Plan") for the initial purchase of a number of shares of common stock of the Company equal to 1% of the Company's fully-diluted outstanding shares as of the date hereof, at a price per share equal to the fair market value at the time of Board approval, which option shall be granted within 30 days of your first day of employment. The Time-Based Option shall vest (i) as to 25% of the shares on the one-year anniversary of grant, and (ii) as to the remaining shares in equal monthly installments for the next 36 months thereafter, becoming fully vested on the fourth anniversary of grant, provided that you remain employed by us on the applicable vesting date. Subject to the approval of the Board of Directors of the Company, you shall also be granted an option (a "Performance-Based Option") under the Plan to purchase an additional number of shares of common stock of the Company equal to 0.3% of the Company's fully-diluted outstanding shares as of the date hereof, at a price per share equal to the fair market value at the time of Board approval, which option shall be granted within 30 days of your first day of employment and will vest six years from the date of grant, subject to accelerated vesting according to the following schedule: (i) 75% upon achievement of clinical proof of concept; and; (ii) 25% upon the Company's execution of a collaboration agreement, in each case based on parameters approved by the Board. Subject to the foregoing, each of the Time-Based Option and the Performance-Based Option shall be subject to all terms and other provisions set forth in the Plan and in a separate option agreement.

7. You may be eligible to receive such future stock options grants as the Board of Directors of the Company shall deem appropriate.

8. You will be required to execute an Invention and Non-Disclosure Agreement and a Non-Competition and Non-Solicitation Agreement in the forms attached as Exhibit A and Exhibit B, respectively, as a condition of employment (such agreements are referred to as "Ancillary Agreements").

9. You represent that you are not bound by any employment contract, restrictive covenant or other restriction preventing you from entering into employment with or carrying out your responsibilities for the Company, or which is in any way inconsistent with the terms of this letter.

10. You agree to provide to the Company, within three days of your hire date, documentation of your eligibility to work in the United States, as required by the Immigration Reform and Control Act of 1986. You may need to obtain a work visa in order to be eligible to work in the United States. If that is the case, your employment with the Company will be conditioned upon your obtaining a work visa in a timely manner as determined by the Company.

11. This letter shall not be construed as an agreement, either expressed or implied, to employ you for any stated term, and shall in no way alter the Company's policy of employment at will, under which both you and the Company remain free to terminate the

employment relationship, with or without cause, at any time, with or without notice. Similarly, nothing in this letter shall be construed as an agreement, either express or implied, to pay you any compensation or grant you any benefit beyond the end of your employment with the Company.

THE REMAINDER OF THIS PAGE INTENTIONALLY LEFT BLANK

If you agree with the employment provisions of this letter, please sign the letter and exhibits, scan the signature pages and email to Leslie Kaufman at lkaufman@syros.com. If you do not accept this offer by _____, this offer will be revoked.

Very Truly Yours,

By: /s/ Nancy Simonian
Name: Nancy Simonian
Title: CEO

The foregoing correctly sets forth the terms of my employment
by Syros Pharmaceuticals, Inc.

/s/ David A. Roth
David Roth

Date: 12/5/2015

Attachment A

Payments Subject to Section 409A

1. Subject to this Attachment A, any severance payments that may be due under the letter agreement shall begin only upon the date of your "separation from service" (determined as set forth below) which occurs on or after the termination of your employment. The following rules shall apply with respect to distribution of the severance payments, if any, to be provided to you under the letter agreement, as applicable:

(a) It is intended that each installment of the severance payments under the letter agreement provided under shall be treated as a separate "payment" for purposes of Section 409A of the Internal Revenue Code of 1986, as amended ("Section 409A"). Neither the Company nor you shall have the right to accelerate or defer the delivery of any such payments except to the extent specifically permitted or required by Section 409A.

(b) If, as of the date of your "separation from service" from the Company, you are not a "specified employee" (within the meaning of Section 409A), then each installment of the severance payments shall be made on the dates and terms set forth in the letter agreement.

(c) If, as of the date of your "separation from service" from the Company, you are a "specified employee" (within the meaning of Section 409A), then:

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

(ii) Each installment of the severance payments due under the letter agreement that is not described in this Attachment A, Section 1(c)(i) and that would, absent this subsection, be paid within the six-month period following your "separation from service" from the Company shall not be paid until the date that is six months and one day after such separation from service (or, if earlier, your death), with any such installments that are required to be delayed being accumulated during the six-month period and paid in a lump sum on the date that is six months and one day following your separation from service and any subsequent installments, if any, being paid in accordance with the dates and terms set forth herein; provided, however, that the preceding provisions of this sentence shall not apply to any installment of payments if and to the maximum extent that

that such installment is deemed to be paid under a separation pay plan that does not provide for a deferral of compensation by reason of the application of Treasury Regulation 1.409A-1(b)(9)(iii) (relating to separation pay upon an involuntary separation from service). Any installments that qualify for the exception under Treasury Regulation Section 1.409A-1(b)(9)(iii) must be paid no later than the last day of your second taxable year following the taxable year in which the separation from service occurs.

2. The determination of whether and when your separation from service from the Company has occurred shall be made and in a manner consistent with, and based on the presumptions set forth in, Treasury Regulation Section 1.409A-1(h). Solely for purposes of this Attachment A, Section 2, "Company" shall include all persons with whom the Company would be considered a single employer under Section 414(b) and 414(c) of the Internal Revenue Code of 1986, as amended.

3. The Company makes no representation or warranty and shall have no liability to you or to any other person if any of the provisions of the letter agreement (including this Attachment) are determined to constitute deferred compensation subject to Section 409A but that do not satisfy an exemption from, or the conditions of, that section.

/s/ David A. Roth
12/5/2015

INVENTION AND NON-DISCLOSURE AGREEMENT

This Agreement is made by and between Syros Pharmaceuticals, Inc., a Delaware corporation (hereinafter referred to collectively with its subsidiaries as the "Company"), and David Roth (the "Employee").

In consideration of the employment or the continued employment of the Employee by the Company, the Company and the Employee agree as follows:

1. Condition of Employment.

The Employee acknowledges that his/her employment and/or the continuance of that employment with the Company is contingent upon his/her agreement to sign and adhere to the provisions of this Agreement. The Employee further acknowledges that the nature of the Company's business is such that protection of its proprietary and confidential information is critical to the business' survival and success.

2. Proprietary and Confidential Information.

(a) The Employee agrees that all information and know-how, whether or not in writing, of a private, secret or confidential nature concerning the Company's business or financial affairs (collectively, "Proprietary Information") is and shall be the exclusive property of the Company. By way of illustration, but not limitation, Proprietary Information may include discoveries, inventions, products, product improvements, product enhancements, processes, methods, techniques, formulas, compositions, compounds, negotiation strategies and positions, projects, developments, plans (including business and marketing plans), research data, clinical data, financial data (including sales costs, profits, pricing methods), personnel data, computer programs (including software used pursuant to a license agreement), customer, prospect and supplier lists, and contacts at or knowledge of customers or prospective customers of the Company. The Employee will not disclose any Proprietary Information to any person or entity other than employees of the Company or use the same for any purposes (other than in the performance of his/her duties as an employee of the Company) without written approval by an officer of the Company, either during or after his/her employment with the Company, unless and until such Proprietary Information has become public knowledge without fault by the Employee. While employed by the Company, the Employee will use the Employee's best efforts to prevent unauthorized publication or disclosure of any of the Company's Proprietary Information.

(b) The Employee agrees that all files, documents, letters, memoranda, reports, records, data, sketches, drawings, models, laboratory notebooks, program listings, computer equipment or devices, computer programs or other written, photographic, or other tangible or intangible material containing Proprietary Information, whether created by the Employee or others, which shall come into his/her custody or possession, shall be and are the exclusive property of the Company to be used by the Employee only in the performance of his/her duties for the Company and shall not be copied or removed from the Company premises except in the pursuit of the business of the Company. All such materials or copies thereof and all tangible property of the Company in the custody or possession of the Employee shall be delivered to the Company, upon the earlier of (i) a

request by the Company or (ii) termination of his/her employment. After such delivery, the Employee shall not retain any such materials or copies thereof or any such tangible property.

(c) The Employee agrees that his/her obligation not to disclose or to use information and materials of the types set forth in paragraphs 2(a) and 2(b) above, and his/her obligation to return materials and tangible property, set forth in paragraph 2(b) above, also extends to such types of information, materials and tangible property of customers of the Company or suppliers to the Company or other third parties who may have disclosed or entrusted the same to the Company or to the Employee in the course of the Company's business.

3. Developments.

(a) The Employee will make full and prompt disclosure to the Company of all discoveries, inventions, improvements, enhancements, processes, methods, techniques, developments, software, and works of authorship, whether patentable or not, which are created, made, conceived or reduced to practice by him/her or under his/her direction or jointly with others during his/her employment by the Company, whether or not during normal working hours or on the premises of the Company (all of which are collectively referred to in this Agreement as "Developments").

(b) The Employee agrees to assign and does hereby assign to the Company (or any person or entity designated by the Company) all his/her right, title and interest in and to all Developments and all related patents, patent applications, copyrights and copyright applications. However, this paragraph 3(b) shall not apply to Developments which do not relate to the business or research and development conducted or planned to be conducted by the Company at the time such Development is created, made, conceived or reduced to practice and which are made and conceived by the Employee not during normal working hours, not on the Company's premises and not using the Company's tools, devices, equipment or Proprietary Information. The Employee understands that, to the extent this Agreement shall be construed in accordance with the laws of any state which precludes a requirement in an employee agreement to assign certain classes of inventions made by an employee, this paragraph 3(b) shall be interpreted not to apply to any invention which a court rules and/or the Company agrees falls within such classes. The Employee also hereby waives all claims to moral

rights in any Developments.

(c) The Employee agrees to cooperate fully with the Company, both during and after his/her employment with the Company, with respect to the procurement, maintenance and enforcement of copyrights, patents and other intellectual property rights (both in the United States and foreign countries) relating to Developments. The Employee shall sign all papers, including, without limitation, copyright applications, patent applications, declarations, oaths, formal assignments, assignments of priority rights, and powers of attorney, which the Company may deem necessary or desirable in order to protect its rights and interests in any Development. The Employee further agrees that if the Company is unable, after reasonable effort, to secure the signature of the Employee on any such papers, any executive officer of the Company shall be entitled to execute any such papers as the agent and the attorney-in-fact of the Employee, and the Employee hereby irrevocably designates and appoints each executive officer of the Company as his/her agent and attorney-in-fact to execute any such papers on his/her behalf, and to take any and all actions as the

Company may deem necessary or desirable in order to protect its rights and interests in any Development, under the conditions described in this sentence.

4. Other Agreements.

The Employee represents that, except as the Employee has disclosed in writing to the Company, the Employee is not bound by the terms of any agreement with any previous employer or other party to refrain from using or disclosing any trade secret or confidential or proprietary information in the course of his/her employment with the Company, to refrain from competing, directly or indirectly, with the business of such previous employer or any other party or to refrain from soliciting employees, customers or suppliers of such previous employer or other party. The Employee further represents that his/her performance of all the terms of this Agreement and the performance of his/her duties as an employee of the Company do not and will not conflict with or breach any agreement with any prior employer or other party to which the Employee is a party (including without limitation any nondisclosure or non-competition agreement), and that the Employee will not disclose to the Company or induce the Company to use any confidential or proprietary information or material belonging to any previous employer or others.

5. United States Government Obligations.

The Employee acknowledges that the Company from time to time may have agreements with other persons or with the United States Government, or agencies thereof, which impose obligations or restrictions on the Company regarding inventions made during the course of work under such agreements or regarding the confidential nature of such work. The Employee agrees to be bound by all such obligations and restrictions which are made known to the Employee and to take all action necessary to discharge the obligations of the Company under such agreements.

6. Miscellaneous.

(a) Equitable Remedies. The restrictions contained in this Agreement are necessary for the protection of the business and goodwill of the Company and are considered by the Employee to be reasonable for such purpose. The Employee agrees that any breach of this Agreement is likely to cause the Company substantial and irrevocable damage which is difficult to measure. Therefore, in the event of any such breach or threatened breach, the Employee agrees that the Company, in addition to such other remedies which may be available, shall have the right to obtain an injunction from a court restraining such a breach or threatened breach and the right to specific performance of the provisions of this Agreement and the Employee hereby waives the adequacy of a remedy at law as a defense to such relief.

(b) Obligations to Third Parties. The Employee acknowledges and represents that this agreement and the Employee's employment with the Company will not violate any continuing obligation the Employee has to any former employer or other third party.

(c) Disclosure of this Agreement. The Employee hereby authorizes the Company to notify others, including but not limited to customers of the Company and any of the Employee's future employers or prospective business associates, of the terms and existence of this Agreement and the Employee's continuing obligations to the Company hereunder.

(d) Not Employment Contract. The Employee acknowledges that this Agreement does not constitute a contract of employment, does not imply that the Company will continue his/her employment for any period of time and does not change the at-will nature of his/her employment.

(e) Successors and Assigns. This Agreement shall be binding upon and inure to the benefit of both parties and their respective successors and assigns, including any corporation with which, or into which, the Company may be merged or which may succeed to the Company's assets or business, provided, however, that the obligations of the Employee are personal and shall not be assigned by him or her. The Employee expressly consents to be bound by the provisions of this Agreement for the benefit of the Company or any subsidiary or affiliate thereof to whose employ the Employee may be transferred without the necessity that this Agreement be re-signed at the time of such transfer.

(f) Severability. In case any provision of this Agreement shall be invalid, illegal or otherwise unenforceable, the validity, legality and enforceability of the remaining provisions shall in no way be affected or impaired thereby.

(g) Waivers. No delay or omission by the Company in exercising any right under this Agreement will operate as a waiver of that or any other right. A waiver or consent given by the Company on any one occasion is effective only in that instance and will not be construed as a bar to or waiver of any right on any other occasion.

(h) Governing Law. This Agreement shall be governed by and construed in accordance with the laws of the Commonwealth of Massachusetts (without reference to the conflicts of laws provisions thereof). Any action, suit, or other legal proceeding which is commenced to resolve any matter arising under or relating to any provision of this Agreement shall be commenced only in a court of the Commonwealth of Massachusetts (or, if appropriate, a federal court located within Massachusetts), and the Company and the Employee each consents to the jurisdiction of such a court. The Company and the Employee each hereby irrevocably waive any right to a trial by jury in any action, suit or other legal proceeding arising under or relating to any provision of this Agreement.

(i) Entire Agreement; Amendment. This Agreement supersedes all prior agreements, written or oral, between the Employee and the Company relating to the subject matter of this Agreement. This Agreement may not be modified, changed or discharged in whole or in part, except by an agreement in writing signed by the Employee and the Company. The Employee agrees that any change or changes in his/her duties, salary or compensation after the signing of this Agreement shall not affect the validity or scope of this Agreement.

(j) Captions. The captions of the sections of this Agreement are for convenience of reference only and in no way define, limit or affect the scope or substance of any section of this Agreement.

THE EMPLOYEE ACKNOWLEDGES THAT HE/SHE HAS CAREFULLY READ THIS AGREEMENT AND UNDERSTANDS AND AGREES TO ALL OF THE PROVISIONS IN THIS AGREEMENT.

WITNESS our hands and seals:

Date: _____ SYROS PHARMACEUTICALS, INC.

By: /s/ Nancy Simonian

Name: Nancy Simonian
Title: CEO

Date: 12/5/2015 EMPLOYEE NAME

David Roth

/s/ David A. Roth

Exhibit C

NON-COMPETITION AND NON-SOLICITATION AGREEMENT

This Agreement is made between Syros Pharmaceuticals, Inc., a Delaware corporation (hereinafter referred to collectively with its subsidiaries as the "Company"), and David Roth.

For good consideration and in consideration of the employment or continued employment of the Employee by the Company, including the equity consideration in the Company, the Employee and the Company agree as follows:

1. Non-Competition and Non-Solicitation. While the Employee is employed by the Company and for a period of one year after the termination or cessation of such employment for any reason, the Employee will not directly or indirectly:

(a) Engage or assist others in engaging in any business or enterprise (whether as owner, partner, officer, director, employee, consultant, investor, lender or otherwise, except as the holder of not more than 1% of the outstanding stock of a publicly-held company) that is competitive with the Company's business, including but not limited to any business or enterprise that develops, manufactures, markets, licenses, sells or provides any product or service that competes with any product or service developed, manufactured, marketed, licensed, sold or provided, or planned to be developed, manufactured, marketed, licensed, sold or provided, by the Company while the Employee was employed by the Company; or

Notwithstanding the foregoing, Section 1(a) shall not preclude the Employee from becoming an employee of, or from otherwise providing services to, a separate division or operating unit of a multi-divisional business or enterprise (a "Division") if: (i) the Division by which the Employee is employed, or to which the Employee provides services, is not competitive with the Company's business (within the meaning of Section 1(a)), (ii) the Employee does not provide services, directly or indirectly, to any other division or operating unit of such multi-divisional business or enterprise which is competitive with the Company's business (within the meaning of Section 1(a)) (individually, a "Competitive Division" and collectively, the "Competitive Divisions") and (iii) the Competitive Divisions, in the aggregate, accounted for less than one-third of the multi-divisional business or enterprises' consolidated revenues for the fiscal year, and each subsequent quarterly period, prior to the Employee's commencement of employment with the Division.

(b) Either alone or in association with others, solicit, divert or take away, or attempt to divert or take away, the business or patronage of any of the clients, customers, or business partners of the Company which were contacted, solicited, or served by the Company during the 12-month period prior to the termination or cessation of the Employee's employment with the Company; or

(c) Either alone or in association with others: (i) solicit, induce or attempt to induce, any employee or independent contractor of the Company to terminate his or her employment or other engagement with the Company, or (ii) solicit for employment or engagement as an independent contractor any person who was employed or otherwise engaged by the Company at any time during the term of the Employee's employment with the Company;

provided, that this clause (ii) shall not apply to the solicitation of any individual whose employment or other engagement with the Company has been terminated for a period of six months or longer.

(d) Extension. If the Employee violates the provisions of any of the preceding paragraphs of this Section 1, the Employee shall continue to be bound by the restrictions set forth in such paragraph until a period of one year has expired without any violation of such provisions.

2. Miscellaneous.

(a) Equitable Remedies. The restrictions contained in this Agreement are necessary for the protection of the business and goodwill of the Company and are considered by the Employee to be reasonable for such purpose. The Employee agrees that any breach of this Agreement is likely to cause the Company substantial and irrevocable damage which is difficult to measure. Therefore, in the event of any such breach or threatened breach, the Employee agrees that the Company, in addition to such other remedies which may be available, shall have the right to obtain an injunction from a court restraining such a breach or threatened breach and the right to specific performance of the provisions of this Agreement and the Employee hereby waives the adequacy of a remedy at law as a defense to such relief.

(b) Obligations to Third Parties. The Employee acknowledges and represents that this agreement and the Employee's employment with the Company will not violate any continuing obligation the Employee has to any former employer or other third party.

(c) Disclosure of this Agreement. The Employee hereby authorizes the Company to notify others, including but not limited to customers of the Company and any of the Employee's future employers or prospective business associates, of the terms and existence of this Agreement and the Employee's continuing obligations to the Company hereunder.

(d) Not Employment Contract. The Employee acknowledges that this Agreement does not constitute a contract of employment, does not imply that the Company will continue his/her employment for any period of time and does not change the at-will nature of his/her employment.

(e) Successors and Assigns. This Agreement shall be binding upon and inure to the benefit of both parties and their respective successors and assigns, including any corporation with which, or into which, the Company may be merged or which may succeed to the Company's assets or business, provided, however, that the obligations of the Employee are personal and shall not be assigned by him or her. The Employee expressly consents to be bound by the provisions of this Agreement for the benefit of the Company or any subsidiary or affiliate thereof to whose employ the Employee may be transferred without the necessity that this Agreement be re-signed at the time of such transfer. Notwithstanding the foregoing, if the Company is merged with or into a third party which is engaged in multiple lines of business, or if a third party engaged in multiple lines of business succeeds to the Company's assets or business, then for purposes of Section 1(a), the term "Company" shall mean and refer to the business of the Company as it existed immediately prior to such event and as it subsequently develops and not to the third party's other businesses.

(f) Interpretation. If any restriction set forth in Section 1 is found by any court of competent jurisdiction to be unenforceable because it extends for too long a period of time or over too great a range of activities or in too broad a geographic area, it shall be interpreted to extend only over the maximum period of time, range of activities or geographic area as to which it may be enforceable.

(g) Severability. In case any provision of this Agreement shall be invalid, illegal or otherwise unenforceable, the validity, legality and enforceability of the remaining provisions shall in no way be affected or impaired thereby.

(h) Waivers. No delay or omission by the Company in exercising any right under this Agreement will operate as a waiver of that or any other right. A waiver or consent given by the Company on any one occasion is effective only in that instance and will not be construed as a bar to or waiver of any right on any other occasion.

(i) Governing Law. This Agreement shall be governed by and construed in accordance with the laws of the Commonwealth of Massachusetts (without reference to the conflicts of laws provisions thereof). Any action, suit, or other legal proceeding which is commenced to resolve any matter arising under or relating to any provision of this Agreement shall be commenced only in a court of the Commonwealth of Massachusetts (or, if appropriate, a federal court located within Massachusetts), and the Company and the Employee each consents to the jurisdiction of such a court. The Company and the Employee each hereby irrevocably

waive any right to a trial by jury in any action, suit or other legal proceeding arising under or relating to any provision of this Agreement.

(j) Entire Agreement; Amendment. This Agreement supersedes all prior agreements, written or oral, between the Employee and the Company relating to the subject matter of this Agreement. This Agreement may not be modified, changed or discharged in whole or in part, except by an agreement in writing signed by the Employee and the Company. The Employee agrees that any change or changes in his/her duties, salary or compensation after the signing of this Agreement shall not affect the validity or scope of this Agreement.

(k) Captions. The captions of the sections of this Agreement are for convenience of reference only and in no way define, limit or affect the scope or substance of any section of this Agreement.

[Remainder of this page intentionally left blank.]

THE EMPLOYEE ACKNOWLEDGES THAT HE/SHE HAS CAREFULLY READ THIS AGREEMENT AND UNDERSTANDS AND AGREES TO ALL OF THE PROVISIONS IN THIS AGREEMENT.

WITNESS our hands and seals:

Date: _____ SYROS PHARMACEUTICALS, INC.

By: /s/ Nancy Simonian

Name: Nancy Simonian
Title: CEO

Date: 12/5/2015 EMPLOYEE NAME

David Roth

/s/ David A. Roth

Syros Pharmaceuticals, Inc.

January 29, 2016

David Roth

Re: Amendment to Employment Offer Letter

Dear David:

Reference is made to that certain Employment Offer Letter dated December 2, 2015 between Syros Pharmaceuticals, Inc., a Delaware corporation (the "Company"), and you regarding the terms of your employment with the Company (the "Offer Letter"). This letter (the "Amendment") confirms the agreement between the Company and you regarding an amendment to the Offer Letter.

1. Section 4 of the Offer Letter is hereby deleted in its entirety and the following inserted in lieu thereof:

"4. Without otherwise limiting the "at-will" nature of your employment, in the event your employment is terminated by the Company without Cause or by you for Good Reason (each as defined below), you shall be entitled to the base salary that has accrued and to which you are entitled as of the effective date of such termination, and further, subject to the conditions set forth in the second paragraph of this Section 4, the Company shall, for a period of nine (9) months following your termination date: (i) continue to pay you, in accordance with the Company's regularly established payroll procedure, your base salary as severance; and (ii) provided you are eligible for and timely elect to continue receiving group medical insurance pursuant to the "COBRA" law, continue to pay the share of the premium for health coverage that is paid by the Company for active and similarly-situated employees who receive the same type of coverage, unless the Company's provision of such COBRA payments will violate the nondiscrimination requirements of applicable law, in which case this benefit will not apply. If, within the three months prior to a Change in Control or in the twelve months following a Change in Control, the Company terminates your employment without Cause or you resign for Good Reason, the Company, subject to the conditions set forth in the second paragraph of this Section 4, will: (a) extend the severance benefits described in (i) and (ii) above for an additional three months, such that the total severance benefit period shall be one (1) year; (b) pay you a lump sum amount equal to your target bonus in effect for the fiscal year in which your separation from employment occurs; and (c) accelerate the vesting of all unvested stock options held by you as of the date your employment is terminated such that 100% of such options shall become fully vested and exercisable effective as of such date.

Notwithstanding the foregoing, you will not be entitled to receive any severance benefits unless, within sixty (60) days following the date of termination, you (i) have executed a severance and release of claims agreement in a form prescribed

by the Company or persons affiliated with the Company (which will include, at a minimum, a release of all releasable claims and non-disparagement and cooperation obligations). Any severance payments shall be paid, or commence on the first payroll period following the date the release becomes effective (the "Payment Date"). Notwithstanding the foregoing, if the 60th day following the date of termination occurs in the calendar year following the calendar year of the termination, then the Payment Date shall be no earlier than January 1st of such subsequent calendar year.

For purposes of this Agreement, "Change in Control" means any transaction or series of related transactions (a) the result of which is a change in the ownership of the Company, such that more than 50% of the equity securities of the Company are acquired by any person or group (as such terms are defined for purposes of Section 13(d)(3) of the Securities Exchange Act of 1934, as amended) that does not own capital stock of the Company of the effective date of such change in control, (b) that results in the sale of all or substantially all of the assets of the Company, or (c) that results in the consolidation or merger of the Company with or into another corporation or corporations or other entity in which the Company is not the survivor (except any such corporation or entity controlled, directly or indirectly, by the Company).

"Cause" means: (a) your conviction of, or plea of guilty or nolo contendere to, any crime involving dishonesty or moral turpitude or any felony; or (b) you have (i) engaged in material dishonesty, willful misconduct or gross negligence, (ii) breached or threatened to breach either or both of the Ancillary Agreements (as defined below), (iii) materially violated a Company policy or procedure causing or threatening to cause substantial injury to the Company, and/or (iv) willfully refused to perform your assigned duties to the Company, following written notice of such refusal by the Company and a period of thirty (30) days to cure the same.

"Good Reason" means the occurrence of one or more of the following without your written consent: (a) a material reduction in your authority, duties and/or responsibilities as compared to your authority, duties and/or responsibilities in effect immediately prior to the occurrence of the event (for example, but not by way of limitation, this determination will include an analysis of whether you maintain at least the same level, scope and type of duties and responsibilities with respect to the management, strategy, operations and business of the Company), or (b) a material reduction in your base compensation as compared to your base compensation in effect immediately prior to the occurrence of the event; provided, however, that no such occurrence shall constitute Good Reason unless: (i) you give the Company a written notice of termination for Good Reason not more than ninety (90) days after the initial existence of the condition, (ii) the grounds for termination (if susceptible to correction) are not corrected by the Company within thirty (30) days of its receipt of such notice, and (iii) your termination of employment occurs within one (1) year following the Company's receipt of such notice.

2. The following language shall be inserted as a new paragraph following the last enumerated paragraph of the Offer Letter:

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"This letter is intended to provide payments that are exempt from or compliant with 409A, and should be interpreted consistent with that intent."

3. The attached exhibit entitled "Payments Subject to Section 409A" is hereby appended to the Offer Letter as Attachment A and, if applicable, replaces any previous such attachment concerning the same subject matter.

4. Except as specifically provided herein, the Offer Letter remains in full force and effect and is not modified or amended hereby.

5. This Amendment will be construed and interpreted in accordance with the laws of the Commonwealth of Massachusetts (other than choice-of-law provisions).

6. This Amendment may be executed in counterparts, each of which will be considered an original, but all of which together will constitute one agreement. Execution of a facsimile or "pdf" copy will have the same force and effect as execution of an original, and a facsimile or "pdf" signature will be deemed an original and valid signature. From and after the date of this Amendment, all references in the Offer Letter to "this agreement" or "this Agreement" or similar terms shall be deemed to be references to the Offer Letter as amended hereby.

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Please indicate your agreement with the above terms by signing below.

Very truly yours,

SYROS PHARMACEUTICALS, INC.

By: /s/ Nancy Simonian
Nancy Simonian
Chief Executive Officer

Accepted and Agreed as of January 29, 2016

/s/ David Roth
David Roth

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Attachment A

Payments Subject to Section 409A

1. Subject to this Attachment A, any severance payments that may be due under the letter agreement shall begin only upon the date of your “separation from service” (determined as set forth below) which occurs on or after the termination of your employment. The following rules shall apply with respect to distribution of the severance payments, if any, to be provided to you under the letter agreement, as applicable:
- a. It is intended that each installment of the severance payments under the letter agreement provided under shall be treated as a separate “payment” for purposes of Section 409A of the Internal Revenue Code of 1986, as amended (“Section 409A”). Neither the Company nor you shall have the right to accelerate or defer the delivery of any such payments except to the extent specifically permitted or required by Section 409A.
 - b. If, as of the date of your “separation from service” from the Company, you are not a “specified employee” (within the meaning of Section 409A), then each installment of the severance payments shall be made on the dates and terms set forth in the letter agreement.
 - c. If, as of the date of your “separation from service” from the Company, you are a “specified employee” (within the meaning of Section 409A), then:
 - i. Each installment of the severance payments due under the letter agreement that, in accordance with the dates and terms set forth herein, will in all circumstances, regardless of when your separation from service occurs, be paid within the short-term deferral period (as defined under Section 409A) shall be treated as a short-term deferral within the meaning of Treasury Regulation Section 1.409A-1(b)(4) to the maximum extent permissible under Section 409A and shall be paid on the dates and terms set forth in the letter agreement; and
 - ii. Each installment of the severance payments due under the letter agreement that is not described in this Attachment A, Section 1(c)(i) and that would, absent this subsection, be paid within the six-month period following your “separation from service” from the Company shall not be paid until the date that is six months and one day after such separation from service (or, if earlier, your death), with any such installments that are required to be delayed being accumulated during the six-month period and paid in a lump sum on the date that is six months and one day following your separation from service and any subsequent installments, if any, being paid in accordance with the dates and terms set forth herein; provided, however, that the preceding provisions of this sentence shall not apply to any installment of payments if and to the maximum extent that that such installment is deemed to be paid under a separation pay plan that does not provide for a deferral of compensation by reason of

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the application of Treasury Regulation 1.409A-1(b)(9)(iii) (relating to separation pay upon an involuntary separation from service). Any installments that qualify for the exception under Treasury Regulation Section 1.409A-1(b)(9)(iii) must be paid no later than the last day of your second taxable year following the taxable year in which the separation from service occurs.

2. The determination of whether and when your separation from service from the Company has occurred shall be made and in a manner consistent with, and based on the presumptions set forth in, Treasury Regulation Section 1.409A-1(h). Solely for purposes of this Attachment A, Section 2, “Company” shall include all persons with whom the Company would be considered a single employer under Section 414(b) and 414(c) of the Internal Revenue Code of 1986, as amended.

3. The Company makes no representation or warranty and shall have no liability to you or to any other person if any of the provisions of the letter agreement (including this Attachment) are determined to constitute deferred compensation subject to Section 409A but that do not satisfy an exemption from, or the conditions of, that section.

INDEMNIFICATION AGREEMENT

This Indemnification Agreement (“Agreement”) is made as of _____, 20____ by and between Syros Pharmaceuticals, Inc., a Delaware corporation (the “Company”), and _____ (“Indemnitee”).

RECITALS

WHEREAS, highly competent persons have become more reluctant to serve publicly-held corporations as directors or officers or in other capacities unless they are provided with adequate protection through insurance or adequate indemnification against inordinate risks of claims and actions against them arising out of their service to and activities on behalf of the corporation;

WHEREAS, the Board of Directors of the Company (the “Board”) has determined that, in order to attract and retain qualified individuals, the Company will attempt to maintain on an ongoing basis, at its sole expense, liability insurance to protect persons serving the Company and its subsidiaries from certain liabilities. Although the furnishing of such insurance has been a customary and widespread practice among United States-based corporations and other business enterprises, the Company believes that, given current market conditions and trends, such insurance may be available to it in the future only at higher premiums and with more exclusions. At the same time, directors, officers, and other persons in service to corporations or business enterprises are being increasingly subjected to expensive and time-consuming litigation relating to, among other things, matters that traditionally would have been brought only against the Company or business enterprise itself. The Certificate of Incorporation of the Company (the “Certificate of Incorporation”) requires indemnification of the officers and directors of the Company. Indemnitee may also be entitled to indemnification pursuant to the General Corporation Law of the State of Delaware (the “DGCL”). The Certificate of Incorporation and the DGCL expressly provide that the indemnification provisions set forth therein are not exclusive, and thereby contemplate that contracts may be entered into between the Company and members of the board of directors, officers and other persons with respect to indemnification;

WHEREAS, the uncertainties relating to such insurance and to indemnification have increased the difficulty of attracting and retaining such persons;

WHEREAS, the Board has determined that the increased difficulty in attracting and retaining such persons is detrimental to the best interests of the Company and its stockholders and that the Company should act to assure such persons that there will be increased certainty of such protection in the future;

WHEREAS, it is reasonable, prudent and necessary for the Company contractually to obligate itself to indemnify, and to advance expenses on behalf of, such persons to the fullest extent permitted by applicable law so that they will serve or continue to serve the Company free from undue concern that they will not be so indemnified;

WHEREAS, this Agreement is a supplement to and in furtherance of the Certificate of Incorporation and any resolutions adopted pursuant thereto, and shall not be deemed a substitute therefor, nor to diminish or abrogate any rights of Indemnitee thereunder; and

WHEREAS, Indemnitee does not regard the protection available under the Certificate of Incorporation and insurance as adequate in the present circumstances, and may not be willing to serve as an officer or director without adequate protection, and the Company desires Indemnitee to serve in such capacity. Indemnitee is willing to serve, continue to serve and to take on additional service for or on behalf of the Company on the condition that he be so indemnified.

NOW, THEREFORE, in consideration of the premises and the covenants contained herein, the Company and Indemnitee do hereby covenant and agree as follows:

Section 1. Services to the Company. Indemnitee agrees to serve as a [director] [officer] of the Company. Indemnitee may at any time and for any reason resign from such position (subject to any other contractual obligation or any obligation imposed by operation of law), in which event the Company shall have no obligation under this Agreement to continue Indemnitee in such position. This Agreement shall not be deemed an employment contract between the Company (or any of its subsidiaries or any Enterprise) and Indemnitee. Indemnitee specifically acknowledges that Indemnitee’s employment with the Company (or any of its subsidiaries or any Enterprise), if any, is at will, and the Indemnitee may be discharged at any time for any reason, with or without cause, except as may be otherwise provided in any written employment contract between Indemnitee and the Company (or any of its subsidiaries or any Enterprise), other applicable formal severance policies duly adopted by the Board, or, with respect to service as a director or officer of the Company, by the Certificate of Incorporation, the Company’s By-laws, and the DGCL. The foregoing notwithstanding, this Agreement shall continue in force after Indemnitee has ceased to serve as an [officer] [director] of the Company, as provided in Section 16 hereof.

Section 2. Definitions. As used in this Agreement:

(a) References to “agent” shall mean any person who is or was a director, officer, or employee of the Company or a subsidiary of the Company or other person authorized by the Company to act for the Company, to include such person serving in such capacity as a director, officer, employee, fiduciary or other official of another corporation, partnership, limited liability company, joint venture, trust or other enterprise at the request of, for the convenience of, or to represent the interests of the Company or a subsidiary of the Company.

(b) A “Change in Control” shall be deemed to occur upon the earliest to occur after the date of this Agreement of

any of the following events:

i. Acquisition of Stock by Third Party. Any Person (as defined below) is or becomes the Beneficial Owner (as defined below), directly or indirectly, of securities of the Company representing fifty (50%) or more of the combined voting power of the Company's then outstanding securities unless the change in relative Beneficial Ownership of the Company's securities by any Person results solely from a reduction in the aggregate number of outstanding shares of securities entitled to vote generally in the election of directors;

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ii. Change in Board of Directors. During any period of two (2) consecutive years (not including any period prior to the execution of this Agreement), individuals who at the beginning of such period constitute the Board, and any new director (other than a director designated by a person who has entered into an agreement with the Company to effect a transaction described in Sections 2(b)(i), 2(b)(iii) or 2(b)(iv)) whose election by the Board or nomination for election by the Company's stockholders was approved by a vote of at least two-thirds of the directors then still in office who either were directors at the beginning of the period or whose election or nomination for election was previously so approved, cease for any reason to constitute at least a majority of the members of the Board;

iii. Corporate Transactions. The effective date of a merger or consolidation of the Company with any other entity, other than a merger or consolidation which would result in the voting securities of the Company outstanding immediately prior to such merger or consolidation continuing to represent (either by remaining outstanding or by being converted into voting securities of the surviving entity) more than 51% of the combined voting power of the voting securities of the surviving entity outstanding immediately after such merger or consolidation and with the power to elect at least a majority of the board of directors or other governing body of such surviving entity;

iv. Liquidation. The approval by the stockholders of the Company of a complete liquidation of the Company or an agreement for the sale or disposition by the Company of all or substantially all of the Company's assets; and

v. Other Events. There occurs any other event of a nature that would be required to be reported in response to Item 6(e) of Schedule 14A of Regulation 14A (or a response to any similar item on any similar schedule or form) promulgated under the Exchange Act (as defined below), whether or not the Company is then subject to such reporting requirement.

For purposes of this Section 2(b), the following terms shall have the following meanings:

(A) "Exchange Act" shall mean the Securities Exchange Act of 1934, as amended from time to time.

(B) "Person" shall have the meaning as set forth in Sections 13(d) and 14(d) of the Exchange Act; provided, however, that Person shall exclude (i) the Company, (ii) any trustee or other fiduciary holding securities under an employee benefit plan of the Company, and (iii) any corporation owned, directly or indirectly, by the stockholders of the Company in substantially the same proportions as their ownership of stock of the Company.

(C) "Beneficial Owner" shall have the meaning given to such term in Rule 13d-3 under the Exchange Act; provided, however, that Beneficial Owner shall exclude any Person otherwise becoming a Beneficial Owner by reason of the stockholders of the Company approving a merger of the Company with another entity.

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(c) "Corporate Status" describes the status of a person who is or was a director, officer, employee or agent of the Company or of any other corporation, limited liability company, partnership or joint venture, trust or other enterprise which such person is or was serving at the request of the Company.

(d) "Disinterested Director" shall mean a director of the Company who is not and was not a party to the Proceeding in respect of which indemnification is sought by Indemnitee.

(e) "Enterprise" shall mean the Company and any other corporation, limited liability company, partnership, joint venture, trust or other enterprise of which Indemnitee is or was serving at the request of the Company as a director, officer, trustee, partner, managing member, employee, agent or fiduciary.

(f) "Expenses" shall include all reasonable attorneys' fees, retainers, court costs, transcript costs, fees of experts and other professionals, witness fees, travel expenses, duplicating costs, printing and binding costs, telephone charges, postage, delivery service fees, any federal, state, local or foreign taxes imposed on Indemnitee as a result of the actual or deemed receipt of any payments under this Agreement, ERISA excise taxes and penalties, and all other disbursements or expenses of the types customarily incurred in connection with prosecuting, defending, preparing to prosecute or defend, investigating, being or preparing to be a witness in, or otherwise participating in, a Proceeding. Expenses also shall include (i) Expenses incurred in connection with any appeal resulting from any Proceeding, including without limitation the premium, security for, and other costs relating to any cost bond, supersedeas bond, or other appeal bond or its equivalent, and (ii) for purposes of Section 14(d) only, Expenses incurred by Indemnitee in connection with the interpretation, enforcement or defense of Indemnitee's rights under this Agreement, by litigation or otherwise. The parties agree that for the purposes of any advancement of Expenses for which Indemnitee has made written demand to the Company in accordance with this

Agreement, all Expenses included in such demand that are certified by affidavit of Indemnitee's counsel as being reasonable shall be presumed conclusively to be reasonable. Expenses, however, shall not include amounts paid in settlement by Indemnitee or the amount of judgments or fines against Indemnitee.

(g) "Independent Counsel" shall mean a law firm, or a member of a law firm, that is experienced in matters of corporation law and neither presently is, nor in the past five years has been, retained to represent: (i) the Company or Indemnitee in any matter material to either such party (other than with respect to matters concerning the Indemnitee under this Agreement, or of other indemnitees under similar indemnification agreements), or (ii) any other party to the Proceeding giving rise to a claim for indemnification hereunder. Notwithstanding the foregoing, the term "Independent Counsel" shall not include any person who, under the applicable standards of professional conduct then prevailing, would have a conflict of interest in representing either the Company or Indemnitee in an action to determine Indemnitee's rights under this Agreement. The Company agrees to pay the reasonable fees and expenses of the Independent Counsel referred to above and to fully indemnify such counsel against any and all Expenses, claims, liabilities and damages arising out of or relating to this Agreement or its engagement pursuant hereto.

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(h) The term "Proceeding" shall include any threatened, pending or completed action, suit, claim, counterclaim, cross claim, arbitration, mediation, alternate dispute resolution mechanism, investigation, inquiry, administrative hearing or any other actual, threatened or completed proceeding, whether brought in the right of the Company or otherwise and whether of a civil, criminal, administrative, legislative, or investigative (formal or informal) nature, including any appeal therefrom, in which Indemnitee was, is or will be involved as a party, potential party, non-party witness or otherwise by reason of the fact that Indemnitee is or was a director or officer of the Company, by reason of any action taken by him (or a failure to take action by him) or of any action (or failure to act) on his part while acting pursuant to his Corporate Status, in each case whether or not serving in such capacity at the time any liability or Expense is incurred for which indemnification, reimbursement, or advancement of Expenses can be provided under this Agreement. If the Indemnitee believes in good faith that a given situation may lead to or culminate in the institution of a Proceeding, this shall be considered a Proceeding under this paragraph.

(i) Reference to "other enterprise" shall include employee benefit plans; references to "fines" shall include any excise tax assessed with respect to any employee benefit plan; references to "serving at the request of the Company" shall include any service as a director, officer, employee or agent of the Company which imposes duties on, or involves services by, such director, officer, employee or agent with respect to an employee benefit plan, its participants or beneficiaries; and a person who acted in good faith and in a manner he reasonably believed to be in the best interests of the participants and beneficiaries of an employee benefit plan shall be deemed to have acted in manner "not opposed to the best interests of the Company" as referred to in this Agreement.

Section 3. Indemnity in Third-Party Proceedings. The Company shall indemnify Indemnitee in accordance with the provisions of this Section 3 if Indemnitee is, or is threatened to be made, a party to or a participant in any Proceeding, other than a Proceeding by or in the right of the Company to procure a judgment in its favor. Pursuant to this Section 3, Indemnitee shall be indemnified to the fullest extent permitted by applicable law against all Expenses, judgments, fines and amounts paid in settlement (including all interest, assessments and other charges paid or payable in connection with or in respect of such Expenses, judgments, fines and amounts paid in settlement) actually and reasonably incurred by Indemnitee or on his behalf in connection with such Proceeding or any claim, issue or matter therein, if Indemnitee acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the Company and, in the case of a criminal Proceeding had no reasonable cause to believe that his conduct was unlawful. The parties hereto intend that this Agreement shall provide to the fullest extent permitted by law for indemnification in excess of that expressly permitted by statute, including, without limitation, any indemnification provided by the Certificate of Incorporation, the By-laws, vote of its stockholders or disinterested directors or applicable law.

Section 4. Indemnity in Proceedings by or in the Right of the Company. The Company shall indemnify Indemnitee in accordance with the provisions of this Section 4 if Indemnitee is, or is threatened to be made, a party to or a participant in any Proceeding by or in the right of the Company to procure a judgment in its favor. Pursuant to this Section 4, Indemnitee shall be indemnified to the fullest extent permitted by applicable law against all Expenses actually and reasonably incurred by him or on his behalf in connection with such

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Proceeding or any claim, issue or matter therein, if Indemnitee acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the Company. No indemnification for Expenses shall be made under this Section 4 in respect of any claim, issue or matter as to which Indemnitee shall have been finally adjudged by a court to be liable to the Company, unless and only to the extent that the Delaware Court (as hereinafter defined) or any court in which the Proceeding was brought shall determine upon application that, despite the adjudication of liability but in view of all the circumstances of the case, Indemnitee is fairly and reasonably entitled to indemnification.

Section 5. Indemnification for Expenses of a Party Who is Wholly or Partly Successful. Notwithstanding any other provisions of this Agreement, to the fullest extent permitted by applicable law and to the extent that Indemnitee is a party to (or a participant in) and is successful, on the merits or otherwise, in any Proceeding or in defense of any claim, issue or matter therein, in whole or in part, the Company shall indemnify Indemnitee against all Expenses actually and reasonably incurred by him in connection therewith. If Indemnitee is not wholly successful in such Proceeding but is successful, on the merits or otherwise, as to one or more but less than all claims, issues or matters in such Proceeding, the Company shall indemnify Indemnitee against all Expenses actually and reasonably incurred by him or on his behalf in connection with or related to each successfully resolved claim, issue or matter to the fullest

extent permitted by law. For purposes of this Section and without limitation, the termination of any claim, issue or matter in such a Proceeding by dismissal, with or without prejudice, shall be deemed to be a successful result as to such claim, issue or matter.

Section 6. Indemnification For Expenses of a Witness. Notwithstanding any other provision of this Agreement, to the fullest extent permitted by applicable law and to the extent that Indemnitee is, by reason of his Corporate Status, a witness or otherwise asked to participate in any Proceeding to which Indemnitee is not a party, he shall be indemnified against all Expenses actually and reasonably incurred by him or on his behalf in connection therewith.

Section 7. Partial Indemnification. If Indemnitee is entitled under any provision of this Agreement to indemnification by the Company for some or a portion of Expenses, but not, however, for the total amount thereof, the Company shall nevertheless indemnify Indemnitee for the portion thereof to which Indemnitee is entitled.

Section 8. Additional Indemnification.

(a) Notwithstanding any limitation in Sections 3, 4, or 5, the Company shall indemnify Indemnitee to the fullest extent permitted by applicable law if Indemnitee is a party to or threatened to be made a party to any Proceeding (including a Proceeding by or in the right of the Company to procure a judgment in its favor) against all Expenses, judgments, fines and amounts paid in settlement (including all interest, assessments and other charges paid or payable in connection with or in respect of such Expenses, judgments, fines and amounts paid in settlement) actually and reasonably incurred by Indemnitee in connection with the Proceeding.

(b) For purposes of Section 8(a), the meaning of the phrase “to the fullest extent permitted by applicable law” shall include, but not be limited to:

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i. to the fullest extent permitted by the provision of the DGCL that authorizes or contemplates additional indemnification by agreement, or the corresponding provision of any amendment to or replacement of the DGCL, and

ii. to the fullest extent authorized or permitted by any amendments to or replacements of the DGCL adopted after the date of this Agreement that increase the extent to which a corporation may indemnify its officers and directors.

Section 9. Exclusions. Notwithstanding any provision in this Agreement, the Company shall not be obligated under this Agreement to make any indemnification payment in connection with any claim made against Indemnitee:

(a) for which payment has actually been made to or on behalf of Indemnitee under any insurance policy or other indemnity provision, except with respect to any excess beyond the amount paid under any insurance policy or other indemnity provision; or

(b) for (i) an accounting of profits made from the purchase and sale (or sale and purchase) by Indemnitee of securities of the Company within the meaning of Section 16(b) of the Exchange Act (as defined in Section 2(b) hereof) or similar provisions of state statutory law or common law, or (ii) any reimbursement of the Company by the Indemnitee of any bonus or other incentive-based or equity-based compensation or of any profits realized by the Indemnitee from the sale of securities of the Company, as required in each case under the Exchange Act (including any such reimbursements that arise from an accounting restatement of the Company pursuant to Section 304 of the Sarbanes-Oxley Act of 2002 (the “Sarbanes-Oxley Act”), or the payment to the Company of profits arising from the purchase and sale by Indemnitee of securities in violation of Section 306 of the Sarbanes-Oxley Act); or

(c) except as provided in Section 14(d) of this Agreement, in connection with any Proceeding (or any part of any Proceeding) initiated by Indemnitee, including any Proceeding (or any part of any Proceeding) initiated by Indemnitee against the Company or its directors, officers, employees or other indemnitees, unless (i) the Board authorized the Proceeding (or any part of any Proceeding) prior to its initiation or (ii) the Company provides the indemnification, in its sole discretion, pursuant to the powers vested in the Company under applicable law.

Section 10. Advances of Expenses. Notwithstanding any provision of this Agreement to the contrary (other than Section 14(d)), the Company shall advance, to the extent not prohibited by law, the Expenses incurred by Indemnitee in connection with any Proceeding (or any part of any Proceeding) not initiated by Indemnitee, and such advancement shall be made within thirty (30) days after the receipt by the Company of a statement or statements requesting such advances from time to time, whether prior to or after final disposition of any Proceeding. Advances shall be unsecured and interest free. Advances shall be made without regard to Indemnitee’s ability to repay the Expenses and without regard to Indemnitee’s ultimate entitlement to indemnification under the other provisions of this Agreement. In accordance with Section 14(d), advances shall include any and all reasonable Expenses incurred pursuing an action to enforce this right of advancement, including Expenses incurred preparing and forwarding statements to the Company to support the advances claimed. The Indemnitee shall

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qualify for advances upon the execution and delivery to the Company of this Agreement, which shall constitute an undertaking providing that the Indemnitee undertakes to repay the amounts advanced (without interest) to the extent that it is ultimately determined that Indemnitee is not entitled to be indemnified by the Company. No other form of undertaking shall be required other than the execution of this Agreement. This Section 10 shall not apply to any claim made by Indemnitee for which indemnity is excluded pursuant to Section 9.

Section 11. Procedure for Notification and Defense of Claim.

(a) Indemnitee shall notify the Company in writing of any matter with respect to which Indemnitee intends to seek indemnification or advancement of Expenses hereunder as soon as reasonably practicable following the receipt by Indemnitee of written notice thereof. The written notification to the Company shall include a description of the nature of the Proceeding and the facts underlying the Proceeding. To obtain indemnification under this Agreement, Indemnitee shall submit to the Company a written request, including therein or therewith such documentation and information as is reasonably available to Indemnitee and is reasonably necessary to determine whether and to what extent Indemnitee is entitled to indemnification following the final disposition of such Proceeding. The omission by Indemnitee to notify the Company hereunder will not relieve the Company from any liability which it may have to Indemnitee hereunder or otherwise than under this Agreement, and any delay in so notifying the Company shall not constitute a waiver by Indemnitee of any rights under this Agreement. The Secretary of the Company shall, promptly upon receipt of such a request for indemnification, advise the Board in writing that Indemnitee has requested indemnification.

(b) The Company will be entitled to participate in the Proceeding at its own expense.

Section 12. Procedure Upon Application for Indemnification.

(a) Upon written request by Indemnitee for indemnification pursuant to Section 11(a), a determination, if required by applicable law, with respect to Indemnitee's entitlement thereto shall be made in the specific case: (i) if a Change in Control shall have occurred, by Independent Counsel in a written opinion to the Board, a copy of which shall be delivered to Indemnitee; or (ii) if a Change in Control shall not have occurred, (A) by a majority vote of the Disinterested Directors, even though less than a quorum of the Board, (B) by a committee of Disinterested Directors designated by a majority vote of the Disinterested Directors, even though less than a quorum of the Board, (C) if there are no such Disinterested Directors or, if such Disinterested Directors so direct, by Independent Counsel in a written opinion to the Board, a copy of which shall be delivered to Indemnitee or (D) if so directed by the Board, by the stockholders of the Company; and, if it is so determined that Indemnitee is entitled to indemnification, payment to Indemnitee shall be made within ten (10) days after such determination. Indemnitee shall cooperate with the person, persons or entity making such determination with respect to Indemnitee's entitlement to indemnification, including providing to such person, persons or entity upon reasonable advance request any documentation or information which is not privileged or otherwise protected from disclosure and which is reasonably available to Indemnitee and reasonably necessary to such determination. Any costs or Expenses (including attorneys' fees and disbursements) incurred by Indemnitee in so

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cooperating with the person, persons or entity making such determination shall be borne by the Company (irrespective of the determination as to Indemnitee's entitlement to indemnification) and the Company hereby indemnifies and agrees to hold Indemnitee harmless therefrom. The Company promptly will advise Indemnitee in writing with respect to any determination that Indemnitee is or is not entitled to indemnification, including a description of any reason or basis for which indemnification has been denied.

(b) In the event the determination of entitlement to indemnification is to be made by Independent Counsel pursuant to Section 12(a) hereof, the Independent Counsel shall be selected as provided in this Section 12(b). If a Change in Control shall not have occurred, the Independent Counsel shall be selected by the Board, and the Company shall give written notice to Indemnitee advising him of the identity of the Independent Counsel so selected. If a Change in Control shall have occurred, the Independent Counsel shall be selected by Indemnitee (unless Indemnitee shall request that such selection be made by the Board, in which event the preceding sentence shall apply), and Indemnitee shall give written notice to the Company advising it of the identity of the Independent Counsel so selected. In either event, Indemnitee or the Company, as the case may be, may, within ten (10) days after such written notice of selection shall have been given, deliver to the Company or to Indemnitee, as the case may be, a written objection to such selection; provided, however, that such objection may be asserted only on the ground that the Independent Counsel so selected does not meet the requirements of "Independent Counsel" as defined in Section 2 of this Agreement, and the objection shall set forth with particularity the factual basis of such assertion. Absent a proper and timely objection, the person so selected shall act as Independent Counsel. If such written objection is so made and substantiated, the Independent Counsel so selected may not serve as Independent Counsel unless and until such objection is withdrawn or the Delaware Court has determined that such objection is without merit. If, within twenty (20) days after the later of submission by Indemnitee of a written request for indemnification pursuant to Section 11(a) hereof and the final disposition of the Proceeding, no Independent Counsel shall have been selected and not objected to, either the Company or Indemnitee may petition the Delaware Court for resolution of any objection which shall have been made by the Company or Indemnitee to the other's selection of Independent Counsel and/or for the appointment as Independent Counsel of a person selected by such court or by such other person as such court shall designate, and the person with respect to whom all objections are so resolved or the person so appointed shall act as Independent Counsel under Section 12(a) hereof. Upon the due commencement of any judicial proceeding or arbitration pursuant to Section 14(a) of this Agreement, Independent Counsel shall be discharged and relieved of any further responsibility in such capacity (subject to the applicable standards of professional conduct then prevailing).

Section 13. Presumptions and Effect of Certain Proceedings.

(a) In making a determination with respect to entitlement to indemnification hereunder, the person or persons or entity making such determination shall, to the fullest extent not prohibited by law, presume that Indemnitee is entitled to indemnification under this Agreement if Indemnitee has submitted a request for indemnification in accordance with Section 11(a) of this Agreement, and the Company shall, to the fullest extent not prohibited by law, have the burden of proof to overcome that presumption in connection with the making by any person, persons or entity of any determination contrary to that presumption. Neither the failure of the

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Company (including by its directors or Independent Counsel) to have made a determination prior to the commencement of any action pursuant to this Agreement that indemnification is proper in the circumstances because Indemnitee has met the applicable standard of conduct, nor an actual determination by the Company (including by its directors or Independent Counsel) that Indemnitee has not met such applicable standard of conduct, shall be a defense to the action or create a presumption that Indemnitee has not met the applicable standard of conduct.

(b) Subject to Section 14(e), if the person, persons or entity empowered or selected under Section 12 of this Agreement to determine whether Indemnitee is entitled to indemnification shall not have made a determination within sixty (60) days after receipt by the Company of the request therefor, the requisite determination of entitlement to indemnification shall, to the fullest extent not prohibited by law, be deemed to have been made and Indemnitee shall be entitled to such indemnification, absent (i) a misstatement by Indemnitee of a material fact, or an omission of a material fact necessary to make Indemnitee's statement not materially misleading, in connection with the request for indemnification, or (ii) a prohibition of such indemnification under applicable law; provided, however, that such 60-day period may be extended for a reasonable time, not to exceed an additional thirty (30) days, if the person, persons or entity making the determination with respect to entitlement to indemnification in good faith requires such additional time for the obtaining or evaluating of documentation and/or information relating thereto; and provided, further, that the foregoing provisions of this Section 13(b) shall not apply (i) if the determination of entitlement to indemnification is to be made by the stockholders pursuant to Section 12(a) of this Agreement and if (A) within fifteen (15) days after receipt by the Company of the request for such determination the Board has resolved to submit such determination to the stockholders for their consideration at an annual meeting thereof to be held within seventy-five (75) days after such receipt and such determination is made thereat, or (B) a special meeting of stockholders is called within fifteen (15) days after such receipt for the purpose of making such determination, such meeting is held for such purpose within sixty (60) days after having been so called and such determination is made thereat, or (ii) if the determination of entitlement to indemnification is to be made by Independent Counsel pursuant to Section 12(a) of this Agreement.

(c) The termination of any Proceeding or of any claim, issue or matter therein, by judgment, order, settlement or conviction, or upon a plea of nolo contendere or its equivalent, shall not (except as otherwise expressly provided in this Agreement) of itself adversely affect the right of Indemnitee to indemnification or create a presumption that Indemnitee did not act in good faith and in a manner which he reasonably believed to be in or not opposed to the best interests of the Company or, with respect to any criminal Proceeding, that Indemnitee had reasonable cause to believe that his conduct was unlawful.

(d) For purposes of any determination of good faith, Indemnitee shall be deemed to have acted in good faith if Indemnitee's action is based on the records or books of account of the Enterprise, including financial statements, or on information supplied to Indemnitee by the directors or officers of the Enterprise in the course of their duties, or on the advice of legal counsel for the Enterprise or on information or records given or reports made to the Enterprise by an independent certified public accountant or by an appraiser or other expert selected with the reasonable care by the Enterprise. The provisions of this Section 13(d) shall not be deemed to be exclusive or to limit in any way the other circumstances in which the

Indemnitee may be deemed to have met the applicable standard of conduct set forth in this Agreement.

(e) The knowledge and/or actions, or failure to act, of any director, officer, trustee, partner, managing member, fiduciary, agent or employee of the Enterprise shall not be imputed to Indemnitee for purposes of determining the right to indemnification under this Agreement.

Section 14. Remedies of Indemnitee.

(a) Subject to Section 14(e), in the event that (i) a determination is made pursuant to Section 12 of this Agreement that Indemnitee is not entitled to indemnification under this Agreement, (ii) advancement of Expenses is not timely made pursuant to Section 10 of this Agreement, (iii) no determination of entitlement to indemnification shall have been made pursuant to Section 12(a) of this Agreement within ninety (90) days after receipt by the Company of the request for indemnification, (iv) payment of indemnification is not made pursuant to Section 5, 6 or 7 or the last sentence of Section 12(a) of this Agreement within ten (10) days after receipt by the Company of a written request therefor, (v) payment of indemnification pursuant to Section 3, 4 or 8 of this Agreement is not made within ten (10) days after a determination has been made that Indemnitee is entitled to indemnification, or (vi) in the event that the Company or any other person takes or threatens to take any action to declare this Agreement void or unenforceable, or institutes any litigation or other action or Proceeding designed to deny, or to recover from, the Indemnitee the benefits provided or intended to be provided to the Indemnitee hereunder, Indemnitee shall be entitled to an adjudication by a court of his entitlement to such indemnification or advancement of Expenses. Alternatively, Indemnitee, at his option, may seek an award in arbitration to be conducted by a single arbitrator pursuant to the Commercial Arbitration Rules of the American Arbitration Association. Indemnitee shall commence such proceeding seeking an adjudication or an award in arbitration within 180 days following the date on which Indemnitee first has the right to commence such proceeding pursuant to this Section 14(a); provided, however, that the foregoing clause shall not apply in respect of a proceeding brought by Indemnitee to enforce his rights under Section 5 of this Agreement. The Company shall not oppose Indemnitee's right to seek any such adjudication or award in arbitration.

(b) In the event that a determination shall have been made pursuant to Section 12(a) of this Agreement that Indemnitee is not entitled to indemnification, any judicial proceeding or arbitration commenced pursuant to this Section 14 shall be conducted in all respects as a de novo trial, or arbitration, on the merits and Indemnitee shall not be prejudiced by reason of that adverse determination. In any judicial proceeding or arbitration commenced pursuant to this Section 14 the Company shall have the burden of proving Indemnitee is not entitled to indemnification or advancement of Expenses, as the case may be.

(c) If a determination shall have been made pursuant to Section 12(a) of this Agreement that Indemnitee is entitled to indemnification, the Company shall be bound by such determination in any judicial proceeding or arbitration commenced pursuant to this Section 14, absent (i) a misstatement by Indemnitee of a material fact, or an omission of a material fact

necessary to make Indemnitee's statement not materially misleading, in connection with the request for indemnification, or (ii) a prohibition of such indemnification under applicable law.

(d) The Company shall, to the fullest extent not prohibited by law, be precluded from asserting in any judicial proceeding or arbitration commenced pursuant to this Section 14 that the procedures and presumptions of this Agreement are not valid, binding and enforceable and shall stipulate in any such court or before any such arbitrator that the Company is bound by all the provisions of this Agreement. It is the intent of the Company that, to the fullest extent permitted by law, the Indemnitee not be required to incur legal fees or other Expenses associated with the interpretation, enforcement or defense of Indemnitee's rights under this Agreement by litigation or otherwise because the cost and expense thereof would substantially detract from the benefits intended to be extended to the Indemnitee hereunder. The Company shall, to the fullest extent permitted by law, indemnify Indemnitee against any and all Expenses and, if requested by Indemnitee, shall (within ten (10) days after receipt by the Company of a written request therefor) advance, to the extent not prohibited by law, such Expenses to Indemnitee, which are incurred by Indemnitee in connection with any action brought by Indemnitee for indemnification or advance of Expenses from the Company under this Agreement or under any directors' and officers' liability insurance policies maintained by the Company if, in the case of indemnification, Indemnitee is wholly successful on the underlying claims; if Indemnitee is not wholly successful on the underlying claims, then such indemnification shall be only to the extent Indemnitee is successful on such underlying claims or otherwise as permitted by law, whichever is greater.

(e) Notwithstanding anything in this Agreement to the contrary, no determination as to entitlement of Indemnitee to indemnification under this Agreement shall be required to be made prior to the final disposition of the Proceeding.

Section 15. Non-exclusivity; Survival of Rights; Insurance; Subrogation.

(a) The rights of indemnification and to receive advancement of Expenses as provided by this Agreement shall not be deemed exclusive of any other rights to which Indemnitee may at any time be entitled under applicable law, the Certificate of Incorporation, the By-laws, any agreement, a vote of stockholders or a resolution of directors, or otherwise. No amendment, alteration or repeal of this Agreement or of any provision hereof shall limit or restrict any right of Indemnitee under this Agreement in respect of any action taken or omitted by such Indemnitee in his Corporate Status prior to such amendment, alteration or repeal. To the extent that a change in Delaware law, whether by statute or judicial decision, permits greater indemnification or advancement of Expenses than would be afforded currently under the Certificate of Incorporation and this Agreement, it is the intent of the parties hereto that Indemnitee shall enjoy by this Agreement the greater benefits so afforded by such change. No right or remedy herein conferred is intended to be exclusive of any other right or remedy, and every other right and remedy shall be cumulative and in addition to every other right and remedy given hereunder or now or hereafter existing at law or in equity or otherwise. The assertion or employment of any right or remedy hereunder, or otherwise, shall not prevent the concurrent assertion or employment of any other right or remedy.

(b) To the extent that the Company maintains an insurance policy or policies providing liability insurance for directors, officers, employees, or agents of the Enterprise, Indemnitee shall be covered by such policy or policies in accordance with its or their terms to the maximum extent of the coverage available for any such director, officer, employee or agent under such policy or policies. If, at the time of the receipt of a notice of a claim pursuant to the terms hereof, the Company has director and officer liability insurance in effect, the Company shall give prompt notice of such claim or of the commencement of a Proceeding, as the case may be, to the insurers in accordance with the procedures set forth in the respective policies. The Company shall thereafter take all necessary or desirable action to cause such insurers to pay, on behalf of the Indemnitee, all amounts payable as a result of such Proceeding in accordance with the terms of such policies.

(c) In the event of any payment under this Agreement, the Company shall be subrogated to the extent of such payment to all of the rights of recovery of Indemnitee, who shall execute all papers required and take all action necessary to secure such rights, including execution of such documents as are necessary to enable the Company to bring suit to enforce such rights.

(d) The Company shall not be liable under this Agreement to make any payment of amounts otherwise indemnifiable (or for which advancement is provided hereunder) hereunder if and to the extent that Indemnitee has otherwise actually received such payment under any insurance policy, contract, agreement or otherwise.

(e) The Company's obligation to indemnify or advance Expenses hereunder to Indemnitee who is or was serving at the request of the Company as a director, officer, trustee, partner, managing member, fiduciary, employee or agent of any other corporation, limited liability company, partnership, joint venture, trust, employee benefit plan or other enterprise shall be reduced by any amount Indemnitee has actually received as indemnification or advancement of Expenses from such other corporation, limited liability company, partnership, joint venture, trust or other enterprise.

Section 16. Duration of Agreement. This Agreement shall continue until and terminate upon the later of: (a) ten (10) years after the date that Indemnitee shall have ceased to serve as a [director] [officer] of the Company or (b) one (1) year after the final

termination of any Proceeding then pending in respect of which Indemnitee is granted rights of indemnification or advancement of Expenses hereunder and of any proceeding commenced by Indemnitee pursuant to Section 14 of this Agreement relating thereto. The indemnification and advancement of expenses rights provided by or granted pursuant to this Agreement shall be binding upon and be enforceable by the parties hereto and their respective successors and assigns (including any direct or indirect successor by purchase, merger, consolidation or otherwise to all or substantially all of the business or assets of the Company), shall continue as to an Indemnitee who has ceased to be a director, officer, employee or agent of the Company or of any other Enterprise, and shall inure to the benefit of Indemnitee and his or her spouse, assigns, heirs, devisees, executors and administrators and other legal representatives.

Section 17. Severability. If any provision or provisions of this Agreement shall be held to be invalid, illegal or unenforceable for any reason whatsoever: (a) the validity, legality

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and enforceability of the remaining provisions of this Agreement (including without limitation, each portion of any Section of this Agreement containing any such provision held to be invalid, illegal or unenforceable, that is not itself invalid, illegal or unenforceable) shall not in any way be affected or impaired thereby and shall remain enforceable to the fullest extent permitted by law; (b) such provision or provisions shall be deemed reformed to the extent necessary to conform to applicable law and to give the maximum effect to the intent of the parties hereto; and (c) to the fullest extent possible, the provisions of this Agreement (including, without limitation, each portion of any Section of this Agreement containing any such provision held to be invalid, illegal or unenforceable, that is not itself invalid, illegal or unenforceable) shall be construed so as to give effect to the intent manifested thereby.

Section 18. Enforcement.

(a) The Company expressly confirms and agrees that it has entered into this Agreement and assumed the obligations imposed on it hereby in order to induce Indemnitee to serve as a director or officer of the Company, and the Company acknowledges that Indemnitee is relying upon this Agreement in serving as a director or officer of the Company.

(b) This Agreement constitutes the entire agreement between the parties hereto with respect to the subject matter hereof and supersedes and replaces all prior agreements and understandings, oral, written and implied, between the parties hereto with respect to the subject matter hereof, including any indemnification agreement previously entered into between the Company and the Indemnitee; provided, however, that this Agreement is a supplement to and in furtherance of the Certificate of Incorporation, the By-laws and applicable law, and shall not be deemed a substitute therefor, nor to diminish or abrogate any rights of Indemnitee thereunder.

Section 19. Modification and Waiver. No supplement, modification or amendment of this Agreement shall be binding unless executed in writing by the parties hereto. No waiver of any of the provisions of this Agreement shall be deemed or shall constitute a waiver of any other provisions of this Agreement nor shall any waiver constitute a continuing waiver.

Section 20. Notice by Indemnitee. Indemnitee agrees promptly to notify the Company in writing upon being served with any summons, citation, subpoena, complaint, indictment, information or other document relating to any Proceeding or matter which may be subject to indemnification or advancement of Expenses covered hereunder. The failure of Indemnitee to so notify the Company shall not relieve the Company of any obligation which it may have to the Indemnitee under this Agreement or otherwise.

Section 21. Notices. All notices, requests, demands and other communications under this Agreement shall be in writing and shall be deemed to have been duly given if (a) delivered by hand and receipted for by the party to whom said notice or other communication shall have been directed, (b) mailed by certified or registered mail with postage prepaid, on the third business day after the date on which it is so mailed, (c) mailed by reputable overnight courier and receipted for by the party to whom said notice or other communication shall have been directed or (d) sent by facsimile transmission, with receipt of oral confirmation that such transmission has been received:

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(a) If to Indemnitee, at the address indicated on the signature page of this Agreement, or such other address as Indemnitee shall provide to the Company.

(b) If to the Company to

Syros Pharmaceuticals, Inc.
620 Memorial Drive, Suite 300
Cambridge, MA 02139

or to any other address as may have been furnished to Indemnitee by the Company.

Section 22. Contribution. To the fullest extent permissible under applicable law, if the indemnification provided for in this Agreement is unavailable to Indemnitee for any reason whatsoever, the Company, in lieu of indemnifying Indemnitee, shall contribute to the amount incurred by Indemnitee, whether for judgments, fines, penalties, excise taxes, amounts paid or to be paid in settlement and/or for Expenses, in connection with any claim relating to an indemnifiable event under this Agreement, in such proportion as is deemed fair and reasonable in light of all of the circumstances of such Proceeding in order to reflect (i) the relative benefits received by the Company and Indemnitee as a result of the event(s) and/or transaction(s) giving cause to such Proceeding; and/or (ii) the relative fault of the

Company (and its directors, officers, employees and agents) and Indemnitee in connection with such event(s) and/or transaction(s).

Section 23. Applicable Law and Consent to Jurisdiction. This Agreement and the legal relations among the parties shall be governed by, and construed and enforced in accordance with, the laws of the State of Delaware, without regard to its conflict of laws rules. Except with respect to any arbitration commenced by Indemnitee pursuant to Section 14(a) of this Agreement, the Company and Indemnitee hereby irrevocably and unconditionally (i) agree that any action or proceeding arising out of or in connection with this Agreement shall be brought only in the Chancery Court of the State of Delaware (the "Delaware Court"), and not in any other state or federal court in the United States of America or any court in any other country, (ii) consent to submit to the exclusive jurisdiction of the Delaware Court for purposes of any action or proceeding arising out of or in connection with this Agreement, (iii) appoint, to the extent such party is not otherwise subject to service of process in the State of Delaware, irrevocably RL&F Service Corp., 920 North King Street, 2nd Floor, Wilmington, New Castle County, Delaware 19801 as its agent in the State of Delaware as such party's agent for acceptance of legal process in connection with any such action or proceeding against such party with the same legal force and validity as if served upon such party personally within the State of Delaware, (iv) waive any objection to the laying of venue of any such action or proceeding in the Delaware Court, and (v) waive, and agree not to plead or to make, any claim that any such action or proceeding brought in the Delaware Court has been brought in an improper or inconvenient forum.

Section 24. Identical Counterparts. This Agreement may be executed in one or more counterparts, each of which shall for all purposes be deemed to be an original but all of which together shall constitute one and the same Agreement. Only one such counterpart signed by the party against whom enforceability is sought needs to be produced to evidence the existence of this Agreement.

Section 25. Miscellaneous. Use of the masculine pronoun shall be deemed to include usage of the feminine pronoun where appropriate. The headings of this Agreement are inserted for convenience only and shall not be deemed to constitute part of this Agreement or to affect the construction thereof.

IN WITNESS WHEREOF, the parties have caused this Agreement to be signed as of the day and year first above written.

SYROS PHARMACEUTICALS, INC.

INDEMNITEE

By: _____
Name: _____
Title: _____

Name: _____
Address: _____

