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

Form 10-K

(Mark One)

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

For the fiscal year ended December 31, 2017

OR

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

For the transition period from to

Commission file number 001-37813

SYROS PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in Its Charter)

Delaware	**45-3772460**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
620 Memorial Drive, Suite 300 **Cambridge, Massachusetts**	**02139**
(Address of principal executive offices)	(Zip code)

(617) 744-1340
(Registrant's telephone number, including area code)

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

Title of Class	Name of Exchange on Which Registered
Common Stock, $0.001 par value	**Nasdaq Global Select Market**

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

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☑

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☑

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

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☑ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of the registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☑

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, 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. (Check one):

Large accelerated filer	☐	Accelerated filer	☑
Non-accelerated filer	☐	Smaller reporting company	☐
(Do not check if a smaller reporting company)		Emerging growth company	☑

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

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☑

As of June 30, 2017, the last business day of the registrant's most recently completed second fiscal quarter, the aggregate market value of the registrant's common stock held by non-affiliates was $289,542,157, based on the last reported sale price of such stock on the Nasdaq Global Select Market as of such date.

Portions of the registrant's definitive proxy statement for its 2018 Annual Meeting of Stockholders, which the registrant intends to file pursuant to Regulation 14A with the Securities and Exchange Commission not later than 120 days after the registrant's fiscal year ended December 31, 2017, are incorporated by reference into Items 10, 11, 12, 13 and 14 of Part III of this Annual Report on Form 10-K.As of February 28, 2018, the registrant had 32,193,961 shares of Common Stock, $0.001 par value per share, outstanding.

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Cautionary Note Regarding Forward-Looking Statements and Industry Data

This Annual Report on Form 10-K, or Annual Report, contains forward-looking statements that involve substantial risks and uncertainties. The forward-looking statements are contained principally in the sections of this Annual Report entitled "Business," "Risk Factors," and "Management's Discussion and Analysis of Financial Condition and Results of Operations," but are also contained in other sections of this Annual Report. All statements, other than statements of historical facts, contained in this Annual Report, 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 Annual Report are based upon information available to us as of the date of this Annual Report 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, expand and/or report data from our clinical trials for SY-1425 and SY-1365;
- 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, manufacture and commercialize our current and future product candidates;
- our plans to develop and seek approval of companion diagnostic tests for use in identifying patients who may benefit from treatment with our products and product candidates;
- our expectations regarding the potential benefits of our gene control platform and our approach;
- our ability to enter into, and the terms and timing of, any collaborations, license agreements, or other arrangements;
- whether our collaboration with Incyte Corporation, or Incyte, will yield any validated targets, whether Incyte will exercise any of its options to exclusively license intellectual property directed to such targets, and whether and when any of the target validation fees, option exercise fees, milestone payments or royalties under the Incyte collaboration will ever be paid;
- 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 our current cash, cash equivalents and marketable securities and the period of time in which such capital will be sufficient to fund our planned operations;

- 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 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 Annual Report. We have included important factors in the cautionary statements included in this Annual Report, particularly in the "Risk Factors" section, that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, collaborations, joint ventures or investments that we may make or enter into.

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

This Annual Report also 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 Annual Report 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 "Risk Factors" section. These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us.

PART I

Item 1. BUSINESS

Overview

We are a biopharmaceutical company pioneering an understanding of the non-coding regulatory region of the genome controlling the activation and repression of genes. Our goal is to advance a new wave of medicines to control the expression of genes. We have built a proprietary gene control platform designed to systematically and efficiently analyze this unexploited region of DNA in human disease tissue to identify novel targets linked to genomically defined patient populations and to develop drugs against those targets based on our expertise in transcriptional chemistry. Because gene expression is fundamental to the function of all cells, we believe that our gene control platform has broad potential to create medicines that achieve profound and durable benefit across therapeutic areas and a range of diseases. We are currently focused on developing treatments for cancer and diseases resulting from modifications of a single gene, also known as monogenic diseases, and are building a pipeline of gene control medicines.

Our lead product candidates are:

- SY-1425, a selective retinoic acid receptor alpha, or RARα, agonist that is being evaluated in combination with azacitidine, a hypomethylating agent frequently used to treat acute myeloid leukemia, or AML, and myelodysplastic syndrome, or MDS, patients, and with daratumumab, an anti-CD38 therapeutic antibody approved to treat multiple myeloma, in a Phase 2 clinical trial in genomically defined subsets of patients with AML and MDS; and

- SY-1365, a selective inhibitor of cyclin-dependent kinase 7, or CDK7, in a Phase 1 clinical trial in patients with advanced solid tumors for which expansions in ovarian and breast cancer are planned.

We also have multiple programs in earlier stages of research and development in oncology, including immuno-oncology, and monogenic diseases. Our goal is to build a fully integrated biopharmaceutical company based on our leadership position in gene control.

At the 59th American Society of Hematology Annual Meeting and Exposition in December 2017, or ASH 2017, we presented clinical data from our Phase 2 clinical trial evaluating SY-1425 as a single agent in defined subsets of AML and MDS patients with our proprietary *RARA* and *IRF8* biomarkers. In the trial, we observed that chronic daily dosing of SY-1425 administered at 6 mg/m^2 orally divided in two doses was generally well-tolerated and that clinical and biological activity was observed in patients enrolled in the trial. Specifically, clinical activity was observed in ten of 23 (43%) evaluable patients with relapsed or refractory AML and higher-risk MDS, including improvement in blood counts, reduction in leukemic blasts and one bone marrow complete response. Thirteen of the 23 (57%) evaluable relapsed or refractory AML and higher-risk MDS patients had stable disease. Myeloid differentiation was also observed in the bone marrow, consistent with the underlying mechanism of action of SY-1425 as a differentiating agent. Induction of CD38, a marker of cell differentiation, was observed after one 28-day cycle of treatment in 11 of 13 (85%) patients with pre- and post-treatment immunophenotyping samples.

We believe that these clinical data, when combined with preclinical data showing the tumor-killing activity of SY-1425 in combination with azacitidine and with daratumumab, support the ongoing development of SY-1425 as a combination agent. SY-1425 has shown synergistic tumor-killing activity in combination with azacitidine as well as with daratumumab in preclinical models of *RARA* biomarker-positive AML. In combination with azacitidine, SY-1425 demonstrated greater clearance of tumor cells in bone marrow and other tissues and greater depth and duration of tumor response in preclinical models, compared to either azacitidine or SY-1425 alone. In combination with daratumumab, SY-1425 induced robust immune cell-mediated tumor death *in vitro*. Notably, AML cells do not normally express high levels of CD38. We have shown that by inducing CD38 expression, SY-1425 sensitizes biomarker-positive AML models to the tumor-killing effects of daratumumab.

Our ongoing Phase 2 clinical trial is assessing the safety and efficacy of SY-1425 in combination with azacitidine in approximately 25 newly diagnosed AML patients who are not suitable candidates for standard chemotherapy, and in combination with daratumumab in approximately 12 relapsed or refractory AML and higher-risk MDS patients. All patients enrolled or to be enrolled in the trial have been or will be prospectively selected using our

proprietary *RARA* or *IRF8* biomarkers. In December 2017, we entered into a clinical supply agreement with Janssen Research and Development, LLC, or Janssen, pursuant to which Janssen agreed to supply us daratumumab for use in the trial. We are no longer enrolling patients in the cohorts of the trial in which SY-1425 was being evaluated as a single agent. We expect to report initial clinical data from the combination cohorts of the trial in the fourth quarter of 2018.

We are continuing to dose patients in the dose-escalation phase of our ongoing Phase 1 clinical trial of SY-1365 and expect to report data from this phase of the trial in the fourth quarter of 2018. Once a maximum tolerated dose is reached in the dose escalation phase of the Phase 1 clinical trial and the recommended dosing schedule is identified, we intend to open expansion cohorts evaluating SY-1365 in multiple ovarian cancer populations as a single agent as well as in combination with carboplatin, a chemotherapeutic agent. The ovarian cancer populations include a 24-patient cohort evaluating SY-1365 as a single agent in patients who have relapsed after three or more prior therapies, a 24-patient cohort evaluating SY-1365 in combination with carboplatin in patients who relapsed after one or more prior therapies but who may still benefit from additional platinum-based treatment, and a 12-patient pilot cohort evaluating SY-1365 as a single agent in primary platinum-refractory disease. We also plan to evaluate SY-1365 in combination with fulvestrant, a hormonal medicine, in 12 patients with hormone-receptor positive, or HR+, HER-2-negative metastatic breast cancer who have progressed after treatment with a CDK4/6 inhibitor plus an aromatase inhibitor. In addition, we plan to evaluate the mechanism of action of SY-1365 in ten patients with any solid tumor accessible for biopsies. We expect that the expansion cohorts in our Phase 1 clinical trial will be open to enrollment in mid-2018.

We currently have five programs in our preclinical and discovery pipeline, including preclinical programs directed to the development of a novel CDK7 inhibitor that can be administered orally, inhibitors of cyclin-dependent kinase 12/13, and inhibitors of an immuno-oncology target, as well as discovery programs related to a gene control target to treat sickle cell disease and in the field of cancer. We plan to nominate a development candidate from one of our preclinical programs during 2018 that we can advance into studies to support a potential investigational new drug application, or IND, filing in 2019. We have and are continuing to use our gene control platform in collaboration with third parties to identify and validate targets in diseases beyond our current areas of focus. To this end, we entered a target discovery, research collaboration and option agreement with Incyte Corporation, or Incyte, in January 2018 under which we will use our platform to identify novel therapeutic targets with a focus on myeloproliferative neoplasms. See "— License and Collaboration Agreements – Incyte" below.

Our Focus—Gene Control Medicines

There are approximately 200 different cell types in the human body. 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. What determines cell type and function is the specific set of genes that is expressed, or turned "on" or "off," in that given cell. This coordinated activation and repression of genes, known as the cell's gene expression program, is controlled in part by a number of cellular components acting on non-coding regions of the genome. These components include transcription factors, transcriptional kinases, other transcriptional and regulatory proteins, and RNA. These transcriptional and regulatory proteins bind with specific regions of non-coding DNA, including a specific category called enhancers, to control the rate and magnitude of gene transcription.

In some diseases, alterations in the physical state or function of the non-coding regions of the genome can change a cell's gene expression program, altering the type and function of that cell. Because the altered gene expression program is implemented by transcription factors, transcriptional kinases, other transcriptional and regulatory proteins, and RNA, these proteins and RNA can be important points for therapeutic intervention. Because this biology is fundamental to the function of all cells, it applies across diseases, whether the cause is genetic, environmental, bacterial, viral or multi-factorial.

Although researchers have long believed that alterations in non-coding regions of DNA, which account for 98% of the genome, play a key role in driving disease, the scientific community has lacked the tools to study these regions of the genome, rendering them poorly understood. As a result, the discovery and development of targeted therapies to date has focused almost exclusively on abnormal proteins resulting from genetic alterations found in regions of DNA that encode for proteins, which represent less than 2% of the entire genome.

While targeted therapies, in which the right drug is matched to the right patient, have dramatically improved the ability to treat certain cancers and other serious diseases, the opportunity to identify new drug targets by sequencing coding regions of DNA is limited, particularly in cancer. Moreover, in cancer, the clinical benefit from inhibiting

abnormal proteins resulting from single genetic alterations is often short-lived due to drug resistance. Furthermore, many serious diseases continue to go unaddressed due to the limitations of current drug discovery approaches. Taken together, these factors underscore the need for fundamentally new approaches to drug discovery and development.

Gene control medicines are intended to modulate the cell's underlying gene expression program, influencing the expression of the crucial set of genes that are associated with disease. The relatively few gene control medicines available today are among the most important targeted therapies and are widely used for their approved indications. Drugs that target transcription factors, such as those which target the estrogen receptor in breast cancer, androgen receptor in prostate cancer and glucocorticoid receptor 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, illustrating the significant therapeutic potential of gene control medicines. However, the difficulty in studying non-coding regions of the genome historically prevented a systematic approach to identifying these critical points of intervention, making gene control a largely untapped field for targeted drug discovery and development.

Based on the work of Syros' scientific founders Richard A. Young, Ph.D., James Bradner, M.D. and Nathanael Gray, Ph.D., and other scientists, there is now a rapidly growing scientific understanding of how alterations in non-coding regions of the genome drive disease and how to modulate gene control targets. One of the seminal discoveries that pushed the field forward came out of Dr. Young's laboratory at the Whitehead Institute for Biomedical Research, or Whitehead. He discovered that a very small unique subset of enhancers, called super-enhancers, are central to orchestrating gene expression programs. These highly specialized regulatory regions of non-coding DNA bring together the cellular components needed for gene expression, assembling large amounts of transcription factors, transcriptional kinases and other transcriptional and regulatory proteins to drive increased expression of genes crucial to a given cell's type and function.

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 that are implicated in cancer, such as *MYC*, are associated with super-enhancers. Notably, analysis of super-enhancers and their associated genes allows us to rapidly and systematically elucidate gene expression programs, pinpointing the genes crucial to the function of a given cell and providing critical insights into changes in gene expression programs that contribute to disease.

These and other discoveries from our scientific founders, coupled with technological advancements, have enabled our pioneering approach to therapeutic gene control. We believe we have built the first proprietary platform designed to systematically and efficiently analyze non-coding regions of the genome in healthy and diseased cells taken from patient tissues to identify alterations in gene expression programs that represent optimal points of therapeutic intervention and develop drugs to control the expression of disease-driving genes. By doing so, we believe our gene control platform will allow us to (i) identify a wide array of potential new drug targets across a range of diseases, (ii) provide a new lens for diagnosing and segmenting patients, including those with complex, multi-factorial diseases that have eluded segmentation with other genomic-based approaches, and (iii) advance a new wave of medicines that have the potential to influence multiple drivers of disease through a single target, making them less susceptible to drug resistance and providing patients with a more profound and durable benefit than many of today's targeted therapies.

Our Gene Control Platform

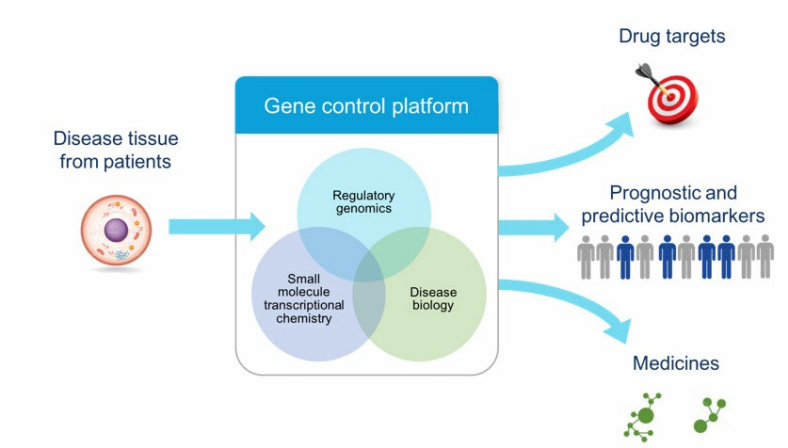
Our proprietary gene control platform consists of two fundamental pillars:

- *Identifying gene control targets that, when modulated with a drug, may provide a therapeutic benefit to a defined patient population.* We analyze gene expression programs and the non-coding regions of the genome associated with those expression programs in diseased and healthy cells taken from patient tissues to identify points of therapeutic intervention and associated biomarkers in specific patient populations.

- *Drugging gene control targets.* We develop product candidates to modulate gene control targets through:

    - internal drug discovery efforts focused on creating small molecule 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 starting points for our own drug discovery programs to accelerate our development path, as we did with SY-1425.



Identifying Novel Gene Control Targets

Our long-term goal is to analyze gene expression programs in serious diseases where we believe currently underserved patients can benefit from gene control medicines. We have invested significant resources in building capabilities to discover novel gene control targets and associated biomarkers. Our approach is disease-focused. Our platform consists of technologies and capabilities to analyze gene expression programs directly from patient tissue samples. We do this by employing our expertise and technologies in computational, gene control and cellular biology. We have in-licensed intellectual property from the laboratories of our scientific founders at Whitehead and the Dana-Farber Cancer Institute, Inc., or 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 expression programs using small amounts of patient tissue. These advancements have enabled us to generate a substantial dataset of gene expression programs and to identify targets across many diseases and cell types. Through those efforts, we have identified drug targets in oncology, immuno-oncology, immunology and monogenic diseases, and have validated several of these targets using biological methods to ablate, or knock out, the target gene or chemical methods to modulate the target's activity. The discovery and validation of these targets has led to the identification of our product candidates SY-1425 and SY-1365 as well as additional novel product candidates in earlier stages of research and preclinical development. We plan to analyze gene expression programs in other cancers, and to collaborate with third parties such as Incyte to identify and validate targets in diseases beyond our current areas of focus.

In some diseases, particularly monogenic diseases, research has revealed that a therapeutic benefit might be possible from modulating expression of a single gene. Another application of our platform is to characterize the regulatory region associated with such a gene and identify protein or RNA components that could be modulated to alter the expression of that single gene. We are applying this approach to sickle cell disease based on the hypothesis that increased expression of the fetal hemoglobin gene in individuals with sickle cell disease could be therapeutically beneficial.

Validation of Our Approach

We have validated our approach by successfully linking known targets of successful, marketed drugs to super-enhancers in human disease tissue. Additionally, using our platform, we have identified super-enhancers associated with genes linked to the hallmarks of a number of serious diseases.

During 2017, we presented data generated by our scientists in collaboration with researchers at Whitehead in which we analyzed regulatory regions of the genome in cancer stem cell enriched triple-negative breast cancer, or TNBC, cell lines. Cancer stem cells, or CSCs, are known to be involved in resistance to chemotherapies, relapse of disease and development of metastasis. The analysis revealed key genes that may be involved in driving disease relapse and metastasis, with implications for the discovery and development of novel therapies for TNBC. Notably, *TP73*, a gene that encodes a DNA-binding transcription factor called p73, was found to be a core driver of transcriptional circuitry in CSCs, controlling super-enhancer associated genes involved in cell migration, signal transduction and developmental processes. The set of *TP73*-controlled genes provide new leads for drug discovery and development with potential to yield much-needed new therapies for TNBC patients.

We also presented data during 2017 from our collaboration with the University of California, San Diego, in which our platform was used to analyze and compare super-enhancers in cells from pancreatic cancer patient tumors to those in cells from normal pancreatic tissues. These data showed that the leukemia inhibitory factor, or *LIF*, gene demonstrated one of the most significant changes in enhancer size from pancreatic tumors in comparison to normal pancreatic tissue. In preclinical mouse models, *LIF* enhanced the anti-tumor activity of chemotherapy and produced a survival benefit when inhibited using a monoclonal antibody.

Finally, we presented data in the last year showing alterations in regulatory regions of the genome in T cells from patients with systemic lupus erythematosus, or SLE, revealing genes critical for activating T cells and driving disease. Specifically, we found that genes regulated by activation of the *SYK* kinase and *IRF4* transcription factor are significantly enriched in SLE naïve and memory T cells, suggesting that they are key drivers of T cell activation in SLE and a core part of the transcriptional regulatory circuitry driving the disease. These findings provide biological insights into the autoimmune response in lupus that could lead to the identification of novel drug targets and therapeutic approaches to treat SLE.

Drugging Gene Control Targets

We develop product candidates against gene control targets through:

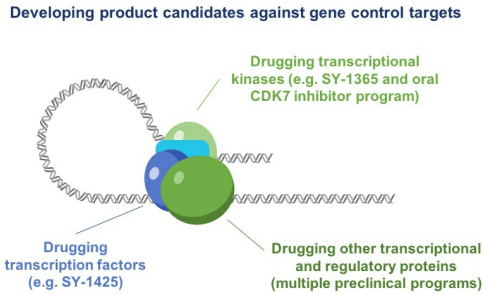
- internal drug discovery efforts focused on creating small molecule drugs targeting transcription factors, transcriptional kinases and other transcriptional and regulatory proteins; and

- linking existing drugs, which we could in-license, to specific patient populations identified through our platform—a strategy we implemented by in-licensing SY-1425 to accelerate our clinical development path.

We have developed significant core internal capabilities in small molecule chemistry, biochemistry and structural biology to characterize the structure and function of transcription factors such as nuclear hormone receptors, transcriptional kinases, chromatin regulators, and other transcriptional and regulatory proteins in order to generate novel chemical matter. We have also developed a sophisticated suite of proprietary assays, which are internally developed tests to measure the biochemical, biophysical, cellular and genomic activity of known and novel compounds against gene control targets.

While our platform is designed to identify drug targets across a broad range of therapeutic areas and therapeutic modalities, our drug discovery and development efforts are focused on small molecule drugs to target specialized proteins responsible for gene expression, including transcription factors, transcriptional kinases and other transcriptional and regulatory proteins. Because these specialized proteins play a central role in implementing gene expression

programs, they are among the most promising and high potential gene control targets for therapeutic intervention. The graphic below illustrates our areas of focus for development of product candidates.



Drugging Transcriptional Kinases

SY-1365 demonstrates 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 have the most advanced inhibitor of CDK7 in clinical development.

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. We are using our capabilities and expertise in structure-based drug design and medicinal chemistry to identify small molecules that that interact with transcription factors.

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 identify in human disease tissue. To date, we have identified multiple drug and enhancer relationships, the most advanced leading to the identification of SY-1425. This program exemplifies the general approach of using our platform to identify compounds that could accelerate our clinical development path.

Our Clinical Programs

SY-1425

Overview

SY-1425 (tamibarotene) is an oral, potent and selective agonist of the transcription factor RARα. In September 2015, we in-licensed from TMRC Co., Ltd., or TMRC, the exclusive right to use intellectual property and data rights controlled by TMRC to develop and commercialize SY-1425 for oncology indications in North America and Europe. We are currently conducting a Phase 2 clinical trial assessing the safety and efficacy of SY-1425 in combination with azacitidine, a hypomethylating agent frequently used to treat patients with AML and MDS, in approximately 25 newly diagnosed AML patients who are not suitable candidates for standard chemotherapy, and in combination with daratumumab, an anti-CD38 therapeutic antibody approved to treat multiple myeloma, in approximately 12 relapsed or refractory AML and higher-risk MDS patients. All patients enrolled or to be enrolled in the trial have been or will be prospectively selected using our proprietary *RARA* or *IRF8* biomarkers. We expect to report initial clinical data from the combination cohorts of the trial in the fourth quarter of 2018.

Linking SY-1425 to Novel Patient Populations

We leveraged our platform to analyze gene expression programs in primary AML and breast cancer patient tissue samples. We discovered that *RARA*, the gene that codes for RARα, was associated with a super-enhancer in some patients' tumors but not in others. A super-enhancer is a highly specialized region of non-coding DNA central to orchestrating gene expression programs and driving increased expression of genes crucial to the function of a given cell. The function of RARα differs depending on whether it is bound to its ligand. In the absence of a ligand, RARα represses differentiation. We believe that in tumors with the *RARA*-associated super-enhancer, there is an abundance of unliganded RARα, resulting in the repression of differentiation, thereby locking the cell in an immature, proliferative and undifferentiated state. Introducing a RARα agonist, such as SY-1425, simulates the activity of a ligand, activating differentiation.

In collaboration with researchers at Stanford University School of Medicine, we published data in the journal *Cancer Discovery* during 2017 where we used our gene control platform to analyze 66 AML patients' tumor samples and identified six distinct patient subsets based on super-enhancer profiles. The data showed that:

- super-enhancer profiles were strongly associated with survival outcomes, often independent of known genetic mutations in AML;
- the *RARA* super-enhancer was associated with high expression of the *RARA* gene, which codes for the RARα transcription factor;
- *RARA* pathway activation was predictive of response to SY-1425 as demonstrated by reduced proliferation and increased differentiation in AML cells with high *RARA* expression. Moreover, SY-1425 decreased tumor burden and prolonged survival in mouse models in which the mice are implanted with human tumors, which are referred to as patient-derived xenograft models, or PDX models, of AML with high *RARA* expression, while no effect was found on AML cells or PDX models with low *RARA* expression;
- all trans retinoic acid, or ATRA, a less potent and non-selective retinoid, produced no survival benefit in PDX models with high *RARA* expression; and
- SY-1425 induced significant transcriptional changes promoting cell differentiation in AML cells with high *RARA* expression, but little to no transcriptional changes in AML cells with low *RARA* expression.

SY-1425 Development Plan

We plan to develop SY-1425 in North America and Europe for treatment of AML and MDS in genomically defined subsets of patients with either the *RARA* or *IRF8* biomarker, or both. In September 2016, we initiated a multi-center, open-label Phase 2 clinical trial enrolling genomically-defined subsets of patients with AML and MDS pursuant to an IND accepted by the U.S. Food and Drug Administration, or FDA, in May 2016. In the fourth quarter of 2016, an investigational device exemption for the assay being used to select patients with the *RARA* and *IRF8* biomarkers for inclusion in this trial was approved by the FDA. In this trial, we have explored the safety and efficacy of SY-1425 as a single agent, and are continuing to explore the safety and efficacy of SY-1425 in combination with other approved and investigational agents, in the following patient cohorts:

- Single-agent SY-1425 in approximately 25 patients with relapsed or refractory AML or relapsed higher-risk MDS;
- Single-agent SY-1425 in approximately 25 newly-diagnosed AML patients who are not suitable candidates for standard chemotherapy;
- Single-agent SY-1425 in approximately 25 patients with lower-risk, transfusion-dependent MDS;
- SY-1425 in combination with azacitidine in approximately 25 newly-diagnosed AML patients who are not suitable candidates for standard chemotherapy; and

- SY-1425 in combination with daratumumab in approximately 12 patients with relapsed or refractory AML or relapsed higher-risk MDS.

All patients enrolled or to be enrolled in the trial are prospectively selected using our proprietary *RARA* or *IRF8* biomarkers. At the European School of Hematology's 4th International Conference on AML in October 2017, or ESH, we presented data from 201 evaluable patients screened in our ongoing Phase 2 clinical trial demonstrating that approximately 40% of patients were positive for either the *RARA* or *IRF8* biomarker, or both, and that approximately one-third of the relapsed or refractory AML and higher-risk MDS patients tested were biomarker positive.

Tamibarotene, the active pharmaceutical ingredient of SY-1425, has been extensively studied and has a well-established safety profile. In our Phase 2 clinical trial, we are using the same dosage used in the treatment of acute promyelocytic leukemia, or APL, in Japan. 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 exclusively in-licensed from TMRC certain intellectual property rights controlled by TMRC and the preclinical data package that was used for approval in Japan and the IND filing in the United States for use in all cancer indications in North America and Europe.

At ASH 2017, we presented clinical data from our Phase 2 clinical trial evaluating SY-1425 as a single agent in 29 patients with relapsed or refractory AML or relapsed higher-risk MDS, and in 29 patients with lower-risk transfusion-dependent MDS. The median age of patients in the relapsed or refractory and higher-risk AML cohort was 72, with more than half of the patients having poor risk cytogenetics and 45% having two or more prior therapies. The median age of patients in the lower-risk MDS cohort was 76. In the trial, we observed that chronic daily dosing of SY-1425 administered at 6 mg/m^2 orally divided in two doses was generally well-tolerated, with a median treatment duration of 80 days and patients treated up to eight months and remaining on study. The majority of adverse events observed in the trial were low grade, with the most commonly-reported adverse events across all grades and causality being elevated triglycerides (36%), fatigue (31%), and dermatologic effects (28%). The most common Grade 3 or 4 adverse event was elevated triglycerides (16%).

At the time of the data cut-off for presenting data at ASH 2017, 48 patients were evaluable for response assessment, including 23 patients in the relapsed or refractory AML or relapsed higher-risk MDS cohort and 25 patients in the lower-risk transfusion-dependent MDS cohort. Clinical activity was observed in ten of 23 (43%) evaluable patients with relapsed or refractory AML and higher-risk MDS, and two of the 25 (8%) evaluable lower-risk MDS patients, including:

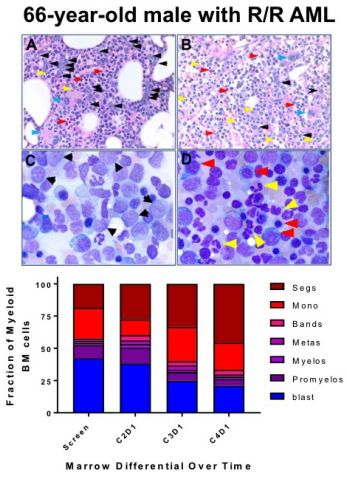
- Nine patients with improvements in hematologic parameters, four of whom achieved hematologic improvement lasting at least eight weeks, as defined by the Revised International Working Group, or IWG, criteria;

- Five patients with reductions in bone marrow blasts, with one relapsed or refractory higher-risk MDS patient achieving a marrow complete response as defined by IWG criteria;

- Thirteen of the 23 (57%) evaluable relapsed or refractory AML and higher-risk MDS patients had stable disease; and

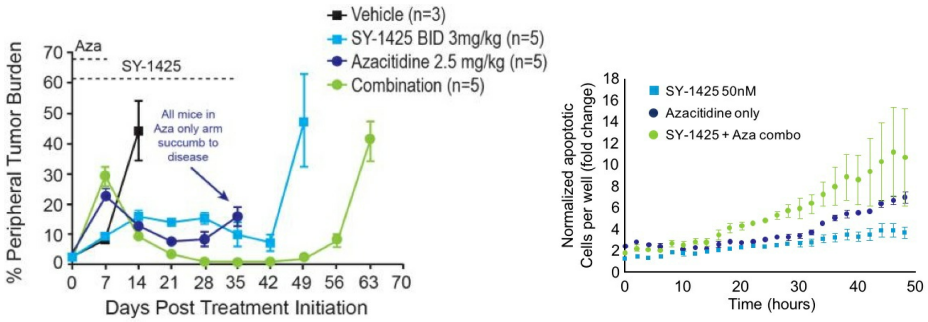
- No patients with lower-risk MDS achieved transfusion independence.

In addition, myeloid differentiation was observed in the bone marrow, consistent with the underlying mechanism of action of SY-1425 as a differentiating agent. The graphic below depicts myeloid differentiation in one relapsed or refractory AML patient starting after one cycle, with marrow blast reduction of greater than 25% beginning after two cycles and continuing to the start of the fourth cycle:



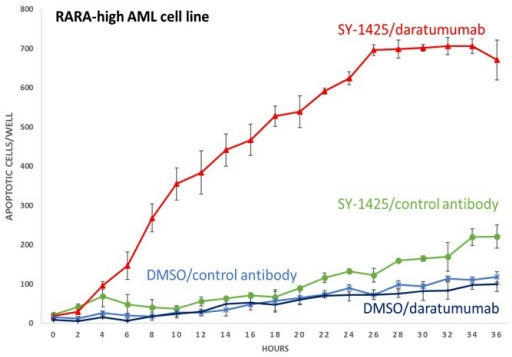
In addition to morphologic evidence of differentiation, immunophenotyping of bone marrow samples demonstrated induction of CD38, a marker of cell differentiation, after one 28-day cycle of treatment in 11 of 13 (85%) patients with pre- and post-treatment immunophenotyping samples.

We are no longer enrolling patients in the cohorts of the trial in which SY-1425 was being evaluated as a single agent. We believe that these clinical data, when combined with preclinical data showing the tumor-killing activity of SY-1425 in combination with azacitidine and with daratumumab, support the ongoing development of SY-1425 as a combination agent. SY-1425 has shown synergistic tumor-killing activity in combination with azacitidine as well as with daratumumab in preclinical models of *RARA* biomarker-positive AML. In combination with azacitidine, SY-1425 demonstrated greater cell death *in vitro* as well as greater clearance of tumor cells in bone marrow and other tissues and greater depth and duration of tumor response in PDX models, compared to either azacitidine or SY-1425 alone:



In combination with daratumumab, SY-1425 induced robust immune cell-mediated tumor death *in vitro*. Notably, AML cells do not normally express high levels of CD38. We have shown that by inducing CD38 expression, SY-1425 sensitizes biomarker-positive AML models to the tumor-killing effects of daratumumab. At the European Hematology Association 22nd Congress held in June 2017, we presented data showing that, by inducing CD38 expression, SY-1425 sensitizes biomarker-positive AML models to the tumor-killing effects of daratumumab. The preclinical studies showed that SY-1425 induced levels of CD38 expression in *RARA*-high AML cells comparable to those in multiple myeloma cells that are known to be responsive to daratumumab, and led to robust cell-mediated tumor

cell death in *RARA*-high AML cells when combined with daratumumab, as shown below:



Our ongoing Phase 2 clinical trial is assessing the safety and efficacy of SY-1425 in combination with azacitidine in approximately 25 newly diagnosed AML patients who are not suitable candidates for standard chemotherapy and in combination with daratumumab in approximately 12 relapsed or refractory AML and higher-risk MDS patients. All patients enrolled or to be enrolled in the trial have been or will be prospectively selected using our proprietary *RARA* or *IRF8* biomarkers. The primary endpoints for each of these cohorts of the trial are overall response rate, as determined by IWG criteria, as well as safety and tolerability. Secondary endpoints include duration of response, hematologic improvement and, for the daratumumab combination cohort, CD38 induction. In December 2017, we entered into a clinical supply agreement with Janssen pursuant to which Janssen agreed to supply us daratumumab for use in the trial. We expect to report initial clinical data from the combination cohorts of the trial in the fourth quarter of 2018.

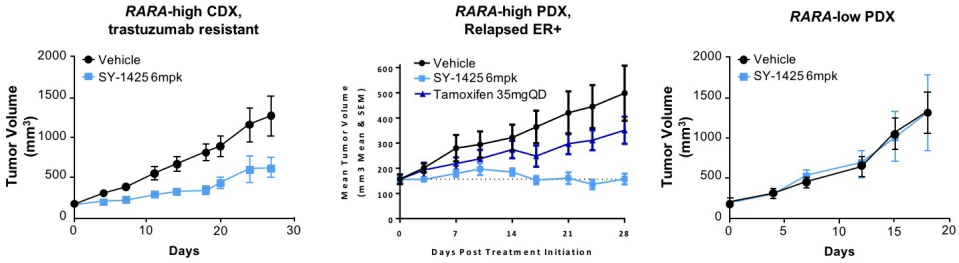
We have entered into an agreement with a third party commercial provider to provide a validated laboratory test under Clinical Laboratory Improvement Amendment, or CLIA, guidelines using a well-established diagnostic platform and approach that is being used to prospectively enroll *RARA* and *IRF8* biomarker-positive 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 these biomarkers, but have not yet selected a platform for development of a companion diagnostic test or entered in to an agreement with a third party for this work. We expect to do so in 2018.

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, upon establishing proof-of-concept in AML and MDS. Our preclinical data in breast cancer supports the development of SY-1425 in genomically defined subsets of patients with breast cancers with our *RARA* biomarker. We also believe there are subsets of patients with other tumor types with our *RARA* biomarker and continue to research the role of the super-enhancer associated with *RARA* in additional cancers.

Preclinical Data in Breast Cancer

Additionally, in our preclinical studies in breast cancer, many of which were presented at the San Antonio Breast Cancer Symposium in December 2016, we observed a strong link between sensitivity to treatment with SY-1425 and breast cancer tumors with the *RARA* biomarker. As shown below, 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. Our *in vitro* studies have also shown that SY-1425 increased the anti-

tumor effects of standard-of-care therapies, including tamoxifen and palbociclib, in ER-positive breast cancer cells with high *RARA* expression and lapatinib in HER2-positive breast cancer cells with high RARA expression.



Prior Clinical Data

Tamibarotene, the active pharmaceutical ingredient of SY-1425, is approved and marketed in Japan under the brand name Amnolake® for treatment of acute recurrent or intractable APL. Given the demonstrated efficacy of the drug in acute recurrent or intractable APL, we may evaluate SY-1425 for treatment of APL in North America and Europe, but we do not have any current plans to do so. Extensive clinical work had been conducted on tamibarotene prior to us 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 treatment 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 seven-year relapse-free survival rate in high-risk patients treated with tamibarotene was 89%, compared to 62% in high-risk patients treated with ATRA (p=0.034). In all patients, the seven-year relapse-free survival rate was 93% in the tamibarotene arm and was 84% in the ATRA arm (p=0.031).

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/m² daily, discontinued at CR	CR = 58% (14/24 evaluable) (≥ 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]	134	Front-line following ATRA-induced CR and consolidation	Tamibarotene 6 mg/m² vs. ATRA 45 mg/m² 14 days every 3 months for 2 years	Overall 7-year RFS: 93% vs. 84%; 7-year RFS in high risk: 89% vs. 62% (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/m² 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/m²/day tamibarotene, 25 mg/m²/day ATRA add-on to 0.15 mg/kg/day ATO for 56 days	**Tamibarotene +ATO** / **ATRA + ATO** CR 80% / 54% CRm 23% / 3%

Table legend:

CR = complete remission
RFS = relapse-free survival
BMT = bone marrow transplant
CRm = complete molecular remission
mEFS = median event-free survival
CT = chemotherapy
CRi = complete remission with incomplete blood count recovery
mOS = median overall survival

1. Tobita, et al. *Blood*, August 1997.
2. Takeshita, et al. American Society of Hematology presentation, December 2017.
3. Sanford D, et al. *British Journal of Haematology*, July 2015.
4. Wang et al, American Society of Hematology 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. The trial evaluated the efficacy and safety of adding tamibarotene or placebo to paclitaxel and carboplatin in patients with stage IIIb (plus pleural effusion) or IV non-small cell lung cancer. 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. Interim data also showed that tamibarotene combined with paclitaxel and carboplatin chemotherapy was associated with increased toxicity in this non-selected non-small cell lung cancer patient population.

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. At ESH, we presented data from 201 evaluable patients screened in our ongoing Phase 2 clinical trial demonstrating that approximately 40% of patients were positive for either the *RARA* or *IRF8* biomarker, or both, and that approximately one-third of the relapsed or refractory AML and higher-risk MDS patients tested were biomarker positive.

There are an estimated 33,000 new AML diagnoses in the United States, Canada and the five largest European countries each year. While several new drugs for the treatment of AML have been approved in the last year, AML remains an area of significant unmet medical need. According to the American Cancer Society, newly diagnosed AML patients in the United States have a 27% five-year survival rate. More than half of newly diagnosed AML patients are elderly or unfit for treatment with standard therapies, leaving this group with limited treatment options and an average survival of less than one year. Despite initial responses to therapy in select patients, the majority of AML patients relapse or become refractory to current treatment options. There are an estimated 10,000 cases of relapsed or refractory AML each year in the United States, Canada and the five largest European countries each year. In the absence of adequate therapies, these relapsed or refractory patients may be put into clinical trials for new and emerging therapies, and average survival of these patients is estimated to be less than six months.

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. Of these patients, approximately 7,500 MDS patients have newly-diagnosed, higher-risk MDS. In the United States, newly-diagnosed, higher-risk MDS patients are expected to survive for 0.8-1.6 years, and relapsed or refractory higher-risk AML patients have an average survival of less than six months. As with AML, treatment options for these patients are limited, with no new drugs having been approved for the treatment relapsed or refractory, higher-risk MDS in over a decade.

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, approximately 20-30% of APL patients relapse and require salvage therapy.

SY-1365

Overview

SY-1365 is a highly potent and selective small molecule CDK7 inhibitor. CDK7, a member of the cyclin-dependent kinase, or CDK, family, is a transcriptional kinase that plays a central role in the expression of key tumor-driving genes, transcription factors, and anti-apoptotic proteins. CDK7 activity has been implicated in various solid tumors with transcriptional dependencies. Inhibiting CDK7 preferentially lowers the expression of disease-driving transcription factors controlled by super-enhancers, and results in the preferential killing of cancer cells over non-cancerous cells. Using our platform, we have generated several potent and selective small molecule CDK7 inhibitors, including SY-1365.

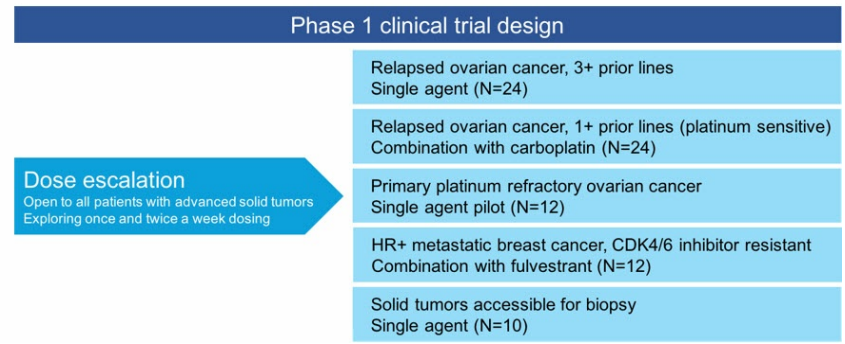
SY-1365 is currently in a Phase 1 clinical trial in patients with advanced solid tumors. We believe that SY-1365 is the most advanced selective CDK7 inhibitor in clinical development. SY-1365, alone and in combination with other therapeutic agents, has shown significant anti-proliferative and pro-apoptotic activity in multiple *in vitro* and *in vivo* models of difficult-to-treat solid tumors, including ovarian and breast cancers. SY-1365 has induced anti-tumor activity in both cell line-derived xenograft and patient-derived xenograft models, including tumor regressions at a twice weekly dosing regimen consistent with the initial regimen being evaluated in our Phase 1 clinical trial. SY-1365 has also shown to anti-tumor activity in models of blood cancers such as acute leukemias, as evidenced by *in vitro* cell death or complete tumor growth inhibition in cell-derived xenografts. Finally, SY-1365 has been shown to lower the expression of oncogenic transcription factors, including *MYC*, a mechanistic effect consistent with inhibition of CDK7.

SY-1365 Clinical Development Plan

In April 2017, the FDA accepted our investigational new drug, or IND, application to advance SY-1365 into a Phase 1 clinical trial in patients with advanced solid tumor malignancies for whom standard curative or palliative measures do not exist or are no longer effective. This trial began enrolling patients in the second quarter of 2017. The trial is testing the safety and tolerability of escalating doses of SY-1365 with the goal of establishing a maximum tolerated dose and a recommended Phase 2 dose and schedule. Additional study objectives include assessing pharmacodynamic changes and early signs of biological activity using biomarkers and clinical efficacy as measured by response rate using radiographic measures. We are currently exploring both a twice-weekly and a once-weekly dosing regimen, and we anticipate that approximately 35 patients will be enrolled in the dose escalation phase of the trial.

Once a maximum tolerated dose is reached in the dose escalation phase of the Phase 1 clinical trial and the recommended dosing schedule is identified, we intend to open expansion cohorts evaluating SY-1365 in multiple ovarian cancer populations as a single agent as well as in combination with carboplatin, a chemotherapeutic agent. The ovarian cancer populations include a 24-patient cohort evaluating SY-1365 as a single agent in patients who have relapsed after three or more prior therapies, a 24-patient cohort evaluating SY-1365 in combination with carboplatin in patients who relapsed after one or more prior therapies but who may still benefit from additional platinum-based treatment, and a 12-patient pilot cohort evaluating SY-1365 as a single agent in primary platinum-refractory disease. We also plan to evaluate SY-1365 in combination with fulvestrant, a hormonal medicine, in 12 patients with HR+, HER-2-negative metastatic breast cancer who have progressed after treatment with a CDK4/6 inhibitor and aromatase inhibitor.

In addition, we plan to evaluate the mechanism of action of SY-1365 in ten patients with any solid tumor accessible for biopsies. A schematic of our Phase 1 clinical trial of SY-1365 is below:

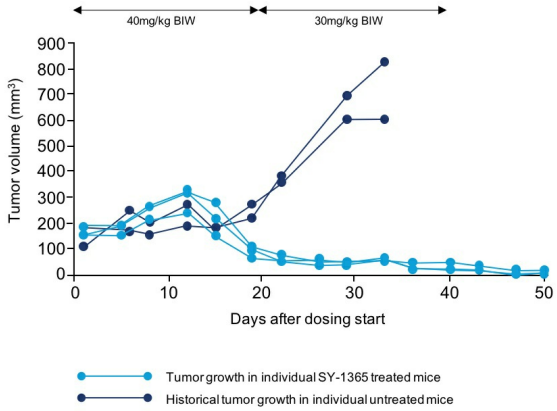


We expect that the expansion cohorts in our Phase 1 clinical trial will be open to enrollment in mid-2018 and that we will report clinical data from the dose-escalation phase of our Phase 1 trial, including safety and pharmacokinetic/pharmacodynamic data, in the fourth quarter of 2018.

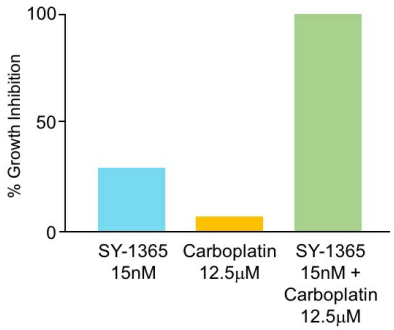
Our Preclinical Data

Our clinical development program for SY-1365 is based on a robust preclinical development program showing significant anti-proliferative activity of SY-1365 in multiple *in vitro* and *in vivo* models of difficult-to-treat solid tumors and blood cancers, including ovarian cancer, breast cancer and AML.

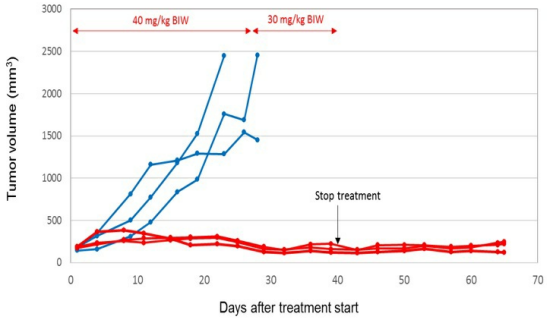
To evaluate the *in vivo* activity of SY-1365 in ovarian cancer, we evaluated SY-1365 in a number of patient-derived xenograft models derived from heavily-pretreated ovarian cancer patients and compared tumor growth in mice administered SY-1365 twice-weekly at the maximum tolerated dose in that species to untreated mice. Significant tumor growth inhibition was observed in many of these models following administration of SY-1365, with data from a representative model set forth in the graphic below:



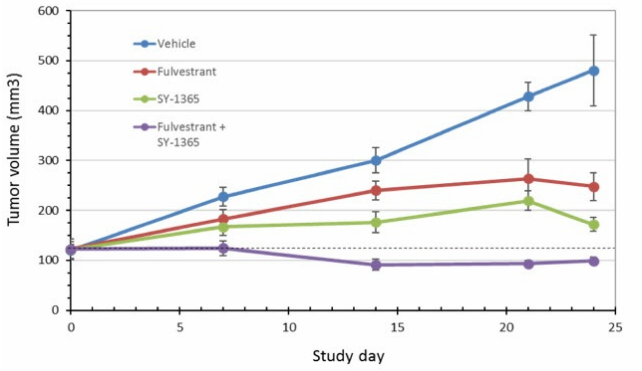
We have also shown the synergistic effect of treatment with SY-1365 and platinum-based chemotherapy in several ovarian cancer cell lines, as exemplified in the graphic below:



The inhibitory activity of SY-1365 was evaluated *in vitro* in many breast cancer cell lines, representing different subgroups of breast cancer. SY-1365 showed anti-tumor activity in all subgroups, inducing cell death in 15 of 19 TNBC cell lines and 17 of 21 HR+ and HER2-positive cell lines. At the San Antonio Breast Cancer Conference held in December 2017, we presented the results of our analysis of the anti-tumor activity of SY-1365 in xenograft models of TNBC. In the graphic below, we showed a complete response in mice administered SY-1365 twice weekly at the maximum tolerated dose in that species as compared to untreated mice.



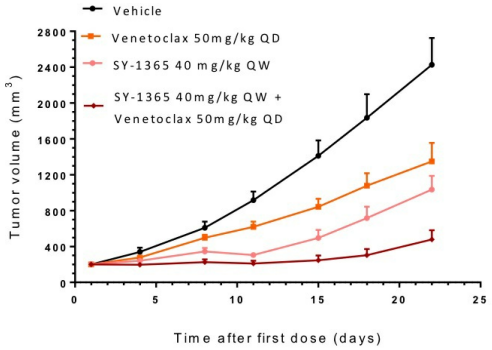
We, together with several of our academic collaborators, have demonstrated that SY-1365 could inhibit many HR+ cancer cells, including those with a form of acquired resistance to a class of hormonal treatments known as aromatase inhibitors, and that SY-1365 was able to inhibit breast cancer cell lines *in vitro* that no longer respond to inhibitors of CDK4/6. In addition, SY-1365 showed *in vitro* synergy with fulvestrant in several HR+ breast cancer cell lines. SY-1365 also showed a combination effect with fulvestrant in an *in vivo* model of HR+ breast cancer, as shown in the graphic below. We believe that these data, taken together, provide a mechanistic rationale for evaluating SY-1365 in combination with fulvestrant in patients with HR+ metastatic breast cancer who have progressed following treatment with a CDK4/6 inhibitor plus an aromatase inhibitor.



We also believe that SY-1365 has potential in blood cancers as well as in other solid tumor malignancies. The preclinical rationale for potential development of SY-1365 in blood cancers includes data we presented at ASH 2017 demonstrating that SY-1365:

- inhibited proliferation *in vitro* in leukemia and lymphoma cells, as well as leukemia cells from primary patient cultures;
- induced cell death in the majority of AML, leukemia and lymphoma cell lines tested; and
- inhibited tumor growth, including inducing tumor regression, using bi-weekly dosing in preclinical mouse models of AML.

In addition, we demonstrated that SY-1365 synergized with venetoclax, an investigational product being developed in AML, in AML cell lines *in vitro*, and that, as shown in the graphic below, the administration of SY-1365 plus venetoclax in an *in vivo* model resulted in greater tumor growth inhibition than either agent alone.



We also presented data at the 2017 AACR-NCI-EORTC Molecular Targets and Cancer Therapeutics conference showing the relationship between the pharmacokinetic, pharmacodynamic and anti-tumor activity of SY-1365 in multiple preclinical models of TNBC and AML, across a range of doses and regimens from daily to weekly dosing. These data showed a prolonged pharmacodynamic effect, as measured by CDK7 target occupancy, with a half-life of approximately three days, which supports the intermittent dosing regimen being evaluated in our ongoing Phase 1 clinical trial. We are using an assay measuring target occupancy as a target engagement marker in this trial. These data also showed a dose-dependent relationship between CDK7 target occupancy and anti-tumor activity in a preclinical model of AML, and sustained tumor regressions in multiple *in vivo* models using a twice-weekly dosing regimen.

SY-1365 Market Opportunity

With SY-1365, we believe we have the opportunity to address significant unmet medical needs across a range of cancers. The initial disease-specific focus of our clinical development program for SY-1365 is expected to be in ovarian cancer and HR+ breast cancer.

Ovarian cancer is the fifth most common cause of cancer death in women. There are an estimated 59,000 ovarian cancer diagnoses each year in what we refer to as the developed pharmaceutical markets – the United States, Canada, Japan and the five largest European countries by population, which are Germany, the United Kingdom, France Spain and Italy. Of these, approximately 70% have high-grade serous ovarian cancer and present with advanced disease at initial diagnosis. The standard of care treatment for these patients is platinum-based chemotherapy. It is estimated that 10-15% of these patients are "platinum-refractory," which means that they progress during, or in less than one month of completion of, platinum-based treatment. There are limited treatment options for platinum-refractory patients. Approximately 30% of these patients are "platinum-resistant," which means that they progress within six months of completing platinum-based treatment. We believe that subsequent treatment options for these patients at the present time have limited activity and significant toxicities. Approximately 55-60% of these patients are "platinum-sensitive," which means that they initially respond to platinum-based treatment, but progress after six months or more. The majority of these patients relapse within three to five years. The planned expansion cohorts of our Phase 1 clinical trial of SY-1365 include patients who have progressed after platinum-based treatments.

Breast cancer is the most common tumor type in women and is the leading cause of cancer death in women worldwide. According to the American Cancer Society, approximately 266,000 new breast cancer cases will be diagnosed in the United States in 2018, with approximately 41,000 deaths from the disease. Approximately 80% of breast cancers express estrogen receptors, progesterone receptors, or both. Hormone-based therapies are the cornerstone for these HR+ cancers. In metastatic breast cancer, AIs are frequently used as a first-line treatment option. Recent approvals of a class of drugs that inhibit CDK4/6, such as palbociclib and ribociclib, have resulted in their use in combination with AIs for the treatment of HR+, HER2-negative, breast cancers. Patients who relapse following treatment with an AI in combination with a CDK4/6 inhibitor currently have few effective treatment options.

Other Programs

We currently have five programs in our preclinical and discovery pipeline, including preclinical programs directed to the development of a CDK7 inhibitor that can be administered orally, inhibitors of cyclin-dependent kinase 12/13, and inhibitors of an immuno-oncology target, as well as discovery programs related to a gene control target to treat sickle cell disease and in the field of cancer. We plan to nominate a development candidate from one of our preclinical programs during 2018 that we can advance into studies to support a potential IND filing in 2019, consistent with our objective of filing, on average, an IND every other year.

We are using our platform to analyze gene expression programs in tumors and immune cells across various cancers and monogenic diseases to identify optimal points of therapeutic intervention in specific subsets of patients and to create a pipeline of novel product candidates targeting transcriptional and regulatory proteins. We are also using our platform in collaboration with third parties to identify and validate targets in diseases beyond our current areas of focus. To this end, we entered a target discovery, research collaboration and option agreement with Incyte in January 2018 under which we will use our platform to identify novel therapeutic targets with a focus on myeloproliferative neoplasms. See "—License and Collaboration Agreements–Incyte" below.

Research and Development Expense

During the years ended December 31, 2017, 2016 and 2015, our research and development expenses were $41.9 million, $37.8 million and $24.4 million, respectively. For additional information regarding our research and development expense as well as our revenues, operating loss, and total assets, see the sections of this report entitled, "Financial Statements" in Part II, Item 8 and "Management's Discussion and Analysis of Financial Condition and Results of Operations" in Part II, Item 7.

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 February 28, 2018, we own two issued U.S. patents, 12 pending U.S. provisional patent applications, twelve U.S. pending patent applications, 41 foreign applications pending in a number of jurisdictions, including Europe, Australia, Japan, China, and Canada, and four pending Patent Cooperation Treaty, or PCT, patent applications. In addition, as of February 28, 2018, we have exclusively licensed six issued U.S. patents, three U.S. pending patent applications, five issued foreign patents and 12 foreign patent applications pending in a number of jurisdictions, including Australia, Canada, China, Europe, and Japan. A significant portion of our owned and licensed pending patent applications pertain to our product candidates and associated biomarkers, key discovery and preclinical programs, specifically our CDK7 inhibitor program, and transcription factor modulators, and our gene control platform.

Our intellectual property portfolio as of February 28, 2018 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 U.S. Patent and Trademark Office, or 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. In addition, we may elect to abandon prosecution of some of our pending patent applications, particularly outside of the United States, if we determine that these applications do not have strategic significance to our programs or platform.

SY-1425

Our owned intellectual property portfolio for SY-1425 contains two issued U.S. patents, two U.S. pending patent applications, 11 foreign applications pending in a number of jurisdictions, including Europe, Australia, Japan, China, and Canada, and three pending PCT patent applications directed to patient stratification methods based on biomarkers, combinations and methods of use for agonists of RARα, including SY-1425. One of our issued patents, U.S. Patent 9,845,508, covers a method of diagnosing and treating AML patients by determining whether they have elevated levels of RARA messenger RNA, or mRNA, and, if they do, administering SY-1425. The second patent, U.S. Patent 9,868,994, covers a method of treating AML and MDS by administering SY-1425 to patients known to have elevated levels of IRF8 mRNA. For purposes of these patents, AML does not include acute promyelocytic leukemia, or APL. We believe that our currently-issued U.S. patents related to our SY-1425 program are eligible for listing in the U.S. Food and Drug Administration's Orange Book. The U.S. patents and pending applications and any U.S. or non-U.S. applications claiming priority to these pending applications, if issued, have statutory expiration dates no earlier than March 2036.

In addition, we are exclusively licensed in North America and Europe under 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.

SY-1365

The intellectual property portfolio for SY-1365 and our other CDK7 inhibitors contains patent applications directed to compositions of matter for our compounds and analogs, compositions of matter for CDK7 inhibitors having different structural features (*i.e.,* different compound families), as well as methods of use, biomarkers, and formulations for these novel compounds. As of February 28, 2018, we own six pending U.S. patent applications, 29 pending foreign applications in a number of jurisdictions, including Europe, Canada, China, Japan and Australia and one pending PCT patent application and seven pending U.S. provisional applications, directed to this program. Any U.S. or non-U.S. patents issuing from these pending applications or applications claiming priority to the pending applications covering our compounds and related methods of use will have a statutory expiration date ranging from October 2034 to January 2039. Patent term adjustments or patent term extensions could result in later expiration dates.

We are also exclusively licensed under one U.S. patent, two pending U.S. patent applications and 11 pending foreign patent applications in a number of jurisdictions, including Australia, Canada, Europe, and Japan, 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 and immuno-oncology targets in multiple compound families, and methods of treating various diseases, including cancer and immunological diseases, through inhibition of specific transcription factor(s) or gene products. As of February 28, 2018, we own five U.S. provisional patent applications and three U.S. patent applications and are exclusively licensed to two issued U.S. patents directed to our other programs. The licensed U.S. patents have statutory expiration dates of July 2032 and November 2033. Any U.S. or non-U.S. patents issuing from the pending applications or applications claiming priority to the pending applications covering transcription factor inhibitors, immuno-oncology target inhibitors or methods of treating disease by inhibition of transcription factors or gene products will have statutory expiration dates ranging from February 2031 to December 2038.

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. As of February 28, 2018, 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, one U.S. pending patent application and one pending foreign patent application in Europe, 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 no earlier than 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 no earlier than October 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. Our pending patent applications, and any patent applications that we may in the future file or license from third parties may not, however, 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 and Collaboration Agreements

We are a party to global target discovery collaboration with Incyte under which we intend to identify and validate novel therapeutic targets with a focus on myeloproliferative neoplasms. By entering into this collaboration, we aim to use our platform to benefit patients with diseases beyond our current areas of focus, although we do not have any rights to commercialize any products arising from this collaboration. These collaborations impose certain performance obligations on us. We may enter into agreements similar to this one in the future.

In addition, 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.

Incyte Corporation

In January 2018, we entered into a target discovery, research collaboration and option agreement with Incyte. Under this agreement, we will use our gene control platform to identify novel therapeutic targets with a focus on myeloproliferative neoplasms, and Incyte will receive options to obtain exclusive worldwide rights to intellectual property resulting from the collaboration for the development and commercialization of therapeutic products directed to up to seven validated targets. Incyte will have exclusive worldwide rights to develop and commercialize any therapies under the collaboration that modulate those validated targets.

Under the terms of the collaboration agreement, Incyte paid us $10.0 million in up-front consideration, consisting of $2.5 million in cash and $7.5 million in pre-paid research funding. Our activities under this agreement are subject to a joint research plan and, subject to certain exceptions, Incyte will be responsible for funding our activities under the research plan, including amounts in excess of the pre-paid research funding amount. We are eligible to receive target selection milestone payments and option exercise fees of up to an aggregate of $54.0 million if Incyte selects the maximum number of targets for validation and exercises its option to obtain exclusive rights to collaboration intellectual property for therapeutic products directed to all seven validated targets. Should any therapeutic product be developed by Incyte against a target as to which Incyte has exercised its option to obtain exclusive rights to collaboration intellectual property, we will be eligible to receive milestone payments and, if approved and commercialized, royalty payments from Incyte. For each of the seven validated targets, we would become eligible to receive from Incyte a total of up to $50.0 million in development and regulatory milestone payments. If products arising from the collaboration are approved, we would become eligible to receive from Incyte, for each validated target, a total of up to $65.0 million in commercial milestone payments. Upon approval and commercialization of any therapeutic product resulting from the collaboration, we would become eligible to receive low single-digit royalties on net sales of such product.

The term of the collaboration agreement with Incyte will, unless terminated by a party early, expire when all royalty obligations for products arising from the collaboration expire. The agreement may be terminated by Incyte for convenience on sixty (60) days' prior written notice to us, or by us on thirty (30) days' written notice in the event Incyte or one of its affiliates or sublicensees challenges the validity or enforceability of certain patent rights controlled by us. The agreement may also be terminated by either of the parties on thirty (30) days' prior written notice in the event of an uncured material breach of the agreement by the other party or immediately in the case of certain bankruptcy events. Incyte's right to terminate for convenience and each party's right to terminate for uncured material breach may be exercised either with respect to the agreement in its entirety or, as applicable, in relation to the relevant validated target and associated therapeutic products.

In connection with the collaboration agreement, we sold 793,021 shares of our common stock to Incyte for an aggregate purchase price of $10.0 million in cash, or $12.61 per share, in a private placement. In addition, from the closing of this sale until the earlier of the second anniversary of such closing or the expiration or termination of the collaboration agreement, we have granted to Incyte the right to purchase up to its *pro rata* share of the securities offered in certain subsequent offerings of our common stock or common stock equivalents, subject to the terms and conditions set forth in the stock purchase agreement. In February 2018, we sold 144,505 additional shares of our common stock to Incyte at a price of $9.55 per share, resulting in proceeds to us of $1.4 million.

We are obligated to make a payment to Whitehead representing a percentage of the up-front cash consideration and equity premium received from Incyte.

TMRC

In September 2015, we entered into, and in April 2016, we amended and restated, 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 low single-digit royalties based on net sales with respect to know-how licensed by TMRC during a predefined royalty term, and to make payments to TMRC upon meeting specified clinical and regulatory milestones in an aggregate amount of approximately $13.0 million per indication, of which $1.0 million was paid in the third quarter of 2016 upon successful dosing of the first patient in our Phase 2 clinical trial of SY-1425. 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. If we have reason to do so, we may also terminate the agreement after one year from the original effective date at our sole discretion.

In connection with the TMRC license agreement, in April 2016 we entered into a supply management agreement with TMRC. Pursuant to the supply management agreement, we and TMRC have agreed to establish a joint manufacturing committee to discuss strategy for supply of SY-1425. In addition, we have agreed to pay TMRC a fee for each kilogram of SY-1425 active pharmaceutical ingredient we procure for clinical trial or commercial use. The supply management agreement terminates on the expiration or termination of the TMRC license agreement, and our obligation to pay these fees survives the termination of the supply management agreement. In April 2016, we also entered into a standby license with TMRC and Toko Pharmaceuticals Ind. Co. Ltd., or Toko, the owner of the patent rights licensed to TMRC from which our license agreement with TMRC derives its rights, pursuant to which we obtain a standby license from Toko if Toko's license with TMRC is terminated.

Dana-Farber Cancer Institute, Inc.

In February 2013, we entered into a license agreement with 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 licensed 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 sale of licensed products 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

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 an exclusive, sublicensable with certain restrictions, license under specified patents relating to *MYC* modulators 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. 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. 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 98,099 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 was 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. As of February 28, 2018, our license continued to be

exclusive in all fields. 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 73,575 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.

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 product 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 RARα agonist, for patients with AML or MDS. We will select patients for our clinical trials based on high-levels of RARα as measured by our proprietary *RARA* and *IRF8* biomarkers. We are aware of four new drugs approved by the FDA during 2017 for the treatment of AML or patient subsets within AML: midostaurin, enasidanib, daunorubicin + cytarabine liposome, and gemtuzumab. SY-1425 may also face competition from other investigational products currently in clinical development for AML and MDS, including venetoclax, which is currently being evaluated by AbbVie, Inc. in two randomized pivotal studies in patients with AML, as well as investigational products in development from Takeda Pharmaceutical Co. Ltd., Daiichi Sankyo Company, Limited, Agios Pharmaceuticals, Inc., Novartis AG, Bristol-Myers Squibb Co., Eli Lilly & Co., Eisai Inc., Celgene Corporation, Pfizer, Inc., Incyte Corporation and FORMA Therapeutics, LLC. We are aware of only one other selective RARα program, a compound in development from Io Therapeutics, Inc. which, according to a government-sponsored website, is in an investigator initiated Phase 1/2 study in a non-selective patient group in relapsed and refractory AML, high-risk MDS and chronic myelomonocytic leukemia.

SY-1365

We are conducting a Phase 1 clinical trial of SY-1365 in patients with advanced solid tumors and plan to open expansion cohorts in various ovarian and breast cancer populations once we establish the maximum tolerated dose during the dose escalation phase of the trial. We believe that SY-1365 is the most advanced selective CDK7 inhibitor in clinical development. We are aware of an oral CDK7 inhibitor being developed by Carrick Therapeutics Ltd. that has recently entered Phase 1 clinical development, and are aware of several other selective CDK7 inhibitor programs that we believe are in preclinical development, including programs from Aurigene Discovery Technologies Ltd., Ube Industries Ltd., Qurient Co. Ltd., and Beta Pharma, Inc. SY-1365 may face competition from these selective CDK7 inhibitors.

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

Approval and Regulation of Drugs in the United States

In the United States, drug products are regulated under the Federal Food, Drug and Cosmetic Act, or FDCA, and applicable implementing regulations and guidance. The failure of an applicant to comply with the applicable regulatory requirements at any time during the product development process, including non-clinical testing, clinical testing, the approval process or post-approval process, may result in delays to the conduct of a study, regulatory review and approval and/or administrative or judicial sanctions. These sanctions may include, but are not limited to, the FDA's refusal to allow an applicant to proceed with clinical trials, refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, warning letters, adverse publicity, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines and civil or criminal investigations and penalties brought by the FDA or Department of Justice, or DOJ, or other government entities, including state agencies.

An applicant seeking approval to market and distribute a new drug in the United States generally must satisfactorily complete each of the following steps before the product candidate will be licensed by the FDA:

- preclinical testing including laboratory tests, animal studies and formulation studies, which must be performed in accordance with the FDA's good laboratory practice, or GLP, regulations and standards;
- submission to the FDA of an IND for human clinical testing, which must become effective 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 to establish the safety, potency and purity of the product candidate for each proposed indication, in accordance with current good clinical practices, or GCP;
- preparation and submission to the FDA of a new drug application, or NDA, for a drug product which includes not only the results of the clinical trials, but also, detailed information on the chemistry, manufacture and quality controls for the product candidate and proposed labelling for one or more proposed indication(s);
- review of the product candidate by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities, including those of third parties, at which the product candidate or components thereof are manufactured 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 any FDA audits of the non-clinical and clinical trial sites to assure compliance with GCP and the integrity of clinical data in support of the NDA;
- payment of applicable user fees and securing FDA approval of the NDA to allow marketing of the new drug product; 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 any post-approval studies required by the FDA.

Preclinical Studies

Before an applicant begins testing a product candidate with potential therapeutic value in humans, the product candidate enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, formulation and stability, as well as other studies to evaluate, among other things, the toxicity of the product candidate. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements, including GLP regulations and standards. The results of the preclinical tests, together with manufacturing information and analytical data, 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, and long-term toxicity studies, may continue after the IND is submitted.

The IND and IRB Processes

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

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a specific protocol or part of a protocol is not allowed to proceed, while other protocols may do so. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all FDA IND requirements must be met unless waived. When a foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA in order to use the study as support for an IND or application for marketing approval. Specifically, on April 28, 2008, the FDA amended its regulations governing the acceptance of foreign clinical studies not conducted under an investigational new drug application as support for an IND or a new drug application. The final rule provides that such studies must be conducted in accordance with good clinical practice, or GCP, including review and approval by an independent ethics committee, or IEC, and informed consent from subjects. The GCP requirements in the final rule encompass both ethical and data integrity standards for clinical studies. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

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

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

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

Human Clinical Trials in Support of an NDA

Clinical trials involve the administration of the investigational product candidate to human subjects under the supervision of a qualified investigator 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 clinical trial protocols detailing, among other things, the objectives of the study, inclusion and exclusion criteria, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

Human clinical trials are typically conducted in three sequential phases, but the phases may overlap or be combined. Additional studies may also be required after approval.

Phase 1 clinical trials are initially conducted in a limited population to test the product candidate for safety, including adverse effects, dose tolerance, absorption, metabolism, distribution, excretion and pharmacodynamics in healthy humans or in patients. During Phase 1 clinical trials, information about the investigational drug product's pharmacokinetics and pharmacological effects may be obtained to permit the design of well-controlled and scientifically valid Phase 2 clinical trials.

Phase 2 clinical trials are generally conducted in a limited patient population to identify possible adverse effects and safety risks, evaluate the efficacy of the product candidate for specific targeted indications and determine dose tolerance and optimal dosage and dosage schedule. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more costly Phase 3 clinical trials. Phase 2 clinical trials are well controlled, closely monitored and conducted in a limited patient population.

Phase 3 clinical trials proceed if the Phase 2 clinical trials demonstrate that a dose range of the product candidate is potentially effective and has an acceptable safety profile. Phase 3 clinical trials are undertaken within an expanded patient population to further evaluate dosage, provide substantial evidence of clinical efficacy and further test for safety in an expanded and diverse patient population at multiple, geographically dispersed clinical trial sites. A well-controlled, statistically robust Phase 3 clinical trial may be designed to deliver the data that regulatory authorities will use to decide whether or not to approve, and, if approved, how to appropriately label a drug: such Phase 3 studies are referred to as "pivotal."

In some cases, the FDA may approve an NDA for a product candidate but require the sponsor to conduct additional clinical trials to further assess the product candidate's safety and effectiveness after approval. Such post-approval trials are typically referred to as Phase 4 clinical trials. These studies are used to gain additional experience from the treatment of a larger number of patients in the intended treatment group and to further document a clinical benefit in the case of drugs approved under accelerated approval regulations. Failure to exhibit due diligence with regard to conducting Phase 4 clinical trials could result in withdrawal of approval for products.

Progress reports detailing the status and a brief description of available results of the clinical trials must be submitted at least annually to the FDA. 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 product; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or completed at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product has been associated with unexpected serious harm to patients. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

Concurrent with clinical trials, companies often complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product 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 product candidate does not undergo unacceptable deterioration over its shelf life.

Review and Approval of an NDA

In order to obtain approval to market a drug product in the United States, a marketing application must be submitted to the FDA that provides sufficient data establishing the safety, purity and potency of the proposed drug product for its intended indication. The application includes all relevant data available from pertinent preclinical and clinical trials, together with detailed information relating to the product's chemistry, manufacturing, controls and proposed labeling, among other things. Data can come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety, purity and potency of the drug product to the satisfaction of the FDA.

The NDA is a vehicle through which applicants formally propose that the FDA approve a new product for marketing and sale in the United States for one or more indications. Every new drug product candidate must be the subject of an approved NDA before it may be commercialized in the United States. Under federal law, the submission of most NDAs is subject to an application user fee, which for federal fiscal year 2018 is $2,421,495 for an application requiring clinical data. The sponsor of an approved NDA is also subject to an annual program fee, which for fiscal year 2018 is $304,162. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for products with orphan designation and a waiver for certain small businesses.

Following submission of an NDA, the FDA conducts a preliminary review of the application 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 whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept the application 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 the FDA accepts the application 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 products that are not NMEs, the ten-month and six-month review periods run from the date that the FDA receives the application. The review process and the Prescription Drug User Fee Act, or PDUFA, goal date may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an application, 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 component manufacturing, finished product manufacturing and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Under the FDA Reauthorization Act of 2017, the FDA must implement a protocol to expedite review of responses to inspection reports pertaining to certain applications, including applications for products in shortage or those for which approval is dependent on remediation of conditions identified in the inspection report.

In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events and whether the product is a new molecular entity.

The FDA may refer an application for a novel product 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

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, as applicable to our business, are referred to as fast track designation, breakthrough therapy designation and priority review designation.

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

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

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

Accelerated Approval Pathway

The FDA may grant accelerated approval to a 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 drug, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a 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. Thus, the benefit of accelerated approval derives from the potential to receive approval based on surrogate endpoints sooner than possible for trials with clinical or survival endpoints, rather than deriving from any explicit shortening of the FDA approval timeline, as is the case with priority review.

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

If the FDA approves a new product, it may limit the approved indications for use of the product. The agency may also 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, to help ensure the safe use of the product. REMS can include medication guides, communication plans for health care professionals, and elements to assure safe use, or ETASU. ETASU can 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 patent registries. 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 Regulation

If regulatory approval for marketing of a product or new indication for an existing product is obtained, the sponsor will be required to comply with all regular post-approval regulatory requirements as well as any post-approval requirements that the FDA may have imposed as part of the approval process. The sponsor will be required to report, among other things, certain adverse reactions and manufacturing problems to the FDA, provide updated safety and efficacy information and comply with requirements concerning advertising and promotional labeling requirements. Manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMP regulations, which impose certain procedural and documentation requirements upon manufacturers. Accordingly, the sponsor and its third-party manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain compliance with cGMP regulations and other regulatory requirements.

A product may also be subject to official lot release, meaning that the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release, the manufacturer must submit samples of each lot, together with a release protocol showing a summary of the history of

manufacture of the lot and the results of all of the manufacturer's tests performed on the lot, to the FDA . The FDA may in addition perform certain confirmatory tests on lots of some products before releasing the lots for distribution. Finally, the FDA will conduct laboratory research related to the safety, purity, potency and effectiveness of pharmaceutical products.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements 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 safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

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

The FDA strictly regulates the marketing, labeling, advertising and promotion of prescription drug products placed on the market. This regulation includes, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and promotional activities involving the Internet and social media. Promotional claims about a drug's safety or effectiveness are prohibited before the drug is approved. After approval, a drug product generally may not be promoted for uses that are not approved by the FDA, as reflected in the product's prescribing information. In the United States, health care professionals are generally permitted to prescribe drugs for such uses not described in the drug's labeling, known as off-label uses, because the FDA does not regulate the practice of medicine. However, FDA regulations impose rigorous restrictions on manufacturers' communications, prohibiting the promotion of off-label uses. It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in nonpromotional, non-misleading communication regarding off-label information, such as distributing scientific or medical journal information.

If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the DOJ, or the Office of the Inspector General of the Department of Health and Human Services, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion, and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

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

Pediatric Studies and Exclusivity

Under the Pediatric Research Equity Act of 2003, an NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the 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. Sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design,

any deferral or waiver requests and other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

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

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

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

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

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition, generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a product available in the United States for treatment of the disease or condition will be recovered from sales of the product. A company must seek orphan drug designation before submitting an NDA for the candidate product. 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 PDUFA goal dates 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 condition for seven years, except in certain limited circumstances. Orphan exclusivity does not block the approval of a different product for the same rare disease or condition, nor does it block the approval of the same product for different conditions. 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 drug exclusivity will not bar approval of another product under certain circumstances, including if a subsequent product with the same drug for the same condition is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. This is the case despite an earlier court opinion holding that the

Orphan Drug Act unambiguously required the FDA to recognize orphan exclusivity regardless of a showing of clinical superiority.

Section 505(b)(2) NDAs

NDAs for new drug products are based on well controlled studies that provide substantial evidence of the safety and efficacy of the proposed new product for the proposed use. These applications are submitted under Section 505(b)(1) of the FDCA. The FDA is, however, authorized to approve an alternative type of NDA under Section 505(b)(2) of the FDCA. This type of application allows the applicant to rely, in part, on the FDA's previous findings of safety and efficacy for a similar product, or published literature. Specifically, Section 505(b)(2) applies to NDAs for a drug for which the investigations made to show whether or not the drug is safe for use and effective in use and relied upon by the applicant for approval of the application "were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted."

Thus, Section 505(b)(2) authorizes the FDA to approve an NDA based on safety and effectiveness data that were not developed by the applicant. NDAs filed under Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval for new or improved formulations or new uses of previously approved products. If the 505(b)(2) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, the applicant 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 to support the change from the approved product. The FDA may then approve the new product candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

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 therapeutic equivalent generic drug to be fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of therapeutic equivalence often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

Under the Hatch-Waxman Amendments, the FDA may not approve an ANDA until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity. For the purposes of this provision, 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.

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

Hatch-Waxman Patent Certification and the 30-Month Stay

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

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

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

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

If the ANDA 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 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 ANDA 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 ANDA applicant.

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. As a result, approval of a Section 505(b)(2) NDA can be stalled until all the listed patents claiming the referenced product have expired, until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired, and, in the case of a Paragraph IV certification and subsequent patent infringement suit, until the earlier of 30

months, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) applicant.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted on a patent covering a product is typically one-half the time between the effective date of a clinical investigation involving human beings is begun and the submission date of an application, plus the time between the submission date of an application and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved 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 products for which approval is sought can only be extended in connection with one of the approvals. The United States Patent and Trademark Office reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

The 21st Century Cures Act

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

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

FDA Approval and Regulation of Companion Diagnostics

If safe and effective use of a therapeutic depends on an *in vitro* diagnostic, then the FDA generally will require approval or clearance of that diagnostic, known as a companion diagnostic, at the same time that the FDA approves the therapeutic product. In August 2014, the FDA issued final guidance clarifying the requirements that will apply to approval of therapeutic products and *in vitro* companion diagnostics. According to the guidance, if the FDA determines that a companion diagnostic device is essential to the safe and effective use of a novel therapeutic product or indication, the FDA generally will not approve the therapeutic product or new therapeutic product indication if the companion diagnostic device is not approved or cleared for that indication. Approval or clearance of the companion diagnostic device will ensure that the device has been adequately evaluated and has adequate performance characteristics in the intended population. The review of *in vitro* companion diagnostics in conjunction with the review of our therapeutic treatments for cancer will, therefore, likely involve coordination of review by the FDA's Center for Drug Evaluation and Research and the FDA's Center for Devices and Radiological Health Office of In Vitro Diagnostics Device Evaluation and Safety.

Under the FDCA, *in vitro* diagnostics, including companion diagnostics, are regulated as medical devices. In the United States, the FDCA and its implementing regulations, and other federal and state statutes and regulations govern, among other things, medical device design and development, preclinical and clinical testing, premarket clearance or approval, registration and listing, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import, and post-market surveillance. Unless an exemption applies, diagnostic tests require

marketing clearance or approval from the FDA prior to commercial distribution. The two primary types of FDA marketing authorization applicable to a medical device are premarket notification, also called 510(k) clearance, and premarket approval, or PMA approval.

The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, can take several years or longer. It involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications are subject to an application fee, which exceeds $250,000 for most PMAs. In addition, PMAs for certain devices must generally include the results from extensive preclinical and adequate and well-controlled clinical trials to establish the safety and effectiveness of the device for each indication for which FDA approval is sought. In particular, for a diagnostic, a PMA application typically requires data regarding analytical and clinical validation studies. As part of the PMA review, the FDA will typically inspect the manufacturer's facilities for compliance with the Quality System Regulation, or QSR, which imposes elaborate testing, control, documentation and other quality assurance requirements.

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

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

Health care Law and Regulation

Health care 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, patient privacy laws and regulations and other health care laws and regulations that may constrain business and/or financial arrangements. Restrictions under applicable federal and state health care laws and regulations, include the following:

- the 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 health care program such as Medicare and Medicaid;

- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or

causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government.

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any health care benefit program or making false statements relating to health care matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal false statements statute, which 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 health care benefits, items or services;

- 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 the ACA, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the 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 health care items or services that are reimbursed by non-government 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 manufacturers to report information related to payments to physicians and other 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.

Pharmaceutical Insurance Coverage and Health Care Reform

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

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

product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

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

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

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

- establishment of a Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Other legislative changes have been proposed and adopted since the ACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 and 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 and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Further, there have been several recent U.S. congressional inquiries and proposed state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products.

These healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price for any approved product and/or the level of reimbursement physicians receive for administering any approved product. Reductions in reimbursement levels may negatively impact the prices or the frequency with which products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. Since enactment of the ACA, there have been numerous legal challenges and Congressional actions to repeal and replace provisions of the law. In May 2017, the U.S. House of Representatives passed legislation known as the American Health Care Act of 2017. Thereafter, the Senate Republicans introduced and then updated a bill to replace the ACA known as the Better Care Reconciliation Act of 2017. The Senate Republicans also introduced legislation to repeal the ACA without companion legislation to replace it, and a "skinny" version of the Better Care Reconciliation Act of 2017. In addition, the Senate considered proposed healthcare reform legislation known as the Graham-Cassidy bill. None of these measures was passed by the U.S. Senate.

The Trump Administration has also taken executive actions to undermine or delay implementation of the ACA. In January 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. In October 2017, the President signed a second Executive Order allowing for the use of association health plans and short-term health insurance, which may provide fewer health benefits than the plans sold through the ACA exchanges. At the same time, the Administration announced that it will discontinue the payment of cost-sharing reduction (CSR) payments to insurance companies until Congress approves the appropriation of funds for such CSR payments. The loss of the CSR payments is expected to increase premiums on certain policies issued by qualified health plans under the ACA. A bipartisan bill to appropriate funds for CSR payments was introduced in the Senate, but the future of that bill is uncertain.

More recently, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by the President on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Congress will likely consider other legislation to replace elements of the ACA, during the next Congressional session.

Further, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, Congress and the Trump

administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing.

Review and Approval of Medicinal Products in the European Union

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

Clinical Trial Approval

The Clinical Trials Directive 2001/20/EC, the Directive 2005/28/EC on Good Clinical Practice, or GCP, and the related national implementing provisions of the individual EU Member States govern the system for the approval of clinical trials in the EU. Under this system, an applicant must obtain prior approval from the competent national authority of the EU Member States 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. The clinical trial application must be accompanied by, among other documents, an investigational medicinal product dossier (the Common Technical Document) with supporting information prescribed by Directive 2001/20/EC, Directive 2005/28/EC, where relevant the implementing national provisions of the individual EU Member States and further detailed in applicable guidance documents.

In April 2014, the new Clinical Trials Regulation, (EU) No 536/2014, or Clinical Trials Regulation, was adopted. The Regulation was published on June 16, 2014 but is not expected to apply until 2019. The Clinical Trials Regulation will be directly applicable in all the EU Member States, repealing the current Clinical Trials Directive 2001/20/EC and replacing any national legislation that was put in place to implement the Directive. Conduct of all clinical trials performed in the EU will continue to be bound by currently applicable provisions until the new Clinical Trials Regulation becomes applicable. The extent to which on-going clinical trials will be governed by the Clinical Trials Regulation will depend on when the Clinical Trials Regulation becomes applicable and on the duration of the individual clinical trial. If a clinical trial continues for more than three years from the day on which the Clinical Trials Regulation becomes applicable the Clinical Trials Regulation will at that time begin to apply to the clinical trial.

The new Clinical Trials Regulation aims to simplify and streamline the approval of clinical trials in the EU. The main characteristics of the regulation include: a streamlined application procedure via a single entry point, the "EU Portal and Database"; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed by the appointed reporting Member State, whose assessment report is submitted for review by the sponsor and all other competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted (Concerned Member States). Part II is assessed separately by each Concerned Member State. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the Concerned Member State. However, overall related timelines will be defined by the Clinical Trials Regulation.

PRIME Designation in the EU

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

Marketing Authorization

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

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid across the European Economic Area (i.e., the EU as well as Iceland, Liechtenstein and Norway). Pursuant to Regulation (EC) No 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy medicinal products, and products with a new active substance indicated for the treatment of certain diseases, including products for the treatment of cancer. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional. The centralized procedure may at the request of the applicant also be used in certain other cases. We anticipate that the centralized procedure will be mandatory for the product candidates we are developing.

Under the centralized procedure, the CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the EU, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. If the CHMP accepts such request, the time limit of 210 days will be reduced to 150 days but it is possible that the CHMP can revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment. At the end of this period, the CHMP provides a scientific opinion on whether or not a marketing authorization should be granted in relation to a medicinal product. Within 15 calendar days of receipt of a final opinion from the CHMP, the European Commission must prepare a draft decision concerning an application for marketing authorization. This draft decision must take the opinion and any relevant provisions of EU law into account. Before arriving at a final decision on an application for centralized authorization of a medicinal product the European Commission must consult the Standing Committee on Medicinal Products for Human Use. The Standing Committee is composed of representatives of the EU Member States and chaired by a non-voting European Commission representative. The European Parliament also has a related "droit de regard". The European Parliament's role is to ensure that the European Commission has not exceeded its powers in deciding to grant or refuse to grant a marketing authorization.

The European Commission may grant a so-called "marketing authorization under exceptional circumstances". Such authorization is intended for products for which the applicant can demonstrate that it is unable to provide

comprehensive data on the efficacy and safety under normal conditions of use, because the indications for which the product in question is intended are encountered so rarely that the applicant cannot reasonably be expected to provide comprehensive evidence, or in the present state of scientific knowledge, comprehensive information cannot be provided, or it would be contrary to generally accepted principles of medical ethics to collect such information. Consequently, marketing authorization under exceptional circumstances may be granted subject to certain specific obligations, which may include the following:

- the applicant must complete an identified program of studies within a time period specified by the competent authority, the results of which form the basis of a reassessment of the benefit/risk profile;
- the medicinal product in question may be supplied on medical prescription only and may in certain cases be administered only under strict medical supervision, possibly in a hospital and in the case of a radiopharmaceutical, by an authorized person; and
- the package leaflet and any medical information must draw the attention of the medical practitioner to the fact that the particulars available concerning the medicinal product in question are as yet inadequate in certain specified respects.

A marketing authorization under exceptional circumstances is subject to annual review to reassess the risk-benefit balance in an annual reassessment procedure. Continuation of the authorization is linked to the annual reassessment and a negative assessment could potentially result in the marketing authorization being suspended or revoked. The renewal of a marketing authorization of a medicinal product under exceptional circumstances, however, follows the same rules as a "normal" marketing authorization. Thus, a marketing authorization under exceptional circumstances is granted for an initial five years, after which the authorization will become valid indefinitely, unless the EMA decides that safety grounds merit one additional five-year renewal.

The European Commission may also grant a so-called "conditional marketing authorization" prior to obtaining the comprehensive clinical data required for an application for a full marketing authorization. Such conditional marketing authorizations may be granted for product candidates (including medicines designated as orphan medicinal products), if (i) the risk-benefit balance of the product candidate is positive, (ii) it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data, (iii) the product fulfills an unmet medical need and (iv) the benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required. A conditional marketing authorization may contain specific obligations to be fulfilled by the marketing authorization holder, including obligations with respect to the completion of ongoing or new studies, and with respect to the collection of pharmacovigilance data. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions and/or specific obligations. The timelines for the centralized procedure described above also apply with respect to the review by the CHMP of applications for a conditional marketing authorization.

The EU medicines rules expressly permit the EU Member States to adopt national legislation prohibiting or restricting the sale, supply or use of any medicinal product containing, consisting of or derived from a specific type of human or animal cell, such as embryonic stem cells. While the products we have in development do not make use of embryonic stem cells, it is possible that the national laws in certain EU Member States may prohibit or restrict us from commercializing our products, even if they have been granted an EU marketing authorization.

Unlike the centralized authorization procedure, the decentralized marketing authorization procedure requires a separate application to, and leads to separate approval by, the competent authorities of each EU Member State in which the product is to be marketed. This application is identical to the application that would be submitted to the EMA for authorization through the centralized procedure. The reference EU Member State prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. The resulting assessment report is submitted to the concerned EU Member States who, within 90 days of receipt, must decide whether to approve the assessment report and related materials. If a concerned EU Member State cannot approve the assessment report and related materials due to concerns relating to a potential serious risk to public health, disputed elements may be referred to the European Commission, whose decision is binding on all EU Member States.

The mutual recognition procedure similarly is based on the acceptance by the competent authorities of the EU Member States of the marketing authorization of a medicinal product by the competent authorities of other EU Member

States. The holder of a national marketing authorization may submit an application to the competent authority of an EU Member State requesting that this authority recognize the marketing authorization delivered by the competent authority of another EU Member State.

Regulatory Data Protection in the EU

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

Periods of Authorization and Renewals

A marketing authorization has an initial validity for five years in principle. The marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the EU Member State. To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. The European Commission or the competent authorities of the EU Member States may decide, on justified grounds relating to pharmacovigilance, to proceed with one further five-year period of marketing authorization. Once subsequently definitively renewed, the marketing authorization shall be valid for an unlimited period. Any authorization which is not followed by the actual placing of the medicinal product on the EU n market (in case of centralized procedure) or on the market of the authorizing EU Member State within three years after authorization ceases to be valid.

Orphan Drug Designation and Exclusivity

Regulation (EC) No. 141/2000, as implemented by Regulation (EC) No. 847/2000 provides that a drug can be designated as an orphan drug 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 EU when the application is made, or (2) a life-threatening, seriously debilitating or serious and chronic condition in the EU and that without incentives it is unlikely that the marketing of the drug in the EU would generate sufficient return to justify the necessary investment. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the EU or, if such method exists, the drug 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 and a range of other benefits during the development and regulatory review process including scientific assistance for study protocols, authorization through the centralized marketing authorization procedure covering all member countries and a reduction or elimination of registration and marketing authorization fees. However, marketing authorization may be granted to a similar medicinal product with the same orphan indication during the ten-year period with the consent of the marketing authorization holder for the original orphan medicinal product or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities. 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. The period of market exclusivity may, in addition,

be reduced to six years if it can be demonstrated on the basis of available evidence that the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity.

Regulatory Requirements after a Marketing Authorization has been Obtained

In case an authorization for a medicinal product in the EU is obtained, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include:

- Compliance with the EU's stringent pharmacovigilance or safety reporting rules must be ensured. These rules can impose post-authorization studies and additional monitoring obligations.

- The manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the applicable EU laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice. These requirements include compliance with EU cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the EU with the intention to import the active pharmaceutical ingredients into the EU.

- The marketing and promotion of authorized drugs, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the EU notably under Directive 2001/83EC, as amended, and EU Member State laws. Direct-to-consumer advertising of prescription medicines is prohibited across the EU.

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the EU, which is commonly referred to as "Brexit". Thereafter, on March 29, 2017, the country formally notified the EU of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. The withdrawal of the United Kingdom from the EU will take effect either on the effective date of the withdrawal agreement or, in the absence of agreement, two years after the United Kingdom provides a notice of withdrawal pursuant to the EU Treaty. Since the regulatory framework for pharmaceutical products in the United Kingdom, covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from EU directives and regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the United Kingdom. It remains to be seen how, if at all, Brexit will impact regulatory requirements for product candidates and products in the United Kingdom.

Pricing Decisions for Approved Products

In the EU, 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 product candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the EU 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. 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 EU have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage health care expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the EU. The downward pressure on health care costs in general, particularly prescription products, 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 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 products, if approved in those countries.

Sales and Marketing

We hold North American and European commercialization rights to SY-1425 for all cancer indications, and worldwide rights to SY-1365 and all of our other preclinical programs for all potential indications. 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.

Employees

As of December 31, 2017 we had 56 full-time employees, including 29 employees with M.D. or Ph.D. degrees. Of these full-time employees, 44 employees are engaged in research and development activities and 12 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.

Corporate Information

We were incorporated under the laws of the State of Delaware on November 9, 2011 under the name LS22, Inc. We changed our name to Syros Pharmaceuticals, Inc. on August 15, 2012. Our principal executive office is located at 620 Memorial Drive, Suite 300, Cambridge, Massachusetts 02139, and our telephone number is (617) 744-1340.

Information Available on the Internet

Our Internet website address is *www.syros.com*. The information contained on, or that can be accessed through, our website is not a part of or incorporated by reference in this Annual Report on Form 10-K. We have included our website address in this in this Annual Report on Form 10-K solely as an inactive textual reference. We make available free of charge through our website our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to those reports filed or furnished pursuant to Sections 13(a) and 15(d) of the Exchange Act. We make these reports available through the "SEC Filings" section of our website as soon as reasonably practicable after we electronically file such reports with, or furnish such reports to, the SEC. We also make available, free of charge on our website, the reports filed with the U.S. Securities and Exchange Commission, or SEC, by our executive officers, directors and 10% stockholders pursuant to Section 16 under the Exchange Act as soon as reasonably practicable after copies of those filings are provided to us by those persons. You can find, copy and inspect information we file at the SEC's public reference room, which is located at 100 F Street, N.E., Room 1580, Washington, DC 20549. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the SEC's public reference room. You can review our electronically filed reports and other information that we file with the SEC on the SEC's website at *http://www.sec.gov*.

ITEM 1A. RISK FACTORS

We operate in a dynamic and rapidly changing business environment that involves multiple risks and substantial uncertainty. The following discussion addresses risks and uncertainties that could cause, or contribute to causing, actual results to differ from expectations in material ways. In evaluating our business, investors should pay particular attention to the risks and uncertainties described below and in other sections of this Annual Report on Form 10-K and in our subsequent filings with the SEC. These risks and uncertainties, or other events that we do not currently anticipate or that we currently deem immaterial also may affect our results of operations, cash flows and financial condition. The trading price of our common stock could also decline due to any of these risks, and you could 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 $29.8 million, $47.7 million and $54.0 million for the years ended December 31, 2015, 2016 and 2017, respectively. As of December 31, 2017, we had an accumulated deficit of $155.3 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 the sale of equity securities. 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' equity (deficit) and working capital.

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

- continue our planned clinical development activities with respect to SY-1425, a selective retinoic acid receptor alpha, or RARα, agonist that is currently being evaluated in combination with azacitidine, a hypomethylating agent, and with daratumumab, an anti-CD38 antibody, in a Phase 2 clinical trial, and SY-1365, a selective inhibitor of cyclin-dependent kinase 7, or CDK7, that is currently in the dose-escalation portion of a Phase 1 clinical trial in patients with advanced solid tumors;
- develop and seek approval of companion diagnostic tests for use in identifying patients who may benefit from treatment with our products and product candidates;
- initiate and continue research, preclinical and clinical development efforts for our research and 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 and add operational, financial and management information systems, including personnel and systems to support our product development and commercialization efforts 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 and early clinical research. We have not yet demonstrated an ability to advance a program into a late-stage clinical trial, obtain marketing approvals, manufacture a product at commercial scale or arrange for a third party to do so on our behalf, develop companion diagnostic tests 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 with respect to our ongoing Phase 2 clinical trial of SY-1425 in combination with azacitidine and daratumumab, as we develop and seek approval of companion diagnostic tests for use in identifying patients who may benefit from treatment with SY-1425, advance the clinical development of SY-1365 into planned Phase 1 expansion cohorts in ovarian and breast cancers, initiate new research and 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 for products or product candidates covered by licensed

intellectual property rights. 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, 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 will be required to expend significant funds in order to advance the development of SY-1425 and SY-1365, as well as our other research and preclinical programs. In addition, while we may seek one or more collaborators for future development of our current product candidates 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, our existing cash, cash equivalents and marketable securities 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 candidates 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 to support our internal research and development efforts. 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 our existing cash, cash equivalents and marketable securities as of December 31, 2017, together with amounts received from Incyte Corporation, or Incyte, in connection with our collaboration and option agreement executed in January 2018 and the net proceeds from the underwritten public offering of our common stock and concurrent private placement of our common stock to Incyte that closed in February 2018, will enable us to fund our planned operating expense and capital expenditure requirements into 2020. Our estimate as to how long we expect our existing cash, cash equivalents, and marketable securities 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 SY-1365 and any associated companion diagnostic tests;
- research and preclinical development efforts for any future product candidates that we may develop;
- the number of future product candidates that we pursue and their development requirements;
- our ability to enter into, and the terms and timing of, any collaborations, licensing agreements or other arrangements;
- whether our target discovery collaboration with Incyte Corporation, or Incyte, will yield any validated targets, whether Incyte will exercise any of its options to exclusively license intellectual property directed to such targets, and whether and when any of the target validation fees, option exercise fees, milestone payments or royalties under the collaboration agreement with Incyte will ever be paid;
- 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, operate as a public company, 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, 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, as we did through a public offering of our common stock that closed in February 2018, the ownership interests of our existing stockholders may be diluted, and the terms of these securities could include liquidation or other preferences and anti-dilution protections that could adversely affect our stockholders' rights. 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 product 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 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 a late-stage clinical trial 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

demonstrated sufficient safety or efficacy of any of our product candidates in clinical trials to warrant further development in the patient population studied.

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:

- insights regarding disease targets that are obtained through the use of our gene control platform may be generated independently through alternative approaches or be published by third parties;
- 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 SY-1365. If we are unable to initiate or complete the clinical development of, obtain marketing approval for or successfully commercialize SY-1425 or SY-1365, 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 SY-1365. 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 SY-1365 will depend on several factors, including the following:

- successful initiation, enrollment and completion of clinical trials;
- a safety, tolerability and efficacy profile, alone or in combination with other approved or investigational products, 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 successful development and approval of companion diagnostic tests for use in identifying patients who may benefit from treatment with SY-1425 or SY-1365;
- 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 suppliers of raw materials and drug substance and drug product manufacturers;
- 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 Co. Ltd., or TMRC;
- 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 SY-1365, 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 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.

We are conducting a Phase 2 clinical trial of SY-1425 in combination with azacitidine in genomically defined subsets of patients with newly-diagnosed acute myeloid leukemia, or AML, who are not suitable candidates for standard chemotherapy, and in combination with daratumumab in genomically defined patients with relapsed or refractory AML or higher-risk myelodysplastic syndrome, or MDS, identified using our biomarkers. We anticipate reporting clinical data from this trial in the fourth quarter of 2018. We are collaborating with a third party with respect to the clinical trial assay being used to select patients with our RARA and IRF8 biomarkers for inclusion in the trial. Our anticipated time to data in this trial is subject to our continued ability to initiate clinical trial sites and recruit eligible patients, the performance of the clinical trial assay and the prevalence of patients with these biomarkers, and the satisfaction by biomarker-positive

patients of other eligibility criteria for participation in the trial. The rate of patient enrollment in the trial is difficult to predict. As a result, there can be no assurance that we will enroll or have data from the trial when we anticipate.

We are also conducting a Phase 1 clinical trial of SY-1365 in patients with advanced solid tumors. We expect to report initial clinical data from the dose escalation portion of this trial in the fourth quarter of 2018. Our anticipated time to data in this trial is subject to our ability to recruit eligible patients and the number of dose cohorts that will need to be enrolled prior to observing pharmacokinetic activity, if achieved at all. Our assumption as to the activity of SY-1365 at particular dose levels may prove to be incorrect. There can be no assurance that we will enroll or have data from the trial when we anticipate.

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 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. It is also 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. For example, in December 2017 we reported data from our Phase 2 clinical trial evaluating SY-1425 as a single agent in genomically defined subsets of patients with relapsed or refractory AML and higher risk MDS. While biological and clinical activity was observed in certain patients enrolled in the trial, the data were not sufficiently robust to warrant further development of SY-1425 as a single agent in these patient populations and we elected to stop enrollment in the portions of our Phase 2 clinical trial evaluating SY-1425 as a single agent. We face a similar risk of failure in our ongoing evaluation of SY-1425 in combination with azacitidine and daratumumab. 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 of 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, SY-1365 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 control approaches may be unpredictable. Tamibarotene, the active ingredient in SY-1425, 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 (also known as ATRA), Retin-A, retinol (found in over-the-counter skin creams), isotretinoin and bexarotene. In addition, our experience administering SY-1365 to humans has been limited to date, so the safety profile that SY-1365 will demonstrate in human clinical trials is unknown. We are and expect to continue evaluating the administration of tamibarotene in combination with other biological and pharmaceutical products, including azacitidine and daratumumab, in patients with AML, MDS and other hematologic malignancies, and we plan to evaluate SY-1365 in combination with a chemotherapeutic agent in patients with ovarian cancer. We cannot predict at this time whether the combination of our product candidates with another product will be well tolerated by patients in clinical studies or that any unexpected adverse events or undesirable side effects will not occur. 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;

- 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 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 candidates 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. Genomically defined diseases may, however, 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. Moreover, in light of the recent approval of new products for the treatment of AML, there is substantial competition for patients to be enrolled in clinical trials for this disease. 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.

The data supporting our clinical development strategies for SY-1425 and SY-1365 have been derived entirely 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 candidates 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 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 occur, 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, SY-1365 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 candidates, 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.

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. For example, we are aware of four new drugs approved by the FDA during 2017 for the treatment of AML or patient subsets within AML: midostaurin, enasidanib, daunorubicin + cytarabine liposome, and gemtuzumab. SY-1425 may also face competition from other investigational products currently in clinical development for AML and MDS, including venetoclax, which is currently being evaluated by AbbVie, Inc. in two randomized pivotal studies in patients with AML, as well as investigational products in development from Takeda Pharmaceutical Co. Ltd., Daiichi Sankyo Company, Limited, Agios Pharmaceuticals, Inc., Novartis AG, Bristol-Myers Squibb Co., Eli Lilly & Co., Eisai Inc., Celgene Corporation, Pfizer, Inc., Incyte Corporation and FORMA Therapeutics, LLC. We are aware of only one other selective RARα program, a compound in development from Io Therapeutics, Inc. which, according to a government-sponsored website, is in an investigator initiated Phase 1/2 study in a non-selective patient group in relapsed and refractory AML, high-risk MDS and chronic myelomonocytic leukemia. In addition, we are aware of an oral CDK7 inhibitor being developed by Carrick Therapeutics Ltd. that has recently entered Phase 1 clinical development, and are aware of several other selective CDK7 inhibitor programs that we believe are in preclinical development, including programs from Aurigene Discovery Technologies Ltd., Ube Industries Ltd., Qurient Co. Ltd., and Beta Pharma, Inc. SY-1365 may face competition from these selective CDK7 inhibitors.

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;
- 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 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 and our license rights to SY-1425 from TMRC are limited to human cancer indications, 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.

Our internal computer systems, or those used by our third-party research institution collaborators, vendors or other contractors or consultants, may fail or suffer security breaches.

Despite the implementation of security measures, our internal computer systems and those of our vendors and other contractors and consultants may be vulnerable to damage from computer viruses and unauthorized access. Although to our knowledge we have not experienced any such material system failure or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations. For example, the loss of clinical trial data from completed, ongoing or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on our third-party research institution collaborators for research and development of our product candidates and other third parties for the manufacture of our product candidates and to conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or systems, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our product candidates could be delayed.

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 by 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 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. 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.

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.

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, or to use our gene control platform to identify and validate targets in diseases beyond our current areas of focus, as we have with Incyte in the field of myeloproliferative neoplasms. If and when 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 collaborators' abilities to successfully perform the functions assigned to them in these arrangements. In addition, 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.

We expect to seek to establish additional 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 additional collaborators for the development and commercialization of one or more of our product candidates or to validate targets. 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.

Our target discovery collaboration with Incyte contains, and any collaboration agreement that we enter into in the future may contain, restrictions on our ability to enter into potential collaborations, to conduct research or development in certain fields, 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.

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 Cancer Institute, or 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 Dana-Farber, pursuant to which we were granted a predominantly exclusive, with certain non-exclusive exceptions, license under specified U.S. patents relating to *MYC* modulators; 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 five and ten years, respectively, because SY-1425 has not been approved in these markets. Composition of matter patent protection in the United States and elsewhere covering SY-1425 has expired, however. We may be limited in our ability to list our method 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 of a generic version of SY-1425 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. In addition, any off-label use of a generic version of SY-1425 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 and commercialize SY-1425 for human cancers in North America and Europe, and SY-1365 for all potential uses worldwide. 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 have entered into a standby license with TMRC and Toko Pharmaceuticals Ind. Co. Ltd., or Toko, providing that if at any time the license agreement between Toko and TMRC relating to the SY-1425 rights that TMRC has licensed to us terminates or otherwise ceases to be in effect for any reason, Toko will grant directly to us such rights and licenses with respect to SY-1425 as are necessary for us to continue to develop SY-1425. If the TMRC license agreement terminates and this standby license 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 except that, 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, or 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 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 issued in-licensed United States patent relating to this subject matter. We are in communication with that third party regarding the timing under which we would grant them a license under our in-licensed patent. If we are unsuccessful in negotiating a license on acceptable terms, 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 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. It is possible, however, that we would be unable 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). The applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authority in other countries, may not agree, however, 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, contractors and vendors 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 regulatory 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.

If we are required by the FDA to obtain approval of a companion diagnostic in connection with approval of a candidate therapeutic product, and we do not obtain or there are delays in obtaining FDA approval of a diagnostic device, we will not be able to commercialize the product candidate and our ability to generate revenue will be materially impaired.

In August 2014, the FDA issued final guidance clarifying the requirements that will apply to approval of therapeutic products and *in vitro* companion diagnostics. According to the guidance, if the FDA determines that a companion diagnostic device is essential to the safe and effective use of a novel therapeutic product or indication, the FDA generally will not approve the therapeutic product or new therapeutic product indication if the companion diagnostic is not also approved or cleared for that indication. Under the Federal Food, Drug, and Cosmetic Act, or FDCA, companion diagnostics are regulated as medical devices and the FDA has generally required companion diagnostics intended to select the patients who will respond to cancer treatment to obtain premarket approval, or a PMA. Consequently, we anticipate that certain of our companion diagnostics may require us or our collaborators to obtain a PMA. The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the

FDA, involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA approval is not guaranteed and may take considerable time, and the FDA may ultimately respond to a PMA submission with a not approvable determination based on deficiencies in the application and require additional clinical trial or other data that may be expensive and time-consuming to generate and that can substantially delay approval. As a result, if we or our collaborators are required by the FDA to obtain approval of a companion diagnostic for a candidate therapeutic product, and we or our collaborators do not obtain or there are delays in obtaining FDA approval of a diagnostic device, we will not be able to commercialize the product candidate and our ability to generate revenue will be materially impaired.

In its August 2014 guidance, the FDA also indicated that companion diagnostics used to make treatment decisions in clinical trials of a therapeutic product generally will be considered investigational devices. When a companion diagnostic is used to make critical treatment decisions, such as patient selection, the FDA stated that the diagnostic will be considered a significant risk device requiring an investigational device exemption. The FDA may find that a companion diagnostic that we, alone or with a third party, plan to develop does not comply with those requirements and, if this were to occur, we would not be able to proceed with our planned trial of the applicable product candidate in these patient populations.

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.

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

We, or any future collaborators, may not be able to obtain orphan drug designation or 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 have obtained orphan drug designation for SY-1425 for the treatment of AML in the United States. In the future, however, we or any future collaborators may seek orphan drug designations for SY-1425 in other indications or territories or for other 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.

On August 3, 2017, Congress passed the FDA Reauthorization Act of 2017 which, among other things, codified the FDA's pre-existing regulatory interpretation, to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

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.

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 products 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 the FDA.

Designation as a Breakthrough Therapy is within the discretion of the FDA. Accordingly, even if we believe that one of our product candidates meets the criteria for designation as a Breakthrough Therapy, the FDA may disagree and instead determine not to make such designation. Even if we receive Breakthrough Therapy designation, the receipt of such designation for a product candidate may not result in a faster development or regulatory review or approval process compared to 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. Even if we receive Fast Track designation, however, 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.

Under the Cures Act and the Trump Administration's regulatory reform initiatives, the FDA's policies, regulations and guidance may be revised or revoked and that could prevent, limit or delay regulatory approval of our product candidates, which would impact our ability to generate revenue.

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

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

Current and future legislation may increase the difficulty and cost for us and any future collaborators to obtain marketing approval of 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 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, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA. Among the provisions of the ACA 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;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices;
- extension of manufacturers' Medicaid rebate liability;
- expansion of eligibility criteria for Medicaid programs;

- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report certain financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 and, due to subsequent legislative amendments to the statute, will stay in effect through 2025 unless additional congressional action is taken, and the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Further, there have been several recent U.S. congressional inquiries and proposed state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products.

We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

Since enactment of the ACA, there have been numerous legal challenges and Congressional actions to repeal and replace provisions of the law. In May 2017, the U.S. House of Representatives passed legislation known as the American Health Care Act of 2017. Thereafter, the Senate Republicans introduced and then updated a bill to replace the ACA known as the Better Care Reconciliation Act of 2017. The Senate Republicans also introduced legislation to repeal the ACA without companion legislation to replace it, and a “skinny” version of the Better Care Reconciliation Act of 2017. In addition, the Senate considered proposed healthcare reform legislation known as the Graham-Cassidy bill. None of these measures was passed by the U.S. Senate.

The Trump Administration has also taken executive actions to undermine or delay implementation of the ACA. In January 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. In October 2017, the President signed a second Executive Order allowing for the use of association health plans and short-term health insurance, which may provide fewer health benefits than the plans sold through the ACA exchanges. At the same time, the Administration announced that it will discontinue the payment of cost-sharing reduction, or CSR, payments to insurance companies until Congress approves the appropriation of funds for such CSR payments. The loss of the CSR payments is expected to increase premiums on certain policies issued by qualified health plans under the ACA.

A bipartisan bill to appropriate funds for CSR payments was introduced in the Senate, but the future of that bill is uncertain. More recently, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by the President on December 22, 2017, Congress repealed the “individual mandate.” The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Further, each chamber of Congress has put forth multiple bills designed to

repeal or repeal and replace portions of the ACA. Although none of these measures has been enacted by Congress to date, Congress may consider other legislation to repeal and replace elements of the ACA. Congress will likely consider other legislation to replace elements of the ACA during the next Congressional session.

We will continue to evaluate the effect that the ACA and its possible repeal and replacement could have on our business. It is possible that repeal and replacement initiatives, if enacted into law, could ultimately result in fewer individuals having health insurance coverage or in individuals having insurance coverage with less generous benefits. While the timing and scope of any potential future legislation to repeal and replace ACA provisions is highly uncertain in many respects, it is also possible that some of the ACA provisions that generally are not favorable for the research-based pharmaceutical industry could also be repealed along with ACA coverage expansion provisions Accordingly, such reforms, if enacted, could have an adverse effect on anticipated revenue 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 commercialize product candidates.

The costs of prescription pharmaceuticals in the United States has also been the subject of considerable discussion in the United States, and members of Congress and the Administration have stated that they will address such costs through new legislative and administrative measures. The pricing of prescription pharmaceuticals is also subject to governmental control outside the United States. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost effectiveness of our product candidates to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our ability to generate revenues and become profitable could be impaired. In the European Union, similar political, economic and regulatory developments may affect our ability to profitably commercialize our products. In addition to continuing pressure on prices and cost containment measures, legislative developments at the European Union or member state level may result in significant additional requirements or obstacles that may increase our operating costs.

Moreover, 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 U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us and any future collaborators to more stringent product labeling and post-marketing testing and other requirements.

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 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.

We have adopted a Code of Business Conduct and Ethics that mandates compliance with the FCPA and other anti-corruption laws applicable to our business throughout the world. We cannot assure you, however, 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. We do not, however, 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, and it is unclear what impact the decision by the United Kingdom to leave the European Union will have on the global economy. 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 candidates and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could strain our suppliers, possibly 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; [insert name], our chief financial officer; Eric R. Olson, Ph.D., our chief scientific officer; Gerald E. Quirk, Esq., our chief legal and administrative officer; David A. Roth, M.D., our chief medical officer; and Jeremy P. Springhorn, Ph.D., our chief business officer. Each of our 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.

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. 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.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of clinical development, 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

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

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

Our shares of common stock began trading on the Nasdaq Global Select Market on June 30, 2016. Given the limited trading history of our common stock, there is a risk that an active trading market for our shares will not be sustained, which could put downward pressure on the market price of our common stock and thereby affect the ability of our stockholders to sell their shares. 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.

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

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 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 SY-1365;
- the success of existing or new competitive products or technologies;
- 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 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 from the date of our initial public offering. 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. 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 must maintain effective internal control over financial reporting, and if we are unable to do so, the accuracy and timeliness of our financial reporting may be adversely affected, which could have a material adverse effect on our business and stock price.

We must maintain effective internal control over financial reporting in order to accurately and timely report our results of operations and financial condition. In addition, as a public company, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, requires, among other things, that we assess the effectiveness of our disclosure controls and procedures quarterly and the effectiveness of our internal control over financial reporting at the end of each fiscal year.

The rules governing the standards that must be met for our management to assess our internal control over financial reporting pursuant to Section 404 of the Sarbanes-Oxley Act are complex and require significant documentation, testing and possible remediation. These standards require that our audit committee be advised and

regularly updated on management's review of internal control over financial reporting. Our management may not be able to effectively and timely implement controls and procedures that comply with the increased regulatory compliance and reporting requirements that are applicable to us as a public company. If we fail to staff our accounting and finance function adequately or maintain internal control over financial reporting adequate to meet the demands that are placed upon us as a public company, including the requirements of the Sarbanes-Oxley Act, our business and reputation may be harmed and our stock price may 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, 2017, we had federal and state net operating loss carryforwards of $136.4 million and $138.8 million, respectively, and federal and state research and development tax credit carryforwards of $6.1 million and $1.8 million, respectively, each of which if not utilized will expire at various dates through 2037. 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, 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.

The recently passed comprehensive tax reform bill could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law new legislation that significantly revised the Internal Revenue Code of 1986, as amended. The newly enacted federal income tax law, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the new federal tax law is uncertain and our business and financial condition could be adversely affected. In addition, it is uncertain how various states will respond to the newly enacted federal tax law. The impact of this tax reform on holders of our common stock is also uncertain and could be adverse. We urge you to consult with your legal and tax advisors with respect to this legislation and the potential tax consequences of investing in or holding our common stock.

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.

Our executive officers and directors, combined with our stockholders who own more than 5% of our outstanding common stock and their affiliates, in the aggregate, beneficially own a majority 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.

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 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. 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, 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.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

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.

ITEM 3. LEGAL PROCEEDINGS

None.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS, AND ISSUER PURCHASES OF EQUITY SECURITIES

Certain Information Regarding the Trading of Our Common Stock

Our common stock trades under the symbol "SYRS" on the Nasdaq Global Select Market and has been publicly traded since June 30, 2016. Prior to this time, there was no public market for our common stock The following table sets forth the high and low sales price of our common stock as reported on the Nasdaq Global Select Market for the periods indicated:

	High	Low
Year ended December 31, 2016:		
Second Quarter (beginning June 30, 2016)	$ 19.80	$ 14.58
Third Quarter	$ 21.50	$ 8.16
Fourth Quarter	$ 16.85	$ 11.31
Year ended December 31, 2017:		
First Quarter	$ 16.74	$ 10.22
Second Quarter	$ 19.22	$ 13.27
Third Quarter	$ 24.38	$ 11.21
Fourth Quarter	$ 17.62	$ 6.30

Holders of Our Common Stock

As of February 28, 2018, there were approximately 61 holders of record of shares of our common stock. This number does not include stockholders for whom shares are held in "nominee" or "street" name.

Dividend Policy

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

Stock Performance Graph

The following performance graph and related information shall not be deemed to be "soliciting material" or to be "filed" with the Securities and Exchange Commission, or SEC, for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, nor shall such information be incorporated by reference into any future filing under the Exchange Act or Securities Act of 1933, as amended, or the Securities Act, except to the extent that we specifically incorporate it by reference into such filing.

The following graph compares the performance of our common stock to the Nasdaq Composite Index and to the Nasdaq Biotechnology Index from June 30, 2016 (the first date that shares of our common stock were publicly traded) through December 29, 2017, which was the last trading day of the year. The comparison assumes $100 was invested in our common stock and in each of the foregoing indices after the market closed on June 30, 2016, and it assumes reinvestment of dividends, if any. The stock price performance included in this graph is not necessarily indicative of future stock price performance.

Use of Proceeds from Registered Securities

On July 6, 2016, we closed our initial public offering, or our IPO, in which we issued and sold 4,600,000 shares of our common stock at a public offering price of $12.50 per share, including 600,000 shares of common stock sold pursuant to the underwriters' exercise of their option to purchase additional shares of common stock, for aggregate gross proceeds of $57.5 million. All of the shares issued and sold in the IPO were registered under the Securities Act pursuant to a Registration Statement on Form S-1 (File No. 333-211818), which was declared effective by the SEC on June 29, 2016. Cowen and Company, LLC and Piper Jaffray & Co. acted as joint book-running managers of the offering and as representatives of the underwriters. JMP Securities LLC and Wedbush Securities Inc. acted as co-managers for the offering. The offering commenced on June 29, 2016 and did not terminate until the sale of all of the shares offered.

The net offering proceeds to us, after deducting underwriting discounts and offering expenses payable by us totaling $7.6 million, were approximately $49.9 million. No offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning 10.0% or more of any class of our equity securities or to any other affiliates.

As of December 31, 2017, we estimate that we have used all of the net proceeds from the IPO to fund manufacturing and clinical development activities for SY-1425, IND-enabling studies and manufacturing activities for SY-1365, and other research activities in support of our preclinical programs and gene control platform, and for working capital and other general corporate purposes.

ITEM 6. SELECTED CONSOLIDATED FINANCIAL DATA

The following selected consolidated financial data should be read together with our financial statements and the related notes appearing at the end of this Annual Report on Form 10-K and Item 7 "Management's Discussion and Analysis of Financial Condition and Results of Operations" of this Annual Report on Form 10-K. We have derived the consolidated statement of operations data for the years ended December 31, 2017, 2016 and 2015 and the consolidated balance sheet data as of December 31, 2017 and 2016 from our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K. We have derived consolidated statement of operations data for the years ended December 31, 2014 and 2013, and consolidated balance sheet data as of December 31, 2015 and 2014 from our audited consolidated financial statements and related notes not included in this Annual Report on Form 10-K. The selected historical financial information in this section is not intended to replace our financial statements and the related notes thereto. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period.

	Year ended December 31				
	2017	2016	2015	2014	2013
	(in thousands, except for per share data)				
Statements of operations data:					
Revenue	$ 1,101	$ 317	$ 317	$ —	$ —
Operating expenses:					
Research and development	41,896	$ 37,817	$ 24,408	10,923	6,266
General and administrative	13,891	$ 10,463	$ 5,729	2,512	2,367
Total operating expenses	55,787	48,280	30,137	13,435	8,633
Loss from operations	(54,686)	(47,963)	(29,820)	(13,435)	(8,633)
Other income (expense), net	676	$ 220	$ 2	4	(32)
Net loss	$ (54,010)	$ (47,743)	$ (29,818)	$ (13,431)	$ (8,665)
Net loss per share applicable to common stockholders - basic and diluted (1)	$ (2.13)	$ (4.05)	$ (17.55)	$ (10.26)	$ (8.45)
Weighted-average number of common shares used in net loss per share applicable to common stockholders - basic and diluted (1)	25,406,845	12,696,414	1,980,286	1,525,018	1,095,973

	As of December 31,			
	2017	2016	2015	2014
	(in thousands)			
Balance sheet data:				
Cash, cash equivalents and marketable securities	$ 72,049	$ 83,593	$ 35,909	$ 60,393
Working capital (2)	60,746	75,941	28,493	59,291
Total assets	78,488	91,323	43,631	61,494
Convertible preferred stock (3)	—	—	82,013	82,013
Total stockholders' equity (deficit)	65,324	80,602	(47,964)	(21,772)

(1) See Note 2 to our consolidated financial statements for a description of the method used to calculate 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.
(2) 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.
(3) On July 6, 2016, upon the closing of our IPO, all of the then-outstanding shares of our convertible preferred stock converted into 15,988,800 shares of common stock.

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our audited financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis and set forth elsewhere in this Annual Report, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. You should review the section titled "Risk Factors" in Part I, Item 1A of this Annual Report for a discussion of important factors that could cause actual results to 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 pioneering an understanding of the non-coding regulatory region of the genome controlling the activation and repression of genes. Our goal is to advance a new wave of medicines to control the expression of genes. We have built a proprietary gene control platform designed to systematically and efficiently analyze this unexploited region of DNA in human disease tissue to identify novel targets linked to genomically defined patient populations and to develop drugs against those targets based on our expertise in transcriptional chemistry. Because gene expression is fundamental to the function of all cells, we believe that our gene control platform has broad potential to create medicines that achieve profound and durable benefit across therapeutic areas and a range of diseases. We are currently focused on developing treatments for cancer and diseases resulting from modifications of a single gene, also known as monogenic diseases, and are building a pipeline of gene control medicines.

Our lead product candidates are:

- SY-1425, a selective retinoic acid receptor alpha, or RARα, agonist that is being evaluated in combination with azacitidine, a hypomethylating agent frequently used to treat acute myeloid leukemia, or AML, and myelodysplastic syndrome, or MDS, patients, and with daratumumab, an anti-CD38 therapeutic antibody approved to treat multiple myeloma, in a Phase 2 clinical trial in genomically defined subsets of patients with AML and MDS; and

- SY-1365, a selective inhibitor of cyclin-dependent kinase 7, or CDK7, in a Phase 1 clinical trial in patients with advanced solid tumors for which expansions in ovarian and breast cancer are planned.

We also have multiple programs in earlier stages of research and development in oncology, including immuno-oncology, and monogenic diseases. Our goal is to build a fully integrated biopharmaceutical company based on our leadership position in gene control.

At the 59th American Society of Hematology Annual Meeting and Exposition in December 2017, or ASH 2017, we presented clinical data from our Phase 2 clinical trial evaluating SY-1425 as a single agent in defined subsets of AML and MDS patients with our proprietary *RARA* and *IRF8* biomarkers. In the trial, we observed that chronic daily dosing of SY-1425 administered at 6 mg/m^2 orally divided in two doses was generally well-tolerated and that clinical and biological activity was observed in patients enrolled in the trial. Specifically, clinical activity was observed in ten of 23 (43%) evaluable patients with relapsed or refractory AML and higher-risk MDS, including improvement in blood counts, reduction in leukemic blasts and one bone marrow complete response. Thirteen of the 23 (57%) evaluable relapsed or refractory AML and higher-risk MDS patients had stable disease. Myeloid differentiation was also observed in the bone marrow, consistent with the underlying mechanism of action of SY-1425 as a differentiating agent. Induction of CD38, a marker of cell differentiation, was observed after one 28-day cycle of treatment in 11 of 13 (85%) patients with pre- and post-treatment immunophenotyping samples.

We believe that these clinical data, when combined with preclinical data showing the tumor-killing activity of SY-1425 in combination with azacitidine and with daratumumab support the ongoing development of SY-1425 as a combination agent. SY-1425 has shown synergistic tumor-killing activity in combination with azacitidine as well as with daratumumab in preclinical models of *RARA* biomarker-positive AML. In combination with azacitidine, SY-1425 demonstrated greater clearance of tumor cells in bone marrow and other tissues and greater depth and duration of tumor response in preclinical models, compared to either azacitidine or SY-1425 alone. In combination with daratumumab, SY-1425 induced robust immune cell-mediated tumor death *in vitro*. Notably, AML cells do not normally express high

levels of CD38. We have shown that by inducing CD38 expression, SY-1425 sensitizes biomarker-positive AML models to the tumor-killing effects of daratumumab.

Our ongoing Phase 2 clinical trial is assessing the safety and efficacy of SY-1425 in combination with azacitidine in approximately 25 newly diagnosed AML patients who are not suitable candidates for standard chemotherapy and in combination with daratumumab in approximately 12 relapsed or refractory AML and higher-risk MDS patients. All patients enrolled or to be enrolled in the trial have been or will be prospectively selected using our proprietary *RARA* or *IRF8* biomarkers. In December 2017, we entered into a clinical supply agreement with Janssen Research and Development, LLC, or Janssen, pursuant to which Janssen agreed to supply us daratumumab for use in the trial. We are no longer dosing patients in the cohorts of the trial in which SY-1425 was being evaluated as a single agent. We expect to report initial clinical data from the combination cohorts of the trial in the fourth quarter of 2018.

We are continuing to dose patients in the dose-escalation phase of our ongoing Phase 1 clinical trial of SY-1365 and expect to report data from this phase of the trial in the fourth quarter of 2018. Once a maximum tolerated dose is reached in the dose escalation phase of the Phase 1 clinical trial and the recommended dosing schedule is identified, we intend to open expansion cohorts evaluating SY-1365 in multiple ovarian cancer populations as a single agent as well as in combination with carboplatin, a chemotherapeutic agent. The ovarian cancer populations include a 24-patient cohort evaluating SY-1365 as a single agent in patients who have relapsed after three or more prior therapies, a 24-patient cohort evaluating SY-1365 in combination with carboplatin in patients who relapsed after one or more prior therapies but who may still benefit from additional platinum-based treatment, and a 12-patient pilot cohort evaluating SY-1365 as a single agent in primary platinum-refractory disease. We also plan to evaluate SY-1365 in combination with fulvestrant, a hormonal medicine, in 12 patients with hormone-receptor positive, HER-2 negative metastatic breast cancer who have progressed after treatment with a CDK4/6 inhibitor plus an aromatase inhibitor. We also plan to evaluate the mechanism of action of SY-1365 in ten patients with any solid tumor accessible for biopsies. We expect that the expansion cohorts in our Phase 1 clinical trial will be open to enrollment in mid-2018.

We currently have five programs in our preclinical and discovery pipeline, including preclinical programs directed to the development of a CDK7 inhibitor that can be administered orally, inhibitors of cyclin-dependent kinase 12/13, and inhibitors of an immuno-oncology target, as well as discovery programs related to a gene control target to treat sickle cell disease and in the field of cancer. We plan to nominate a development candidate from one of these programs during 2018 that we can advance into preclinical studies to support a potential investigational new drug application, or IND, filing in 2019. We have and are continuing to use our gene control platform in collaboration with third parties to identify and validate targets in diseases beyond our current areas of focus. To this end, we entered a target discovery, research collaboration and option agreement with Incyte Corporation, or Incyte, in January 2018 under which we will use our platform to identify novel therapeutic targets with a focus on myeloproliferative neoplasms.

Recent Developments

Incyte Corporation

In January 2018, we entered into a target discovery, research collaboration and option agreement with Incyte. Under this agreement, we will use our gene control platform to identify novel therapeutic targets with a focus on myeloproliferative neoplasms, and Incyte will receive options to obtain exclusive worldwide rights to intellectual property resulting from the collaboration for the development and commercialization of therapeutic products directed to up to seven validated targets. Incyte will have exclusive worldwide rights to develop and commercialize any therapies under the collaboration that modulate those validated targets.

Under the terms of the collaboration agreement, Incyte paid us $10.0 million in up-front consideration, consisting of $2.5 million in cash and $7.5 million in pre-paid research funding. Our activities under this agreement are subject to a joint research plan and, subject to certain exceptions, Incyte will be responsible for funding our activities under the research plan, including amounts in excess of the pre-paid research funding amount. We are eligible to receive target selection milestone payments and option exercise fees of up to an aggregate of $54.0 million if Incyte selects the maximum number of targets for validation and exercises its option to obtain exclusive rights to collaboration intellectual property for therapeutic products directed to all seven validated targets. Should any therapeutic product be developed by Incyte against a target as to which Incyte has exercised its option to obtain exclusive rights to collaboration intellectual property, we will be eligible to receive milestone payments and, if approved and commercialized, royalty payments from Incyte. For each of the seven validated targets, we would become eligible to receive from Incyte a total of up to $50.0

million in development and regulatory milestone payments. If products arising from the collaboration are approved, we would become eligible to receive from Incyte, for each validated target, a total of up to $65.0 million in commercial milestone payments. Upon approval and commercialization of any therapeutic product resulting from the collaboration, we would become eligible to receive low single-digit royalties on net sales of such product.

In connection with the collaboration agreement, we sold 793,021 shares of our common stock to Incyte for an aggregate purchase price of $10.0 million in cash, or $12.61 per share, in a private placement. In addition, from the closing of this sale until the earlier of the second anniversary of such closing or the expiration or termination of the collaboration agreement, we have granted to Incyte the right to purchase up to its *pro rata* share of the securities offered in certain subsequent offerings of our common stock or common stock equivalents, subject to the terms and conditions set forth in the stock purchase agreement. In February 2018, we sold 144,505 additional shares of our common stock to Incyte at a price of $9.55 per share, resulting in gross proceeds to us of $1.4 million.

Public Offering

On January 30, 2018, we issued and sold an aggregate of 4,188,481 shares of our common stock in a public offering at a price per share $9.55 per share, resulting in gross proceeds of $40.0 million before deducting underwriting commissions and fees estimated to be approximately $2.7 million. Additionally, on February 2, 2018, the underwriters exercised their option to purchase an additional 628,272 shares at a price per share of $9.55, resulting in additional gross proceeds of $6.0 million.

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. Our only source of revenue to date has been a research agreement with a multinational pharmaceutical company. For the year ended December 31, 2017 and 2016, we recognized $1.1 million and $0.3 million, respectively, in revenue related to this agreement. This research agreement expired on March 31, 2017 in accordance with its terms.

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 the development of product candidates, which include:

- employee-related expenses including salaries and benefits;
- stock-based compensation expense;
- external costs of funding activities performed by third parties that conduct research and development on our behalf and of purchasing supplies used in designing, developing and manufacturing preclinical study and clinical trial materials;
- consulting, licensing and professional fees related to research and development activities; and
- facilities costs, depreciation and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and other operating costs.

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.

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

The following table summarizes our external research and development expenses by program, as well as expenses not allocated to programs, for years ended December 31, 2017 and 2016 (in thousands):

	Year Ended December 31,	
	2017	2016
SY-1425 external costs	$ 9,227	$ 7,940
SY-1365 and other CDK7 program external costs	8,289	8,129
Other research and platform programs external costs	8,161	7,184
Employee-related expenses, including stock-based compensation	11,719	11,214
Facilities and other expenses	4,500	3,350
Total research and development expenses	$ 41,896	$ 37,817

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 activities related to an IND and minimally efficacious dose studies in animals, where applicable and requested under the good laboratory practice, or GLP, requirements of the FDA;
- approval of INDs for our product candidates to commence planned or future clinical trials;
- successful enrollment in, and completion of, clinical trials;
- successful data from our clinical programs that support an acceptable benefit-risk profile of our product candidates in the intended populations;
- successful development, and subsequent clearance or approval, of companion diagnostic tests for use in identifying potential patients;
- receipt of regulatory approvals from applicable regulatory authorities;
- 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. We also anticipate that we will incur increased accounting, audit, legal, compliance and director and officer insurance costs, as well as investor and public relations expenses, associated with operating as a public company.

Other Income, Net

Other income, net consists of interest income on our cash and cash equivalents, interest, dividends, amortization of premiums and discounts, realized gains and losses on sales of marketable securities and interest expense related to our equipment financing arrangement.

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.

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

Revenue

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.

The research agreement we entered with a multinational pharmaceutical company contained a single unit of accounting and we recognized 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 was 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 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 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. Prior to June 30, 2016, we were a privately-held company and lacked company-specific historical and implied volatility information. As such, 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 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.

Prior to becoming a public company, we determined the fair value of our common stock using the option pricing method, or OPM, or a hybrid of the probability-weighted expected return method and OPM. The fair value of our common stock underlying our stock-based awards was determined on each grant date by our board of directors. Upon becoming a public company, the fair value of the underlying shares of common stock equals the closing price of our stock on The Nasdaq Global Select Market on the date of grant.

The amount of stock-based compensation expense recognized is based on the fair value of the award on the date of grant. As a result of the adoption of ASU 2016-09, effective January 1, 2017, we account for forfeitures as they occur instead of estimating forfeitures at the time of grant and revising those estimates in subsequent periods if actual forfeitures differ from its estimates. Ultimately, the actual expense recognized over the vesting period will be for only those options that vest.

We have computed the fair value of stock options at the date of grant using the following weighted-average assumptions:

	Year Ended December 31,		
	2017	2016	2015
Weighted-average risk-free interest rate	2.07 %	1.36 %	1.78 %
Expected dividend yield	— %	— %	— %
Expected option term	6.05	5.98	6.09
Volatility	87.83 %	85.39 %	82.71 %

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.

Results of Operations

Comparison of Years Ended December 31, 2017 and 2016

The following table summarizes our results of operations for the years ended December 31, 2017 and 2016, together with the changes in those items in dollars (in thousands):

	Year Ended December 31,			
	2017	2016	Dollar Change	% Change
Statements of Operations Data:				
Revenue	$ 1,101	$ 317	$ 784	247 %
Operating expenses:				
Research and development	41,896	37,817	4,079	11 %
General and administrative	13,891	10,463	3,428	33 %
Total operating expenses	55,787	48,280	7,507	16 %
Other income, net	676	220	456	207 %
Net loss	$(54,010)	$(47,743)	$ 6,267	13 %

Revenue

In November 2014, we entered into a research agreement with a multinational pharmaceutical company for purposes of mapping immune cell super-enhancers and transcriptional targets in autoimmune disease. Under the research agreement, we were responsible for the conduct of all activities under separate projects, as defined in the research agreement. We recognized revenue on a completed performance basis for each project performed under the agreement. We recognized revenue of $1.1 million and $0.3 million during the years ended December 31, 2017 and December 31, 2016, respectively. The agreement with the multinational pharmaceutical company expired on March 31, 2017 in accordance with its terms.

Research and Development Expense

Research and development expense increased by approximately $4.1 million, or 11%, from $37.8 million for the year ended December 31, 2016 to $41.9 million for the year ended December 31, 2017. The following table summarizes our research and development expenses for the years ended December 31, 2017 and 2016, together with the changes to those items in dollars (in thousands):

	Year Ended December 31,			
	2017	2016	Dollar Change	% Change
External research and development	$23,785	$20,802	$ 2,983	14 %
Employee-related expenses, excluding stock-based compensation	10,053	8,234	1,819	22 %
Stock-based compensation	1,666	2,980	(1,314)	(44)%
Consulting, licensing and professional fees	1,892	2,451	(559)	(23)%
Facilities and other expenses	4,500	3,350	1,150	34 %
Total research and development expenses	$41,896	$37,817	$ 4,079	11 %

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

- an increase of approximately $3.0 million, or 14%, for expenses from third parties that conduct research and development and preclinical activities on our behalf, including an increase of approximately $5.5 million in clinical development for SY-1425 and SY-1365, offset by a decrease of $2.2 million in preclinical development work for SY-1365 as toxicology studies were completed and the Phase 1 clinical trial was initiated;

- an increase of approximately $1.8 million, or 22%, for increased personnel related expenses, including increased salary and benefits primarily due to the hire of key research and development personnel;

- a decrease of approximately $1.3 million, or 44%, for decreased stock-based compensation expense primarily related to the recognition of expense related to performance triggers achieved during 2016 for which no corresponding expense was recognized during 2017;

- a decrease of approximately $0.6 million, or 23% in consulting, licensing, and professional fees, due to the $0.5 million license payment paid to TMRC Co., Ltd., or TMRC, in 2016 under our license agreement with TMRC, which we refer to as the TMRC license agreement; and

- an increase of approximately $1.2 million, or 34%, for increases in the proportion of costs allocated to research and development, as well as increases in facilities costs including depreciation and maintenance expenses associated with our operating lease at our corporate headquarters beginning in August 2015.

General and Administrative Expense

General and administrative expense increased by approximately $3.4 million, or 33% from $10.5 million for the year ended December 31, 2016 to $13.9 million for the year ended December 31, 2017. The change in general and administrative expense was primarily attributable to an increase in employee-related costs, including salary, benefits and stock-based compensation, as well as increased consulting, licensing, and professional fees to support our overall growth as a company.

Other Income, Net

Other income, net consists of interest income on our cash and cash equivalents, interest, amortization of premiums and discounts on marketable securities, and interest expense related to our equipment financing arrangement. The increase in other income from the year ended December 31, 2016 to the year ended December 31, 2017 is due to a full year of investing activities in 2017, as we started investing in marketable securities beginning in October 2016.

Comparison of Years Ended December 31, 2016 and 2015

The following table summarizes our results of operations for the years ended December 31, 2016 and 2015, together with the changes in those items in dollars (in thousands):

	Year Ended December 31,			
	2016	2015	Dollar Change	Dollar Change
Statements of Operations Data:				
Revenue	$ 317	$ 317	$ —	— %
Operating expenses:				
Research and development	37,817	24,408	13,409	55 %
General and administrative	10,463	5,729	4,734	83 %
Total operating expenses	48,280	30,137	18,143	60 %
Other income, net	220	2	218	10,900 %
Net loss	$ (47,743)	$ (29,818)	$ 17,925	60 %

Revenue

In November 2014, we entered into a research agreement with a multinational pharmaceutical company for purposes of mapping immune cell super-enhancers and transcriptional targets in autoimmune disease. Under the research agreement, we were responsible for the conduct of all activities under separate projects, as defined in the research agreement. We recognized revenue on a completed performance basis for each project performed under the agreement. We recognized revenue of $0.3 million during each of the years ended December 31, 2016 and December 31, 2015.

Research and Development Expense

Research and development expense increased by approximately $13.4 million, or 55%, from $24.4 million for the year ended December 31, 2015 to $37.8 million for the year ended December 31, 2016. The following table summarizes our research and development expenses for the year ended December 31, 2016 and 2015, together with the changes to those items in dollars (in thousands):

	Year Ended December 31,			
	2016	2015	Dollar Change	% Change
External research and development	$20,802	$12,749	$ 8,053	63 %
Employee-related expenses, excluding stock-based compensation	8,234	5,344	2,890	54 %
Stock-based compensation	2,980	2,733	247	9 %
Consulting, licensing and professional fees	2,451	1,972	479	24 %
Facilities and other expenses	3,350	1,610	1,740	108 %
Total research and development expenses	$37,817	$24,408	$ 13,409	55 %

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

- an increase of approximately $8.1 million, or 63% for expenses from third parties that conduct research and development and preclinical activities on our behalf, including approximately $6.1 million in contract manufacturing and clinical development for SY-1425, a $1.0 million milestone payment made under our license agreement with TMRC in September 2016, and approximately $0.9 million for preclinical development for SY-1365 and advancement of the CDK7 program;
- an increase of approximately $2.9 million, or 54% for increased personnel related expenses, including increased salary and benefits primarily due to the hire of research and development personnel;
- an increase of approximately $0.2 million, or 9% for increased stock-based compensation expense;
- an increase of approximately $0.5 million, or 24% in consulting, licensing, and professional fees, due to increased preclinical, clinical and regulatory consulting fees for SY-1425 and SY-1365; and
- an increase of approximately $1.7 million, or 108% for increases in facilities costs including depreciation and maintenance expenses associated with our operating lease at our corporate headquarters beginning in August 2015.

General and Administrative Expense

General and administrative expense increased by approximately $4.7 million, or 83% from $5.7 million for the year ended December 31, 2015 to $10.5 million for the year ended December 31, 2016. The change in general and administrative expense was primarily attributable to an increase in employee-related costs, including salary, benefits and stock-based compensation, as well as increased consulting, licensing, 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.

Other Income, Net

Other income, net consists of interest income on our cash, cash equivalents and marketable securities, offset by interest expense related to our equipment financing arrangement. The increase in other income from the year ended December 31, 2015 to the year ended December 31, 2016 is due to a higher level of invested cash and cash equivalents from our proceeds.

Liquidity and Capital Resources

Sources of Liquidity

We funded our operations from inception through December 31, 2017 primarily through gross proceeds of $122.2 million from sales of our preferred stock and the issuance of convertible notes that subsequently converted into preferred stock, $57.5 million in gross proceeds from the sale of common stock in our initial public offering, or IPO, and $35.0 million in gross proceeds from the sale of common stock in a private placement in April 2017.

On July 20, 2017, we filed a universal shelf registration statement on Form S-3 with the SEC to register for sale from time to time up to $225.0 million of common stock, preferred stock, debt securities, warrants and/or units in one or more registered offerings. The shelf registration statement was declared effective on July 31, 2017. Further, in July 2017, we entered into a sales agreement with Cowen and Company, LLC, or Cowen, pursuant to which, from time to time, we may offer and sell shares of our common stock having an aggregate offering price of up to $50.0 million through Cowen pursuant to such universal shelf registration statement.

As of December 31, 2017, we had cash, cash equivalents and marketable securities of approximately $72.0 million.

Cash Flows

The following table provides information regarding our cash flows for the years ended December 31, 2017, 2016 and 2015 (in thousands):

	Year Ended December 31,		
	2017	2016	2015
Net cash provided by (used in):			
Operating activities	$(44,729)	$(40,536)	$(23,030)
Investing activities	(15,591)	(27,342)	(1,176)
Financing activities	33,937	90,557	(278)
Net increase (decrease) in cash and cash equivalents	$(26,383)	$ 22,679	$(24,484)

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 $44.7 million during the year ended December 31, 2017 compared to $40.5 million during the year ended December 31, 2016. The increase in cash used in operating activities was primarily due to an increase in our net loss of $6.3 million for the year ended December 31, 2017 as compared to the year ended December 31, 2016.

Net cash used in operating activities was $40.5 million during the year ended December 31, 2016 compared to $23.0 million during the year ended December 31, 2015. The increase in cash used in operating activities was primarily due to an increase in net loss of $17.9 million for the year ended December 31, 2016 as compared to the year ended December 31, 2015.

Net Cash Used in Investing Activities

Net cash used in investing activities was $15.6 million during the year ended December 31, 2017 compared to $27.3 million during the year ended December 31, 2016. The decrease in cash used in investing activities was primarily due to sales and maturities of marketable securities of $27.0 million during 2017 compared to no sales or maturities of marketable securities during 2016, offset by an increase in purchases of marketable securities during 2017.

Net cash used in investing activities was $27.3 million during the year ended December 31, 2016 compared to $1.2 million during the year ended December 31, 2015. The increase in cash used in investing activities was due to purchases of marketable securities as well as increased purchases of property and equipment associated with our corporate headquarters.

Net Cash Provided by (Used in) Financing Activities

Net cash provided by financing activities was $33.9 million during the year ended December 31, 2017, compared to net cash provided by financing activities of $90.6 million during the year ended December 31, 2016. The decrease in cash provided by financing activities is primarily due to the issuance of common stock in connection with the IPO in July 2016, as well as the issuance of $39.8 million in a preferred stock financing in January 2016, offset by gross proceeds of $35.0 million in connection with the sale of common stock through private placement in April 2017.

Net cash provided by financing activities was $90.6 million during the year ended December 31, 2016 compared to net cash used in financing activities of $0.3 million during the year ended December 31, 2015. The increase in cash provided by financing activities was primarily due to the issuance of common stock in connection with the IPO in July 2016, as well as the issuance of $39.8 million in a preferred stock financing in January 2016.

Funding Requirements

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue clinical trials of SY-1425 and SY-1365, seek to develop companion diagnostic tests for use with our product candidates, 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, 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 favorable terms, we would be forced to delay, reduce, eliminate, or out-license our research and development programs or future commercialization rights to our product candidates.

We believe that our cash, cash equivalents and marketable securities as of December 31, 2017, together with amounts received from Incyte in connection with our collaboration and option agreement executed in January 2018 and the net proceeds from the underwritten public offering of our common stock and concurrent private placement of our common stock to Incyte that closed in February 2018, will enable us to fund our planned operating expense and capital expenditure requirements into 2020. Our future capital requirements will depend on many factors, including:

- the scope, progress, timing, costs and results of clinical trials of SY-1425 and SY-1365 and any associated companion diagnostic tests;
- 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;
- whether our collaboration with Incyte will yield any validated targets, whether Incyte will exercise any of its options to exclusively license intellectual property directed to such targets, and whether and when any of the target validation fees, option exercise fees, milestone payments or royalties under the collaboration agreement with Incyte will ever be paid;

- 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, operate as a public company, 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, the ownership interests of our common stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. 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 and Commitments

As December 31, 2017, we have a capital lease for laboratory equipment that expires in March 2018 and a capital lease for office equipment that ends in April 2020. Additionally, we lease office space at 620 Memorial Drive in Cambridge, Massachusetts under a non-cancellable operating lease that expires in October 2020. The following table summarizes our significant contractual obligations as of payment due date by period at December 31, 2017:

	Payments due by period				
(in thousands)	Total	Less than 1 year	1 to 3 years	3 to 5 years	More than 5 years
Capital lease payments	$ 55	$ 48	$ 7	$ —	$ —
Operating lease payments	3,743	1,288	2,455	—	—
Total	$ 3,798	$ 1,336	$ 2,462	$ —	$ —

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 amended and restated 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. In May 2016, we paid TMRC $0.5 million representing the balance of the remaining upfront license fee and in September 2016, we made a $1.0 million milestone payment to TMRC upon the successful dosing of the first patient in our Phase 2 clinical trial of SY-1425.

We also entered into a supply arrangement with TMRC, under which the Company agreed to pay TMRC a fee for each kilogram of SY-1425 active pharmaceutical ingredient that is produced. During the year ended December 31, 2017, we paid TMRC $0.4 million in payments related to this agreement. No payments were made under this supply management arrangement during the year ended December 31, 2016.

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, or SEC, rules.

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.

As an EGC, we intend to rely on 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 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 our IPO; (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 SEC rules.

ITEM 7A. 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. However, because of the short-term nature of the duration of our portfolio and the low-risk profile of our investments, we believe an immediate 10% change in market interest rates would not be expected to have a material impact on the fair market value of our investments portfolio or on our financial condition or results of operations.

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 December 31, 2017, 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 year ended December 31, 2017.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

SYROS PHARMACEUTICALS, INC.
INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Syros Pharmaceuticals, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Syros Pharmaceuticals, Inc. (the Company) as of December 31, 2017 and 2016, the related consolidated statements of operations, comprehensive loss, convertible preferred stock and stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2017, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2017 and 2016, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2017, in conformity with US generally accepted accounting principles.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

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

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

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2014.
Boston, Massachusetts
March 12, 2018

SYROS PHARMACEUTICALS, INC.
CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share data)

	December 31, 2017	December 31, 2016
Assets		
Current assets:		
Cash and cash equivalents	$ 32,205	$ 58,588
Marketable securities	39,844	25,005
Accounts receivable	—	867
Prepaid expenses and other current assets	917	1,048
Restricted cash	193	—
Total current assets	73,159	85,508
Property and equipment, net	3,938	4,850
Other long-term assets	1,101	482
Restricted cash	290	483
Total assets	$ 78,488	$ 91,323
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 2,283	$ 2,415
Accrued expenses	9,728	6,115
Deferred revenue	—	550
Deferred rent, current portion	355	319
Capital lease obligations, current portion	47	168
Total current liabilities	12,413	9,567
Deferred rent, net of current portion	745	1,101
Capital lease obligations, net of current portion	6	53
Commitments and contingencies (Note 9)		
Stockholders' equity:		
Preferred stock, $0.001 par value; 10,000,000 shares authorized at December 31, 2017 and December 31, 2016, 0 shares issued and outstanding at December 31, 2017 and December 31, 2016	—	—
Common stock, $0.001 par value; 200,000,000 shares authorized at December 31, 2017 and December 31, 2016; 26,423,375 and 23,380,888 shares issued and outstanding at December 31, 2017 and December 31, 2016, respectively	26	23
Additional paid-in capital	220,606	181,844
Accumulated other comprehensive loss	(42)	(9)
Accumulated deficit	(155,266)	(101,256)
Total stockholders' equity	65,324	80,602
Total liabilities and stockholders' equity	$ 78,488	$ 91,323

See accompanying notes to consolidated financial statements.

SYROS PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS
(in thousands, except share and per share data)

	Year Ended December 31,		
	2017	2016	2015
Revenue	$ 1,101	$ 317	$ 317
Operating expenses:			
Research and development	41,896	37,817	24,408
General and administrative	13,891	10,463	5,729
Total operating expenses	55,787	48,280	30,137
Loss from operations	(54,686)	(47,963)	(29,820)
Other income, net	676	220	2
Net loss	$ (54,010)	$ (47,743)	$ (29,818)
Accrued dividends on preferred stock	—	(3,681)	(4,934)
Net loss applicable to common stockholders	$ (54,010)	$ (51,424)	$ (34,752)
Net loss per share applicable to common stockholders - basic and diluted	$ (2.13)	$ (4.05)	$ (17.55)
Weighted-average number of common shares used in net loss per share applicable to common stockholders - basic and diluted	25,406,845	12,696,414	1,980,286

See accompanying notes to consolidated financial statements.

SYROS PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(in thousands, except share and per share data)

	Year Ended December 31,		
	2017	2016	2015
Net loss	$ (54,010)	$ (47,743)	$ (29,818)
Other comprehensive loss:			
Unrealized holding losses on marketable securities	(33)	(9)	—
Comprehensive loss	$ (54,043)	$ (47,752)	$ (29,818)

See accompanying notes to consolidated financial statements.

SYROS PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)
(in thousands except share data)

	Series A Convertible Preferred Stock		Series B Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Stockholders' (Deficit) Equity
	# of Shares	Amount	# of Shares	Amount	# of Shares	Par Value				
Balance at December 31, 2014	30,350,000	$ 29,015	16,893,931	$ 52,998	1,640,009	$ 1	$ 1,922	$ —	$ (23,695)	$ (21,772)
Exercise of stock options and vesting of restricted stock awards	—	—	—	—	723,009	1	392	—	—	393
Stock-based compensation expense	—	—	—	—	—	—	3,233	—	—	3,233
Net loss	—	—	—	—	—	—	—	—	(29,818)	(29,818)
Balance at December 31, 2015	30,350,000	29,015	16,893,931	52,998	2,363,018	2	5,547	—	(53,513)	(47,964)
Issuance of Series B convertible preferred stock, net of issuance costs of $206	—	—	12,714,150	39,794	—	—	—	—	—	—
Conversion of Series A convertible preferred stock into common stock	(30,350,000)	(29,015)	—	—	8,093,326	8	29,007	—	—	29,015
Conversion of Series B convertible preferred stock into common stock	—	—	(29,608,081)	(92,792)	7,895,474	8	92,784	—	—	92,792
Exercise of stock options and vesting of restricted stock awards	—	—	—	—	429,070	—	395	—	—	395
Issuance of common stock under initial public offering, net of issuance costs of $7.6 million	—	—	—	—	4,600,000	5	49,877	—	—	49,882
Stock-based compensation expense	—	—	—	—	—	—	4,234	—	—	4,234
Other comprehensive loss	—	—	—	—	—	—	—	(9)	—	(9)
Net loss	—	—	—	—	—	—	—	—	(47,743)	(47,743)
Balance at December 31, 2016	—	$ —	—	$ —	23,380,888	$ 23	$ 181,844	$ (9)	$ (101,256)	$ 80,602
Exercise of stock options and vesting of restricted stock awards	—	—	—	—	449,896	—	1,799	—	—	1,799
Issuance of common stock through private placement, net of issuance costs of $2.4 million	—	—	—	—	2,592,591	3	32,544	—	—	32,547
Stock-based compensation expense	—	—	—	—	—	—	4,419	—	—	4,419
Other comprehensive loss	—	—	—	—	—	—	—	(33)	—	(33)
Net loss	—	—	—	—	—	—	—	—	(54,010)	(54,010)
Balance at December 31, 2017	—	$ —	—	$ —	26,423,375	$ 26	$ 220,606	$ (42)	$ (155,266)	$ 65,324

See accompanying notes to consolidated financial statements.

SYROS PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Year Ended December 31,		
	2017	2016	2015
Operating activities			
Net loss	$ (54,010)	$ (47,743)	$ (29,818)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	1,527	1,273	602
Loss on disposal of assets	—	4	17
Stock-based compensation expense	4,419	4,234	3,233
Net amortization of premiums and discounts on marketable securities	(102)	6	—
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	131	(508)	(390)
Accounts receivable	867	(317)	—
Other long-term assets	(365)	(482)	—
Restricted cash	—	—	(413)
Accounts payable	141	(404)	2,022
Accrued expenses	3,533	3,685	1,663
Deferred revenue	(550)	—	—
Deferred rent and lease incentive	(320)	(284)	54
Net cash used in operating activities	(44,729)	(40,536)	(23,030)
Investing activities			
Purchases of property and equipment	(821)	(2,322)	(1,176)
Purchases of marketable securities	(41,770)	(25,020)	—
Sales or maturities of marketable securities	27,000	—	—
Net cash used in investing activities	(15,591)	(27,342)	(1,176)
Financing activities			
Payments on capital lease obligations	(168)	(135)	(50)
Proceeds from issuance of common stock through employee benefit plans	1,799	395	392
Proceeds from issuance of convertible preferred stock, net of issuance costs	—	39,813	—
Proceeds from issuance of common stock, net of issuance costs	32,306	50,484	(620)
Net cash provided by (used in) financing activities	33,937	90,557	(278)
(Decrease) increase in cash and cash equivalents	(26,383)	22,679	(24,484)
Cash and cash equivalents			
Beginning of period	58,588	35,909	60,393
End of period	$ 32,205	$ 58,588	$ 35,909
Supplemental disclosure of cash flow information:			
Cash paid for interest	$ 9	$ 19	$ 18
Non-cash investing and financing activities			
Conversion of convertible preferred stock into common stock	$ —	$ 82,013	$ —
Property and equipment received but unpaid as of period end	$ 143	$ 349	$ 1,359
Assets acquired under capital lease	$ —	$ 17	$ 389
Assets acquired through lease incentive	$ —	$ —	$ 1,612
Offering costs incurred but unpaid as of period end	$ 13	$ —	$ 1,280

See accompanying notes to consolidated financial statements.

Syros Pharmaceuticals, Inc.
Notes to Consolidated Financial Statements

1. Nature of Business

Syros Pharmaceuticals, Inc. (the "Company"), a Delaware corporation formed in November 2011, is a biopharmaceutical company seeking an understanding of the non-coding regulatory region of the genome to advance new medicines to control the expression of disease-driving genes. The Company has built a proprietary platform designed to analyze this unexploited region of DNA in human disease tissue to identify and drug novel targets linked to genomically defined patient populations.

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 and discovery activities. If the Company is unable to raise capital when needed or on favorable terms, it would be forced to delay, reduce, eliminate or out-license certain of its research and development programs or future commercialization rights to its product candidates.

On July 6, 2016, the Company completed an initial public offering, in which the Company issued and sold 4,600,000 shares of its common stock at a public offering price of $12.50 per share, including 600,000 shares of common stock sold pursuant to the underwriters' exercise of their option to purchase additional shares of common stock, for aggregate gross proceeds of $57.5 million (the "IPO"). The Company received approximately $49.9 million in net proceeds from the IPO after deducting $7.6 million of underwriting discounts and commissions and offering costs. Upon the closing of the IPO, all of the outstanding shares of the Company's convertible preferred stock automatically converted into 15,988,800 shares of common stock at the applicable conversion ratio then in effect. Subsequent to the closing of the IPO, there were no shares of preferred stock outstanding. In connection with the IPO, the Company amended and restated its certificate of incorporation to change the authorized capital stock to 200,000,000 shares designated as common stock, and 10,000,000 shares designated as preferred stock, all with a par value of $0.001 per share. The significant increase in common stock outstanding in July 2016 relating to the IPO and conversion of convertible preferred stock had an impact on the year-over-year comparability of the Company's net loss per share calculations throughout 2017.

On April 26, 2017, the Company issued and sold an aggregate of 2,592,591 shares of its common stock in a private placement at an offering price of $13.50 per share, for aggregate gross proceeds of $35.0 million, before deducting placement agent fees of $2.1 million and other offering expenses of $0.3 million.

The Company has incurred significant annual net operating losses in every year since its inception. It expects to continue to incur significant and increasing net operating losses for at least the next several years. The Company's net losses were $54.0 million, $47.7 million and $29.8 million for the years ended December 31, 2017, 2016 and 2015, respectively. As of December 31, 2017, the Company had an accumulated deficit of $155.3 million. The Company has not generated any revenues from product sales, has not completed the development of any product candidate and may never have a product candidate approved for commercialization. The Company has financed its operations to date primarily through private placements of its preferred stock, the sale of common stock in the IPO, and a private placement of common stock in April 2017. The Company has devoted substantially all of its financial resources and efforts to research and development and general and administrative expense to support such research and development. The Company's 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 the Company's stockholders' equity and working capital. The Company believes that its cash, cash equivalents and marketable securities of $72.0 million as of December 31, 2017, together with amounts received from Incyte Corporation ("Incyte") in connection with the Company's collaboration and option agreement with Incyte executed in January 2018 and the net proceeds from the underwritten public offering of the Company's common stock and concurrent private placement of the Company's common stock to Incyte that closed in February 2018, will be sufficient to allow the Company to fund its current operating plan for a period of at least 12 months past the issuance date of these consolidated financial statements.

Syros Pharmaceuticals, Inc.
Notes to Consolidated Financial Statements (Continued)

2. Summary of Significant Accounting Policies

Basis of Presentation

The Company's consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States ("U.S. GAAP"). 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").

In connection with preparing for its IPO, the Company effected a one-for-3.75 reverse stock split of the Company's common stock. The reverse stock split became effective on June 17, 2016. The par value and authorized shares of common stock and convertible preferred stock were not adjusted as a result of the reverse stock split. All share and per share amounts in the financial statements and notes thereto have been retroactively adjusted for all periods presented to give effect to this reverse stock split, including reclassifying an amount equal to the reduction in par value of common stock to additional paid-in capital. The financial statements have also been retroactively adjusted to reflect adjustments to the conversion price for each series of convertible preferred stock effected in connection with the reverse stock split.

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 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 prior to the completion of the IPO, accrued expenses and income taxes. Actual results may differ from those estimates or assumptions.

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.

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, as well as overnight repurchase agreements, are stated at fair value. The Company maintains its bank accounts at one major financial institution.

Marketable Securities

The Company determines the appropriate classification of its marketable securities, which consist primarily of debt securities, at the time of purchase and reevaluates such designation at each balance sheet date. All of the Company's marketable securities are considered available-for-sale and carried at estimated fair values and reported in short-term marketable securities. Unrealized gains and losses on available-for-sale securities are excluded from net income and reported in accumulated other comprehensive income (loss) as a separate component of stockholders' equity (deficit). Other income, net, includes interest, dividends, amortization of premiums and discounts, realized gains and losses on sales of securities and other-than-temporary declines in the fair value of securities, if any. The cost of securities sold is based on the specific identification method. The Company regularly reviews all of its investments for other-than-temporary declines in fair value. The Company's review includes the consideration of the cause of the impairment, including the creditworthiness of the security issuers, the number of securities in an unrealized loss position, the severity and duration of the unrealized losses, whether the Company has the intent to sell the securities and whether it is more likely than not that it will be required to sell the securities before the recovery of their amortized cost basis. If the Company were to determine that the decline in fair value of an investment is below its accounting basis and the decline is other-than-temporary, the Company would reduce the carrying value of the security and record a loss for the amount of such decline.

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 equivalents and marketable securities. Under its investment policy, the Company limits amounts invested in such securities by credit rating, maturity, industry group, investment type and issuer, except for securities issued by the U.S. government. The Company is not exposed to any significant concentrations of credit risk from these financial instruments. The goals of the Company's investment policy, in order of priority, are safety and preservation of principal and liquidity of investments sufficient to meet cash flow requirements.

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.

Syros Pharmaceuticals, Inc.
Notes to Consolidated Financial Statements (Continued)

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 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 December 31, 2017.

Other Long-Term Assets

At December 31, 2017, other long-term assets consisted of deferred issuance costs, which included direct and incremental legal and accounting fees related to the shelf registration filed in July 2017, as well as advanced payments made to the contract research organization responsible for conducting the Company's clinical trial of SY-1425 and SY-1365. At December 31, 2016, other long-term assets primarily consisted of advanced payments made to the contract research organization responsible for conducting the Company's clinical trial of SY-1425.

Revenue Recognition

To date, the Company's only source of revenue has been a research agreement with a multinational pharmaceutical company, which expired on March 31, 2017 in accordance with its terms..

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.

Syros Pharmaceuticals, Inc.
Notes to Consolidated Financial Statements (Continued)

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.

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 contained 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 recognized revenue under its research agreement based upon the completed performance method of revenue recognition as it was unable to reasonably estimate the period of performance of the services and the delivery of the final study report was 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 product candidates. Research and development costs include salaries and benefits, materials and supplies, external research, preclinical and clinical development 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.

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 the future 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 acquired research and development in the period in which they are incurred.

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. Prior to June 30, 2016, the Company was a private company and as such lacks Company-specific historical and implied volatility information. Therefore, it estimates its expected stock volatility based on the historical volatility of a publicly traded set of peer companies and expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded stock price. The expected term of the Company's stock options has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. The expected term of stock options granted to non-employees is equal to the contractual term of the option award. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that the Company has never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future. The Company uses the value of its common stock to determine the fair value of restricted stock awards.

Additionally, in March 2016, the FASB issued ASU No. 2016-09, *Compensation—Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting* ("ASU 2016-09"). ASU 2016-09 simplifies several aspects of the accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities, and an option to recognize gross stock-based compensation expense with actual forfeitures as they occur, as well as certain classification on the statement of cash flows. For public entities, ASU 2016-09 is effective for fiscal years beginning after December 15, 2016, and interim periods within those fiscal years. The Company has adopted ASU 2016-09 as of January 1, 2017. The Company has applied ASU 2016-09 using a modified retrospective approach and has adopted the option to recognize stock compensation expense with actual forfeitures recognized as they occur. The adoption of this standard had an immaterial impact to the Company's financial statements. The adoption of ASU 2016-09 also requires all excess tax benefit on stock options to be recorded in the consolidated statements of operations. The adoption did not have a material impact since the expected increase in net deferred tax assets is fully offset by a corresponding increase in the deferred tax asset valuation allowance. The amount of deferred tax assets that had not been previously recognized due to the recognition of excess tax benefits upon adoption was $0.4 million.

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. As a result of the adoption of ASU 2016-09, effective January 1, 2017, the Company accounts for forfeitures as they occur instead of estimating forfeitures at the time of grant and revising those estimates in subsequent periods if actual forfeitures differ from its estimates. Ultimately, the actual expense recognized over the vesting period will be for only those options that vest.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.

Syros Pharmaceuticals, Inc.
Notes to Consolidated Financial Statements (Continued)

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 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

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 dilutive 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.

	As of December 31,		
	2017	2016	2015
Convertible preferred stock	—	—	12,598,370
Stock options	2,846,668	2,543,435	2,226,698
Unvested restricted stock	—	4,885	256,881
	2,846,668	2,548,320	15,081,949

The weighted average number of common shares used in net loss per share applicable to common stockholders on a basic and diluted basis were 25,406,845, 12,696,414 and 1,980,286 for the years ended December 31, 2017, 2016 and 2015, respectively.

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. Entities have the option of using either a full retrospective or a modified retrospective approach to adopt this new guidance. The FASB issued supplemental adoption guidance and clarification to ASU 2014-09 in March 2016, April 2016, May 2016, and December 2016 within ASU 2016-08 "Revenue from Contracts with Customers: Principal vs. Agent Considerations," ASU 2016-10 "Revenue from Contracts with Customers: Identifying Performance Obligations and Licensing," ASU 2016-12 "Revenue from Contracts with Customers: Narrow-Scope Improvements and Practical Expedients," and ASU 2016-20 "Technical Corrections and

Improvements to Topic 606, Revenue from Contracts with Customers," respectively. As of December 31, 2017, the Company had one revenue arrangement, which was completed on March 31, 2017, prior to adoption. The Company plans to use the modified retrospective approach in adopting this standard.

As described further in Note 14 – Subsequent Events, the Company entered into a target discovery, research collaboration and option agreement with Incyte in January 2018 under which the Company will use its gene control platform to identify novel therapeutic targets with a focus on myeloproliferative neoplasms, and Incyte will receive options to obtain exclusive worldwide rights to intellectual property resulting from the collaboration for the development and commercialization of therapeutic products directed to up to seven validated targets. Upon execution of the agreement, Incyte paid the Company $10.0 million in up-front consideration, consisting of $2.5 million in cash and $7.5 million in pre-paid research funding. The Company is eligible to receive target selection milestone payments and option exercise fees of up to an aggregate of $54.0 million, and if products arising from the collaboration are approved, the Company would become eligible to receive from Incyte, for each validated target, a total of up to $50.0 million in development and regulatory milestone payments and up to $65.0 million in commercial milestone payments. No revenue was recognized under this agreement during the year ended December 31, 2017. The Company will recognize revenue related to this agreement using the new standard during 2018.

In February 2016, the FASB issued ASU No. 2016-02, *Leases* ("ASU 2016-02"), which applies to all leases and will require lessees to put most leases on the balance sheet, but recognize expense in a manner similar to the current standard. ASU 2016-02 is effective for fiscal years beginning after December 15, 2018 and interim periods within those years, and, as such, will be effective for the year ended December 31, 2019 for the Company. Entities are required to use a modified retrospective approach of adoption for leases that exist or are entered into after the beginning of the earliest comparative period in the financial statements. Full retrospective application is prohibited. The Company is evaluating the new guidance and the expected effect on the Company's consolidated financial statements. However, the Company anticipates recognition of additional assets and corresponding liabilities related to its operating leases. To date, the Company has one operating lease for its office and laboratory space in Cambridge, Massachusetts (Note 9).

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows (Topic 230)* ("ASU No. 2016-15"), which simplifies certain elements of cash flow classification. The new guidance is intended to reduce diversity of practice in how certain transactions are classified in the statement of cash flows. ASU No. 2016-15 is effective for annual periods beginning after December 15, 2017. The Company is currently evaluating the impact the adoption of ASU No. 2016-15 will have on its consolidated financial statements.

In November 2016, the FASB issued ASU No. 2016-18, *Restricted Cash* ("ASU No. 2016-18"). The amendments in ASU No. 2016-18 require an entity to reconcile and explain the period-over-period change in total cash, cash equivalents and restricted cash within its statements of cash flows. ASU No. 2016-18 is effective for fiscal years (including interim reporting periods within those years) beginning after December 15, 2017. Early adoption is permitted. A reporting entity must apply the amendments in ASU No. 2016-18 using a full retrospective approach. The Company believes that the adoption of this guidance will not have a significant impact on its consolidated financial statements and related disclosures.

In January 2017, the FASB issued ASU No. 2017-01, *Business Combinations (Topic 805): Clarifying the Definition of a Business* ("ASU No. 2017-01"). The amended guidance clarifies the definition of a business with the objective of adding guidance to assist entities with evaluating whether transactions should be accounted for as acquisitions (or disposals) of assets or businesses. The new accounting guidance is effective for annual periods beginning after December 15, 2017, including interim periods within those periods. Early adoption is permitted. The Company will evaluate the impact that the adoption of ASU No. 2017-01 will have on future transactions.

3. Cash Equivalents and Marketable Securities

Cash equivalents are highly liquid investments that are readily convertible into cash with original maturities of three months or less when purchased. Marketable securities consist of securities with original maturities greater than 90 days when purchased. The Company classifies these marketable securities as available-for-sale and records them at fair value in the accompanying consolidated balance sheets. Unrealized gains or losses are included in accumulated other

comprehensive income (loss). Premiums or discounts from par value are amortized to investment income over the life of the underlying security.

Cash equivalents and marketable securities, available-for-sale, consisted of the following at December 31, 2017 and December 31, 2016 (in thousands):

December 31, 2017	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Cash Equivalents:				
Money market funds	$ 17,205	$ —	$ —	$ 17,205
Overnight repurchase agreements	15,000	—	—	15,000
Marketable Securities:				
U.S. treasury obligations	39,886	—	(42)	39,844
Total:	$ 72,091	$ —	$ (42)	$ 72,049

December 31, 2016	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Cash Equivalents:				
Money market funds	$ 58,588	$ —	$ —	$ 58,588
Marketable Securities:				
U.S. treasury obligations	25,014	—	(9)	25,005
Total:	$ 83,602	$ —	$ (9)	$ 83,593

Although available to be sold to meet operating needs or otherwise, securities are generally held through maturity. The cost of securities sold is determined based on the specific identification method for purposes of recording realized gains and losses. During the year ended December 31, 2017, there were no realized gains or losses on sales of investments, and no investments were adjusted for other than temporary declines in fair value.

At December 31, 2017, the Company held 17 securities that were in an unrealized loss position. The aggregate fair value of securities held by the Company in an unrealized loss position for less than twelve months as of December 31, 2017 was $39.8 million and there were no securities held by the Company in an unrealized loss position for more than twelve months. The Company has the intent and ability to hold such securities until recovery. The Company determined that there was no material change in the credit risk of the above marketable securities. As a result, the Company determined it did not hold any marketable securities with an other-than temporary impairment as of December 31, 2017.

4. Fair Value Measurements

Assets measured at fair value on a recurring basis are as follows (in thousands):

Description	December 31, 2017	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Cash equivalents:				
Money market funds	$ 17,205	$ 17,205	$ —	$ —
Overnight repurchase agreements	15,000	—	15,000	—
Marketable securities:				
U.S. treasury obligations	39,844	39,844	—	—
	$ 72,049	$ 57,049	$ 15,000	$ —

Syros Pharmaceuticals, Inc.
Notes to Consolidated Financial Statements (Continued)

Description	December 31, 2016	Active Markets (Level 1)	Observable Inputs (Level 2)	Unobservable Inputs (Level 3)
Cash equivalents:				
Money market funds	$ 58,588	$ 58,588	$ —	$ —
Marketable securities:				
U.S. treasury obligations	25,005	25,005	—	—
	$ 83,593	$ 83,593	$ —	$ —

5. Restricted Cash

At December 31, 2017 and December 31, 2016, the Company had $0.5 million in restricted cash that serves as the security deposit on the lease of the Company's current facility in Cambridge, Massachusetts. At December 31, 2017, approximately $0.2 million of the restricted cash was classified as current as it is expected to be refunded to the Company under the terms of the lease agreement.

6. Property and Equipment

Property and Equipment consists of the following (in thousands):

	Estimated useful life (in years)	December 31, 2017	December 31, 2016
Laboratory equipment	5	$ 3,978	$ 3,612
Computer equipment	3	651	401
Furniture and fixtures	4	396	395
Leasehold improvements	Shorter of 7 years or life of lease	2,613	2,599
Construction in process		—	18
		$ 7,638	$ 7,025
Less: Accumulated depreciation		(3,700)	(2,175)
Total property and equipment, net		$ 3,938	$ 4,850

Depreciation expense, including depreciation expense for assets recorded under capital leases, for the years ended December 31, 2017, 2016 and 2015 was $1.5 million, $1.3 million and $0.6 million, respectively. Laboratory equipment included assets recorded under capital leases of $0.4 million at December 31, 2017 (Note 8). Accumulated depreciation from assets recorded under capital leases was $0.2 million at December 31, 2017.

7. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	December 31, 2017	December 31, 2016
External research and preclinical development	$ 5,875	$ 3,290
Employee compensation and benefits	2,494	1,911
Professional fees	1,225	819
Facilities	134	90
Restricted stock liability	—	5
	$ 9,728	$ 6,115

Syros Pharmaceuticals, Inc.
Notes to Consolidated Financial Statements (Continued)

8. Indebtedness

Equipment Financing

In March 2015, the Company entered into a lease agreement with a vendor for certain laboratory equipment. The Company financed $0.4 million 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. During the year ended December 31, 2017, the Company made payments of $0.2 million, of which $9,000 related to interest. At December 31, 2017, $0.1 million of principal was outstanding with respect to the equipment financing arrangement.

The following table sets forth the Company's future minimum payments due under capital leases as of December 31, 2017:

Year	(in thousands)
2018	$ 48
2019	5
2020	2
	$ 55

9. Commitments and Contingencies

Operating Leases

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. The Company has an option to extend the lease for five additional years. The 2015 Lease 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 $0.9 million, $0.9 million, and $0.3 million for the years ended December 31, 2017, 2016 and 2015, respectively, related to the 2015 Lease. The 2015 Lease agreement required the Company to issue an original letter of credit in the amount of $0.5 million, which is included in restricted cash in the accompanying balance sheet at December 31, 2017 and December 31, 2016. At December 31, 2017, approximately $0.2 million of the restricted cash was classified as current as it is expected to be refunded to the Company under the terms of the lease agreement.

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 following table sets forth the Company's future minimum payments due under operating leases as of December 31, 2017:

Year	(in thousands)
2018	$ 1,288
2019	1,325
2020	1,130
	$ 3,743

Syros Pharmaceuticals, Inc.
Notes to Consolidated Financial Statements (Continued)

License Agreements

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

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. Payments totaling $3.4 million are due to Dana-Farber if and when the Company achieves certain clinical and regulatory milestones for any licensed product, none of which have been achieved as of December 31, 2017. No future potential milestone payments have been accrued as of December 31, 2017 or December 31, 2016, 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. The Company is obligated to pay a tiered royalty on net sales for licensed products in any country subject to the license. Royalty payments, if any, would continue for the duration of the licensed patents.

In April 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 *MYC* modulators owned or controlled by Whitehead and Dana-Farber.

In April 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 connection with the Whitehead agreements, the Company issued 171,674 shares of its common stock to Whitehead in April 2013. Payments totaling $3.6 million are due under the Whitehead agreements when the Company achieves certain milestones. The future potential milestone payments due under the Whitehead agreements have not been accrued as of December 31, 2017 and December 31, 2016, 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. The Company paid Whitehead and the Whitehead Institute for Genome Technology Core $0.9 million and $1.0 million during the years ended December 31, 2017 and 2016, respectively, for annual license maintenance fees and research services. Additionally, at December 31, 2017, the Company had $0.2 million in accounts payable and accrued expenses due to Whitehead and the Whitehead Institute for Genome Technology Core for research services performed during 2017.

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 the treatment of cancer. This agreement was amended and restated in April 2016.

In exchange for this license, the Company agreed to a non-refundable upfront payment of $1.0 million, for which $0.5 million was paid in September 2015 upon execution of the agreement, and the remaining $0.5 million was paid in May 2016. Under the agreement, the Company is also obligated to make payments upon the successful achievement of clinical and regulatory milestones totaling approximately $13.0 million per indication, defined as a distinct tumor type. In September 2016, the Company paid $1.0 million to TMRC for a development milestone achieved upon the successful dosing of the first patient in its Phase 2 clinical trial of SY-1425. In addition, the Company is obligated to pay TMRC a single-digit percentage royalty, on a country-by-country and product-by-product basis, on net product sales of SY-1425 using know-how and patents licensed from TMRC in North America and Europe for a defined royalty term.

The Company also entered into a supply management agreement with TMRC, under which the Company agreed to pay TMRC a fee for each kilogram of SY-1425 active pharmaceutical ingredient that is produced. The Company made payments of $0.4 million under this supply management agreement during the year ended December 31, 2017. No payments were made under this supply management agreement during the year ended December 31, 2016.

Syros Pharmaceuticals, Inc.
Notes to Consolidated Financial Statements (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, 2017 or December 31, 2016.

10. Stock-Based Payments

2016 Stock Incentive Plan

The 2016 Stock Incentive Plan (the "2016 Plan") was adopted by the board of directors on December 15, 2015 and approved by the stockholders on June 17, 2016, and became effective on July 6, 2016 upon the closing of the IPO. The 2016 Plan replaced the 2012 Equity Incentive Plan (the "2012 Plan"). Any options or awards outstanding under the 2012 Plan remained outstanding and effective. Under the 2016 Plan, the Company may grant incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock, restricted stock units and other stock-based awards. The number of shares of the Company's common stock reserved for issuance under the 2016 Plan will automatically increase on January 1 of each calendar year, commencing on January 1, 2017 and ending on December 31, 2025, in an amount equal to the least of (i) 1,600,000 shares of common stock, (ii) 4.0% of the outstanding shares of common stock as of such date, or (iii) such lesser amount as specified by the compensation committee of the board of directors. This number is subject to adjustment in the event of a stock split, stock dividend or other change in the Company's capitalization. For the calendar year beginning January 1, 2017, the number of shares reserved for issuance under the 2016 Plan was increased by 935,430 shares. At December 31, 2017, 2,880,493 shares remained available for future issuance under the 2016 Plan. Under the 2016 Plan, stock options may not be granted at less than fair value on the date of grant.

Terms of stock option agreements, including vesting requirements, are determined by the board of directors, subject to the provisions of the 2016 Plan. Stock option awards granted by the Company generally vest over four years, with 25% vesting on the first 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 may grant performance-based stock option awards 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 may vest in full on the sixth anniversary of the vesting commencement date.

2016 Employee Stock Purchase Plan

The 2016 Employee Stock Purchase Plan (the "2016 ESPP") was adopted by the board of directors on December 15, 2015 and approved by the stockholders on June 17, 2016, and became effective on July 6, 2016 upon the closing of the IPO. The number of shares of the Company's 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) 1,173,333 shares of the Company's common stock, (ii) 1.0% of the total number of shares of the Company's common stock outstanding on the first day of the applicable year, and (iii) an amount determined by the Company's board of directors. For the calendar year beginning January 1, 2017, the number of shares reserved for issuance under the 2016 ESPP was increased by 233,857 shares. At December 31, 2017, 820,523 shares remained available for future issuance under the 2016 ESPP.

Stock Options

Performance-Based Stock Options

The Company has granted stock options to management for which vesting 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 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, 2016, the Company recorded additional stock-based compensation expense of $0.2 million related to the achievement of certain performance-based milestones. The Company did not record any additional stock-based compensation expense related to the achievement of performance-based milestones for the year ended December 31, 2017. As of December 31, 2017, there was $1.0 million of unrecognized stock-based compensation expense related to the performance-based stock options granted to management, with an expected recognition period of 3.2 years.

During the year ended December 31, 2016, the Company granted options to purchase 75,000 shares of common stock to an advisor for which the vesting accelerates upon the achievement of performance-based criteria. As of December 31, 2017, no such performance-based criteria were achieved. As of December 31, 2017, there was $0.6 million of unrecognized stock-based compensation expense related to the performance-based stock options granted to management, with an expected recognition period of 8.7 years.

A summary of the status of stock options as of December 31, 2017 and December 31, 2016 and changes during the year ended December 31, 2017 is presented below:

	Shares	Weighted Average Exercise Price	Remaining Contractual Life (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2016	2,543,435	$ 6.44	8.3	$ 14,898
Granted	1,368,000	11.87		
Exercised	(445,012)	4.03		
Cancelled	(619,755)	7.22		
Outstanding at December 31, 2017	2,846,668	$ 9.25	8.2	$ 5,713
Exercisable at December 31, 2017	858,927	$ 6.06	7.0	$ 3,827
Vested and expected to vest at December 31, 2017	2,846,668	$ 9.25	8.2	$ 5,713

The intrinsic value of options exercised during the years ended December 31, 2017, 2016 and 2015 was $4.6 million, $2.4 million, and $2.0 million, respectively.

Cash received from option exercises during the years ended December 31, 2017, 2016, and 2015 was $1.8 million, $0.4 million, and $0.4 million, respectively.

Restricted Common Stock

From time to time, upon approval by the Company's board of directors, certain employees and advisors have been granted restricted shares of common stock with time- and performance-based vesting criteria. These shares of restricted stock are subject to repurchase rights. Accordingly, the Company has recorded the proceeds from the issuance of restricted stock as a liability in the consolidated balance sheets included as a component of accrued expenses or other long term liabilities based on the scheduled vesting dates. The restricted stock liability is reclassified into stockholders' equity (deficit) as the restricted stock vests over time or upon the achievement of performance.

Syros Pharmaceuticals, Inc.
Notes to Consolidated Financial Statements (Continued)

A summary of the status of unvested restricted common stock as of December 31, 2017 and December 31, 2016 and changes during the year ended December 31, 2017 is presented below:

	Shares	Weighted Average Grant Date Fair Value
Unvested at December 31, 2016	4,885	$ 0.98
Vested	(4,885)	0.98
Repurchased	—	—
Unvested at December 31, 2017	—	$ —

The total fair value of restricted stock vested during the years ended December 31, 2017, 2016, and 2015 was $1,000, $0.1 million, and $0.1 million, respectively, based upon the number of restricted stock awards vested multiplied by the fair value of the Company's common stock on the grant date.

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:

	Year Ended December 31,		
	2017	2016	2015
Weighted-average risk-free interest rate	2.07 %	1.36 %	1.78 %
Expected dividend yield	— %	— %	— %
Expected option term	6.05	5.98	6.09
Volatility	87.83 %	85.39 %	82.71 %

The weighted-average grant date fair value per share of options granted in the years ended December 31, 2017, 2016 and 2015 was $8.75, $8.58 and $4.88, respectively.

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:

	Year Ended December 31,		
	2017	2016	2015
Research and development	$ 1,666	$ 2,980	$ 2,733
General and administrative	2,753	1,254	500
Total stock-based compensation expense	$ 4,419	$ 4,234	$ 3,233

As of December 31, 2017, there was $11.9 million of total unrecognized compensation cost related to non-vested stock options granted to employees, which is expected to be recognized over a weighted-average period of 2.9 years. Additionally, as of December 31, 2017, there was $0.1 million of total unrecognized compensation cost related to non-vested stock options granted to non-employees, excluding those subject to performance-based criteria described above. Due to an operating loss, the Company does not record tax benefits associated with stock-based compensation or option exercises. Tax benefits will be recorded when realized.

11. Income Taxes

The Company accounts for income taxes under FASB Accounting Standards Codification 740 ("ASC 740"). Deferred income tax assets and liabilities are determined based upon differences between financial reporting and tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the

Syros Pharmaceuticals, Inc.
Notes to Consolidated Financial Statements (Continued)

differences are expected to reverse. The components of the income tax provision for the years ended December 31, 2017 and 2016 are as follows:

	Year Ended December 31,	
	2017	2016
Current	$ 7	$ 2
Deferred	—	—
Total	$ 7	$ 2

A reconciliation of the U.S. statutory income tax rate to the Company's effective tax rate is as follows for the years ended December 31, 2017, 2016 and 2015:

	Year ended December 31,		
	2017	2016	2015
Federal income tax computed at federal statutory tax rate	34.00 %	34.00 %	34.00 %
State income tax, net of federal benefit	5.35	4.79	4.70
Permanent items	(1.57)	(2.83)	(3.33)
Federal and state research and development credits	7.36	2.93	2.66
Rate change	(31.79)	—	—
Other	0.66	(0.08)	0.12
Change in valuation allowance	(14.02)	(38.81)	(38.15)
Effective income tax rate	(0.01)%	0.00 %	0.00 %

On December 22, 2017, H.R.1., formerly known as the Tax Cuts and Jobs Act, was signed into law. The new law did not have a significant impact on the Company's consolidated financial statements for the year ended December 31, 2017 because it maintains a valuation allowance on the majority of its net operating losses and other deferred tax assets. However, the reduction of the U.S. federal corporate tax rate from 35% to 21% resulted in increases to the amounts reflected in the effective tax rate attributable to "change in valuation allowance" and "rate change" in the Company's effective tax rate reconciliation table above for the year ended December 31, 2017 compared to the years ended December 31, 2016 and 2015. The change in the U.S. federal corporate tax rate, which is effective January 1, 2018, is also reflected in the Company's deferred tax table below. Lastly, the Company has discussed the possible impact of Staff Accounting Bulletin No. 118 ("SAB 118") on the Company's consolidated financial statements below.

The principal components of the Company's deferred tax assets and liabilities consist of the following at December 31, 2017 and 2016 (in thousands):

	Year ended December 31,	
	2017	2016
Deferred tax assets:		
Federal and state net operating loss carryforwards	$ 37,411	$ 33,846
Tax credit carryforwards	7,573	3,350
Intangible assets	56	197
Stock-based compensation	1,059	247
Leasehold incentive	240	467
Other	1,237	1,605
Total deferred tax assets	47,576	39,712
Less valuation allowance	(47,576)	(39,624)
Net deferred tax assets	—	88
Deferred tax liabilities:		
Fixed assets	—	(88)
Total deferred tax liabilities	—	(88)
Net deferred taxes	$ —	$ —

Syros Pharmaceuticals, Inc.
Notes to Consolidated Financial Statements (Continued)

As of December 31, 2017 the Company had federal net operating loss ("NOL") carryforwards of approximately $136.4 million and state net operating loss carryforwards of $138.8 million which are available to reduce future taxable income. The Company also had federal tax credits of approximately $6.1 million and state tax credits of $1.8 million which may be used to offset future tax liabilities. The NOL and tax credit carryforwards will expire at various dates through 2037. The NOL and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service 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 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, 2017 and 2018, 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 of $8.0 million in 2017 and $18.5 million in 2016 primarily relates to the net loss incurred by the Company.

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. As of December 31, 2017 and 2016 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 federal and state income tax returns are generally subject to examinations for the tax years ended December 31, 2014 through December 31, 2017. To the extent the Company has tax attribute carryforwards, the tax years in which the attribute was generated may still be adjusted upon examination by the Internal Revenue Service or state tax authorities to the extent utilized in a future period. The Company files income tax returns in the U.S. federal and Massachusetts jurisdictions. There are currently no federal or state audits in process.

On December 22, 2017, the SEC staff issued SAB 118 to address the application of GAAP in situations when a registrant does not have the necessary information available, prepared, or analyzed (including computations) in reasonable detail to complete the accounting for certain income tax effects of H.R.1. The Company has recognized the provisional tax impacts related the revaluation of deferred tax assets and liabilities and included these amounts in its financial statements for the year ended December 31, 2017. The ultimate impact may differ from these provisional amounts, possibly materially, due to, among other things, additional analysis, changes in interpretations and assumptions the Company has made, additional regulatory guidance that may be issued, and actions the Company may take as a result of H.R.1. The Company's accounting treatment is expected to be complete when the 2017 U.S. corporate income tax return is filed in 2018.

12. 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 is 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 Counterparty. Upon the completion of each project, the Counterparty determined whether to commence the next project under the research agreement upon written notification.

The research agreement was amended in November 2016 to extend the term to March 31, 2017. The research agreement terminated automatically on March 31, 2017 in accordance with its terms.

Syros Pharmaceuticals, Inc.
Notes to Consolidated Financial Statements (Continued)

The Company recognized 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 $1.1 million and $0.3 million during the years ended December 31, 2017 and December 31, 2016, respectively, under the agreement.

13. 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. Effective September 1, 2017, the Company instituted an employer match of 100% of the amount you contribute to the Plan for each payroll period up to the first 1% of Plan Compensation plus 50% of the amount you contribute between 1% and 6% of Plan Compensation. For the year ended December 31, 2017, the Company contributed $0.3 million to the 401(k) Plan.

14. Subsequent Events

Collaboration Agreement

On January 8, 2018, the Company and Incyte Corporation entered into a Target Discovery, Research Collaboration and Option Agreement (the "Collaboration Agreement"). Under the Collaboration Agreement, the Company will use its proprietary gene control platform to identify novel therapeutic targets with a focus on myeloproliferative neoplasms, and Incyte will receive options to obtain exclusive worldwide rights to intellectual property resulting from the collaboration for the development and commercialization of therapeutic products directed to up to seven validated targets. Incyte will have exclusive worldwide rights to develop and commercialize any therapies under the collaboration that modulate those validated targets.

Under the terms of the Collaboration Agreement, Incyte paid the Company $10.0 million in up-front consideration, consisting of $2.5 million in cash and $7.5 million in pre-paid research funding. The Company's activities under the Collaboration Agreement are subject to a joint research plan and, subject to certain exceptions, Incyte will be responsible for funding the Company's activities under the research plan, including amounts in excess of the pre-paid research funding amount. The Company is obligated to make a payment to Whitehead representing a percentage of the up-front cash consideration received under the Collaboration Agreement.

The Company will be eligible to receive target selection milestone payments and option exercise fees of up to an aggregate of $54.0 million if Incyte selects the maximum number of targets for validation and exercises its option to obtain exclusive rights to collaboration intellectual property for therapeutic products directed to all seven validated targets. Should any therapeutic product be developed by Incyte against a target as to which Incyte has exercised its option to obtain exclusive rights to collaboration intellectual property, the Company will be eligible to receive milestone payments and, if approved and commercialized, royalty payments from Incyte. For each of the seven validated targets, the Company would become eligible to receive from Incyte a total of up to $50.0 million in development and regulatory milestone payments. If products arising from the collaboration are approved, the Company would become eligible to receive from Incyte, for each validated target, a total of up to $65.0 million in commercial milestone payments. Upon approval and commercialization of any therapeutic product resulting from the collaboration, the Company would become eligible to receive low single-digit royalties on net sales of such product.

The term of Collaboration Agreement began on January 8, 2018 and, unless terminated by a party early, will continue until all royalty obligations for products arising from the collaboration expire. The Collaboration Agreement may be terminated by Incyte for convenience on sixty (60) days' prior written notice to the Company, or by the Company on thirty (30) days' written notice in the event Incyte or one of its affiliates or sublicensees challenges the validity or enforceability of certain patent rights controlled by the Company. The Collaboration Agreement may also be terminated by either of the parties on thirty (30) days' prior written notice in the event of an uncured material breach of the Collaboration Agreement by the other party or immediately in the case of certain bankruptcy events. Incyte's right to

terminate for convenience and each party's right to terminate for uncured material breach may be exercised either with respect to the Collaboration Agreement in its entirety or, as applicable, in relation to the relevant validated target and associated therapeutic products.

Following entry into the Collaboration Agreement, the Company's Board of Directors accelerated the vesting of 63,793 shares underlying performance-based stock options granted to members of the Company's management team.

Stock Purchase Agreement

On January 8, 2018, the Company entered into a Stock Purchase Agreement with Incyte (the "SPA"), pursuant to which Incyte agreed to purchase 793,021 shares of the Company's common stock, par value $0.001 per share, for an aggregate purchase price of $10.0 million in cash, or $12.61 per share, in a private placement. The purchase price represents a thirty percent (30%) premium to the volume-weighted sale price of the shares of the Company's common stock over the fifteen (15) trading day period immediately preceding the date of the SPA. The Company is obligated to make a payment to Whitehead representing a percentage of the equity premium received under the SPA. The Shares are subject to a lock-up restriction and a market stand-off agreement for a period of 12 months following the closing of the sale of the shares (the "Closing"). Pursuant to the terms of the SPA, the Company filed a registration statement covering the resale by Incyte of the Shares on January 19, 2018.

In addition, from the Closing until the earlier of the second anniversary of the Closing or the expiration or termination of the Collaboration Agreement, the Company has granted to Incyte the right to purchase up to its pro rata share of the securities offered in certain subsequent offerings of the Company's common stock or common stock equivalents, subject to the terms and conditions set forth in the SPA.

Sale of Securities through Public Offering

On January 30, 2018, the Company issued and sold an aggregate of 4,188,481 shares of its common stock in a public offering at a price per share $9.55 per share, resulting in gross proceeds of $40.0 million before deducting underwriting commissions and fees estimated to be approximately $2.7 million. Additionally, on February 2, 2018, the underwriters exercised their option to purchase an additional 628,272 shares at a price per share of $9.55, resulting in additional gross proceeds of $6.0 million.

In addition, on February 2, 2018, we also closed a concurrent private placement of 125,656 shares of our common stock to Incyte Corporation at a price of $9.55 per share, resulting in proceeds to us of $1.2 million. The Company closed an additional private placement of 18,849 shares of its common stock to Incyte on February 7, 2018 at a price of $9.55 per share, resulting in gross proceeds to the Company of $0.2 million.

15. Selected Quarterly Financial Data (unaudited)

The following table contains selected quarterly financial information for 2017 and 2016. The Company believes that the following information reflects all normal recurring adjustments necessary for a fair statement of the information

Syros Pharmaceuticals, Inc.
Notes to Consolidated Financial Statements (Continued)

for the periods presented. The operating results for any quarter are not necessarily indicative of results for any future period.

	Three Months Ended			
	March 31, 2017	June 30, 2017	September 30, 2017	December 31, 2017
Revenue	$ 1,101	$ —	$ —	$ —
Operating expenses:				
Research and development	9,628	10,041	10,447	11,780
General and administrative	3,086	3,472	3,593	3,740
Total operating expenses	12,714	13,513	14,040	15,520
Loss from operations	(11,613)	(13,513)	(14,040)	(15,520)
Other income, net	98	145	215	218
Net loss applicable to common stockholders	$ (11,515)	$ (13,368)	$ (13,825)	$ (15,302)
Net loss per share applicable to common stockholders - basic and diluted	$ (0.49)	$ (0.52)	$ (0.53)	$ (0.58)
Weighted-average number of common shares used in net loss per share applicable to common stockholders - basic and diluted	23,393,448	25,584,147	26,259,216	26,316,550

	Three Months Ended			
	March 31, 2016	June 30, 2016	September 30, 2016	December 31, 2016
Revenue	$ —	$ —	$ —	$ 317
Operating expenses:				
Research and development	8,265	9,525	11,584	8,443
General and administrative	2,371	2,540	2,633	2,919
Total operating expenses	10,636	12,065	14,217	11,362
Loss from operations	(10,636)	(12,065)	(14,217)	(11,045)
Other income, net	48	44	48	80
Net loss	$ (10,588)	$ (12,021)	$ (14,169)	$ (10,965)
Accrued dividends on preferred stock	(1,737)	(1,823)	(121)	—
Net loss applicable to common stockholders	$ (12,325)	$ (13,844)	$ (14,290)	$ (10,965)
Net loss per share applicable to common stockholders - basic and diluted	$ (5.15)	$ (5.42)	$ (0.65)	$ (0.47)
Weighted-average number of common shares used in net loss per share applicable to common stockholders - basic and diluted	2,394,470	2,553,146	22,012,743	23,374,734

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Management's Evaluation of Disclosure Controls and Procedures

We maintain "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, that are designed to ensure that information required to be disclosed in the reports that we file or submit under the Exchange Act is (1) recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms and (2) accumulated and communicated to our management, including our principal executive and principal financial officer, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our disclosure controls and procedures are designed to provide reasonable assurance of achieving their control objectives.

Our management, with the participation of our Chief Executive Officer, who serves as our principal executive and principal financial officer, has evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2017. Based upon such evaluation, our Chief Executive Officer and Principal Financial Officer has concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of such date.

Internal Control Over Financial Reporting

Management's Report on Internal Control Over Financial Reporting

This Annual Report on Form 10-K does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of our independent registered public accounting firm due to a transition period established by rules of the SEC for newly public companies.

Changes in Internal Control Over Financial Reporting

During the year ended December 31, 2017, we implemented an accounting system for purposes of tracking and accounting for stock-based awards, as well as an enterprise resource system for the purposes of maintaining our general ledger and reporting. There were no other changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the year ended December 31, 2017 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this Item 10 will be included under the captions "Executive Officers," "Election of Directors" and "Section 16(a) Beneficial Ownership Reporting Compliance" in our definitive proxy statement to be filed with the SEC with respect to our 2018 Annual Meeting of Stockholders and is incorporated herein by reference.

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

ITEM 11. EXECUTIVE COMPENSATION

The information required by this Item 11 will be included under the captions "Executive and Director Compensation" and "Compensation Committee Interlocks and Insider Participation" in our definitive proxy statement to be filed with the SEC with respect to our 2018 Annual Meeting of Stockholders and is incorporated herein by reference.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERSHIP AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by this Item 12 will be included under the captions "Security Ownership of Certain Beneficial Owners and Management" and "Securities Authorized for Issuance Under Equity Compensation Plans" in our definitive proxy statement to be filed with the SEC with respect to our 2018 Annual Meeting of Stockholders and is incorporated herein by reference.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this Item 13 will be included, as applicable, under the captions "Employment Agreements," "Potential Payments Upon Termination or Change in Control," "Board Determination of Independence" and "Related Person Transactions" in our definitive proxy statement to be filed with the SEC with respect to our 2018 Annual Meeting of Stockholders and is incorporated herein by reference.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The information required by this Item 14 will be included under the captions "Audit Fees and Services" and "Pre-Approval Policies and Procedures" in our definitive proxy statement to be filed with the SEC with respect to our 2018 Annual Meeting of Stockholders and is incorporated herein by reference.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a) *Financial Statements*

For a list of the consolidated financial statements included herein, see Index to the Consolidated Financial Statements on page 113 of this Annual Report on Form 10-K, which is incorporated into this Item by reference.

(b) *Exhibits*

		Incorporation by Reference			
Exhibit No.	Description	Form	SEC Filing Date	Exhibit Number	Filed with this 10-K
Organizational Documents and Documents Related to Common Stock					
3.1	Restated Certificate of Incorporation of the Registrant	8-K	7/6/16	3.1	
3.2	Amended and Restated Bylaws of the Registrant	8-K	7/6/16	3.2	
4.1	Form of common stock certificate	S-1^	6/3/16	4.1	
4.2	Second Amended and Restated Investors' Rights Agreement dated October 9, 2014, as amended, among the Registrant and the other parties thereto	S-1^	6/3/16	4.2	
4.3	Sales Agreement dated July 20, 2017 by and between the Registrant and Cowen and Company LLC	S-3^^	7/20/17	1.2	
4.4	Stock Purchase Agreement dated January 8, 2018 by and between the Registrant and Incyte Corporation, as amended				X
4.5	Underwriting Agreement dated January 30, 2018 by and among the Registrant, J.P. Morgan Securities LLC, Cowen and Company, LLC and Piper Jaffray and Co., as representatives of the several underwriters named thereing	8-K	1/31/18	1.1	
4.6	Securities Purchase Agreement dated April 20, 2017 by and among the Registrant and the persons party thereto	8-K	4/21/17	10.1	
4.7	Registration Rights Agreement, dated April 20, 2017, by and among the Registrant and the persons party thereto	8-K	4/21/17	10.2	
Equity Plan Documents					
10.1*	2012 Equity Incentive Plan, as amended	S-1^	6/3/16	10.1	
10.2*	Form of Incentive Stock Option Agreement under 2012 Equity Incentive Plan	S-1^	6/3/16	10.2	
10.3*	Form of Nonstatutory Stock Option Agreement under 2012 Equity Incentive Plan	S-1^	6/3/16	10.3	
10.4*	Form of Restricted Stock Agreement under 2012 Equity Incentive Plan	S-1^	6/3/16	10.4	
10.5*	2016 Stock Incentive Plan	S-1^	6/3/16	10.5	
10.6*	Form of Incentive Stock Option Agreement under 2016 Stock Incentive Plan	S-1^	6/3/16	10.6	
10.7*	Form of Nonstatutory Stock Option Agreement under 2016 Stock Incentive Plan	S-1^	6/3/16	10.7	
10.8*	2016 Employee Stock Purchase Plan	S-1^	6/3/16	10.8	
Agreements with Directors and Executive Officers					
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	S-1^	6/3/16	10.9	
10.10*	Offer Letter dated August 25, 2015 by and between the Registrant and Kyle D. Kuvalanka, as amended	S-1^	6/3/16	10.10	
10.11*	Offer Letter dated December 2, 2015 by and between the Registrant and David A. Roth, M.D., as amended	S-1^	6/3/16	10.11	
10.12*	Offer Letter dated September 9, 2016 by and between the Registrant and Gerald E. Quirk, Esq.	10-K	3/20/17	10.12	
10.13*	Offer Letter dated November 6, 2017 by and between the Registrant and Jeremy Springhorn, Ph.D.				X
10.14*	Consulting Agreement dated August 8, 2012 by and between the Registrant and Richard A. Young, Ph.D., as amended	10-K	3/20/17	10.13	

Exhibit No.	Description	Incorporation by Reference: Form	SEC Filing Date	Exhibit Number	Filed with this 10-K
10.15*	Form of Director and Officer Indemnification Agreement by and between the Registrant and each of the directors and executive officers of the Registrant	S-1^	6/3/16	10.12	
License and Collaboration Agreements					
10.16+	Exclusive License Agreement dated February 22, 2013 by and between the Registrant and the Dana-Farber Cancer Institute, Inc.	S-1^	6/3/16	10.13	
10.17+	Exclusive License Agreement dated April 1, 2013 by and among the Registrant, the Whitehead Institute for Biomedical Research and the Dana-Farber Cancer Institute, Inc.	S-1^	6/3/16	10.14	
10.18+	Exclusive License Agreement dated April 4, 2013 by and between the Registrant and the Whitehead Institute for Biomedical Research	S-1^	6/3/16	10.15	
10.19+	Amended and Restated Cancer License Agreement dated April 28, 2016 by and between the Registrant and TMRC Co., Ltd.	S-1^	6/3/16	10.16	
10.20+	Supply Management Agreement dated April 28, 2016 by and between the Registrant and TMRC Co., Ltd.	S-1^	6/3/16	10.18	
10.21	Consent and Stand-by License Agreement dated April 28, 2016 by and among the Registrant, Toko Pharmaceutical Ind. Co., Ltd. and TMRC Co., Ltd.	S-1^	6/3/16	10.19	
10.22+	Target Discovery, Research Collaboration and Option Agreement dated January 8, 2018 by and between the Registrant and Incyte Corporation				X
Leases					
10.23	Lease dated March 13, 2015 by and between the Registrant and 620 Memorial Leasehold LLC	S-1^	6/3/16	10.17	
Subsidiaries, Consents and Certifications					
21.1	Subsidiaries of the Registrant				X
23.1	Consent of Ernst & Young LLP, independent public accounting firm				X
31.1	Certification of principal executive officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended				X
31.2	Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended				X
32.1#	Statement of principal executive officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002				X
32.2#	Statement of principal financial officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002				X
XBRL Documents					
101.INS	XBRL Instance Document				
101.SCH	XBRL Taxonomy Extension Schema Document				
101.CAL	XBRL Calculation Linkbase Document				
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document				
101.LAB	XBRL Label Linkbase Document				
101.PRE	XBRL Taxonomy Presentation Linkbase Document				

* Indicates management contract or compensatory plan.

\+ Confidential treatment has been requested and/or granted as to certain portions, which portions have been omitted and filed separately with the U.S. Securities and Exchange Commission

^ SEC File No. 333-211818

^^ SEC File No. 333-219369

\# This certification will not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liability of that section. Such certification will not be deemed to be incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act, except to the extent specifically incorporated by reference into such filing.

(c) *Financial Statement Schedules*

No financial statement schedules have been submitted because they are not required or are not applicable or because the information required is included in the consolidated financial statements or the notes thereto.

ITEM 16. FORM 10-K SUMMARY

None.

SIGNATURES

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

SYROS PHARMACEUTICALS, INC.

Date: March 12, 2018

By: /s/ Nancy Simonian, M.D.
Nancy Simonian, M.D.
President and Chief Executive Officer

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

Signature	Title	Date
/s/ Nancy Simonian, M.D. Nancy Simonian, M.D.	President, Chief Executive Officer and Director (*Principal Executive and Financial Officer*)	March 12, 2018
/s/ Michael Inbar Michael Inbar	Controller	March 12, 2018
/s/ Peter Wirth Peter Wirth	Chair of the Board of Directors	March 12, 2018
/s/ Srinivas Akkaraju, M.D., Ph.D. Srinivas Akkaraju, M.D., Ph.D.	Director	March 12, 2018
/s/ Marsha H. Fanucci Marsha H. Fanucci	Director	March 12, 2018
/s/ Amir Nashat, Ph.D. Amir Nashat, Ph.D.	Director	March 12, 2018
/s/ Robert T. Nelsen Robert T. Nelsen	Director	March 12, 2018
/s/ Sanj K. Patel Sanj K. Patel	Director	March 12, 2018
/s/ Vicki L Sato, Ph.D. Vicki L. Sato, Ph.D.	Director	March 12, 2018
/s/ Phillip A. Sharp, Ph.D. Phillip A. Sharp, Ph.D.	Director	March 12, 2018
/s/ Richard A. Young, Ph.D. Richard A. Young, Ph.D.	Director	March 12, 2018

Exhibit 4.4

STOCK PURCHASE AGREEMENT

This Stock Purchase Agreement (this "Agreement") is dated as of January 8, 2018, between Syros Pharmaceuticals, Inc., a Delaware corporation (the "Company"), and Incyte Corporation, a Delaware corporation ("Purchaser").

WHEREAS, the Company and Purchaser entered into that certain Target Discovery, Research Collaboration and Option Agreement dated as of the date hereof (the "Collaboration Agreement"); and

WHEREAS, in connection with the execution of the Collaboration Agreement, the Company desires to sell to Purchaser, and Purchaser desires to purchase from the Company, shares of Common Stock of the Company in the amount and upon the terms and conditions set forth in this Agreement.

NOW, THEREFORE, IN CONSIDERATION of the mutual covenants contained in this Agreement, and for other good and valuable consideration the receipt and adequacy of which are hereby acknowledged, the Company and Purchaser agree as follows:

ARTICLE I.
DEFINITIONS

1.1 Definitions. In addition to the terms defined elsewhere in this Agreement, for all purposes of this Agreement, the following terms have the meanings set forth in this Section 1.1:

"Affiliate" means any Person that, directly or indirectly through one or more intermediaries, controls or is controlled by or is under common control with a Person as such terms are used in and construed under Rule 405 under the Securities Act.

"Board of Directors" means the board of directors of the Company.

"Business Day" means any day except Saturday, Sunday and any day on which banking institutions in New York, New York, generally are closed as a result of federal, state or local holiday.

"Closing" has the meaning ascribed to such term in Section 2.1.

"Collaboration Agreement" has the meaning ascribed to such term in the preamble.

"Commission" means the United States Securities and Exchange Commission.

"Common Stock" means the common stock of the Company, par value $0.001 per share, and any other class of securities into which such securities may hereafter be reclassified or changed.

"Common Stock Equivalents" means any securities of the Company which would entitle the holder thereof to acquire at any time Common Stock, including, without

limitation, any debt, preferred stock, right, option, warrant or other instrument that is at any time convertible into or exercisable or exchangeable for, or otherwise entitles the holder thereof to receive, Common Stock.

"Company Counsel" means Wilmer Cutler Pickering Hale and Dorr LLP, with offices located at 60 State Street, Boston, MA 02109.

"Exchange Act" means the Securities Exchange Act of 1934, as amended, and the rules and regulations promulgated thereunder.

"Exempt Issuance" means the issuance of (a) shares of Common Stock or options to employees, consultants, officers or directors of the Company pursuant to any stock or option plan or stock purchase plan, as applicable, duly adopted for such purpose and in existence on the date of this Agreement as such plan is constituted on the date of this Agreement, by a majority of the non-employee members of the Board of Directors or a majority of the members of a committee of non-employee directors established for such purpose, unless otherwise agreed to by the non-employee members of the Board of Directors, (b) securities upon the exercise or exchange of or conversion of any Common Stock Equivalents issued and outstanding on the date of this Agreement, provided that such securities have not been amended on or after the date of this Agreement to increase the number of such securities or to decrease the exercise price, exchange price or conversion price of such securities, (c) securities pursuant to acquisitions or strategic transactions approved by a majority of the disinterested directors of the Company, provided that any such issuance shall not include a transaction in which the Company is issuing securities primarily for the purpose of raising capital or to an entity whose primary business is investing in securities, (d) shares of Common Stock in an "at-the-market" offering, and (e) shares of Common Stock or Common Stock Equivalents issued to banks, equipment lessors or other financial institutions, or to real property lessors, pursuant to a debt financing, equipment leasing or real property leasing transaction approved by the Board of Directors.

"FCPA" means the Foreign Corrupt Practices Act of 1977, as amended.

"FINRA" means the Financial Industry Regulatory Authority.

"GAAP" has the meaning ascribed to such term in Section 3.1(g).

"Governmental Authority" means any court, agency, authority, department, regulatory body or other instrumentality of any government or country or of any national, federal, state, provincial, regional, county, city or other political subdivision of any such government or country or any supranational organization of which any such country is a member.

"Intellectual Property" means patents, patent applications, trademarks, trademark applications, service marks, trade names, trade dress, trade secrets, inventions and discoveries and invention disclosures whether or not patented, copyrights in both published and unpublished works, including without limitation all compilations, data

bases and computer programs, materials and other documentation, licenses, internet domain names and other intellectual property rights and similar rights.

"Liens" means a lien, charge, pledge, security interest, encumbrance, right of first refusal, preemptive right or other restriction.

"Lock-Up Period" has the meaning assigned to such term in Section 5.1(a).

"Material Adverse Effect" means any (i) material adverse effect on the legality, validity or enforceability of this Agreement, (ii) material adverse effect on the results of operations, assets, business or condition (financial or otherwise) of the Company and its Subsidiary, taken as a whole, or (iii) material adverse effect on the Company's ability to perform in any material respect on a timely basis its obligations under this Agreement.

"Order" means any assessment, award, decision, injunction, judgment, order, ruling, verdict or writ entered, issued, made, or rendered by any court, administrative agency, or other Governmental Authority or by any arbitrator.

"Person" means an individual or corporation, partnership, trust, incorporated or unincorporated association, joint venture, limited liability company, joint stock company, government (or an agency or subdivision thereof) or other entity of any kind.

"Purchase Price" has the meaning ascribed to such term in Section 2.1.

"Registration Statement" means a registration statement on Form S-3 (or any successor form related to secondary offerings) required to be filed hereunder as contemplated by Article IV, including any preliminary prospectus, the prospectus, amendments and supplements to such registration statement, preliminary prospectus or prospectus, including pre- and post-effective amendments, all exhibits thereto, and all material incorporated by reference or deemed to be incorporated by reference in such registration statement.

"Rule 144" means Rule 144 promulgated by the Commission pursuant to the Securities Act, as such Rule may be amended or interpreted from time to time, or any similar rule or regulation hereafter adopted by the Commission having substantially the same purpose and effect as such Rule.

"SEC Reports" has the meaning ascribed to such term in Section 3.1(g).

"Securities Act" means the Securities Act of 1933, as amended, and the rules and regulations promulgated thereunder.

"Shares" has the meaning ascribed to such term in Section 2.1.

"Subsidiary" means Syros Securities Corporation, a Massachusetts corporation and the Company's wholly-owned subsidiary.

"Trading Day" means a day on which The NASDAQ Global Select Market is open for trading.

"Transfer Agent" means Computershare Ltd, the current transfer agent of the Company, with a mailing address of 250 Royal Street, Canton, MA 02021 and a facsimile number of (781) 575-4647, and any successor transfer agent of the Company.

ARTICLE II.
PURCHASE AND SALE

2.1 Purchase and Sale of Shares; Closing. Subject to the terms and conditions of this Agreement, the Company agrees to sell to Purchaser at the Closing, free and clear of all Liens, and Purchaser agrees to purchase from the Company at the Closing, 793,021 shares of Common Stock (the "Shares") at a price per share of $12.61 for an aggregate purchase price of $9,999,994.81 (the " Purchase Price"). Subject to the satisfaction or waiver of the conditions set forth in Section 2.4, the Closing shall take place remotely via the exchange of documents and signatures at 10:00 a.m. Eastern Time on the date hereof, or at such other time and location as the Company and Purchaser shall mutually agree (which time and location are designated as the "Closing" and the date thereof as the " Closing Date").

2.2 Delivery and Payment. At the Closing, subject to the terms and conditions hereof, the Company will deliver the Shares to the Purchaser (and the Company will instruct the Transfer Agent to deliver the Shares to the Purchaser via book entry to the applicable balance account registered in the name of the Purchaser) against payment of the Purchase Price in U.S. dollars by wire transfer of immediately available funds made payable to the order of the Company.

2.3 Deliveries at Closing.

(a) Deliveries by the Company. At the Closing, subject to the terms and conditions of this Agreement, the Company shall deliver or cause to be delivered to the Purchaser the following items:

(i) a legal opinion of Company Counsel dated as of the Closing Date substantially in the form of Exhibit A attached hereto;

(ii) a copy of the irrevocable instructions to the Transfer Agent instructing the Transfer Agent to deliver, on an expedited basis, the Shares to the Purchaser, via a book entry position in an account registered in the name of the Purchaser at the Transfer Agent and evidence of Purchaser's ownership of the Shares from the Transfer Agent in the form of Direct Registration Book Entry Advice;

(iii) a compliance certificate, executed by the Chief Executive Officer of the Company, dated as of the Closing Date, to the effect that the conditions specified in Section 2.4(b)(i) and (ii) have been satisfied;

(iv) a certificate of the Company's Secretary certifying as to (A) the Company's certificate of incorporation and bylaws, (B) the resolutions of the Board of Directors approving this Agreement and the transactions contemplated hereby, (C) good standing certificates with respect to the Company from the applicable authorities in the State of Delaware and each state in which the Company is qualified to do business as a foreign corporation, dated a recent date before the Closing, and (D) the incumbency and specimen signature of any officer of the Company executing this Agreement on behalf of the Company; and

(v) all such other documents, certificates and instruments as the Purchaser may reasonably request in order to give effect to the transactions contemplated hereby.

(b) Deliveries by the Purchaser. At the Closing, the Purchaser shall deliver or cause to be delivered to the Company the Purchase Price, by wire transfer of immediately available funds to one or more accounts designated by the Company no later than two (2) Business Days prior to the Closing Date.

2.4 Closing Conditions.

(a) The obligation of the Company to sell the Shares to Purchaser at the Closing is subject to the following conditions being met or waived in writing by the Company:

(i) the representations and warranties of Purchaser contained in Section 3.2 shall be true and correct as of the date hereof (unless specifically made as of another date, in which case as of such other date, and after giving effect to any materiality or other qualifiers contained therein);

(ii) Purchaser shall have performed and complied with all covenants, agreements, obligations and conditions contained in this Agreement that are required to be performed or complied with by Purchaser on or before the Closing;

(iii) Purchaser shall have executed and delivered the Collaboration Agreement; and

(iv) Purchaser shall have delivered the Purchase Price.

(b) The obligation of Purchaser to purchase the Shares at the Closing is subject to the following conditions being met or waived in writing by Purchaser:

(i) the representations and warranties of the Company contained in Section 3.1 shall be true and correct as of the date hereof (unless specifically made as of another date, in which case as of such other date, and after giving effect to any materiality or other qualifiers contained therein);

(ii) the Company shall have performed and complied with all covenants, agreements, obligations and conditions contained in this Agreement

that are required to be performed or complied with by the Company on or before the Closing;

(iii) the Company shall have executed and delivered the Collaboration Agreement;

(iv) the Company shall have delivered or caused to be delivered to the Purchaser the items set forth in Section 2.3(a) of this Agreement;

(v) the sale and issuance of the Shares shall be legally permitted by all laws to which the Purchaser and the Company are subject;

(vi) no Order shall be in effect preventing the consummation of the transactions contemplated by this Agreement or the Collaboration Agreement;

(vii) all consents necessary or appropriate for consummation of the transactions contemplated by this Agreement shall have been obtained;

(viii) no Material Adverse Effect shall have occurred and be continuing; and

(ix) the Company's Common Stock shall continue to be listed on The NASDAQ Global Select Market.

ARTICLE III.
REPRESENTATIONS AND WARRANTIES

3.1 Representations and Warranties of the Company. The Company hereby represents and warrants to Purchaser as of the date hereof (unless specifically made as of another date, in which case as of such other date) as follows:

(a) Capitalization. The capitalization of the Company as of September 30, 2017 is as set forth in the SEC Reports. The Company has not issued any capital stock since its most recently filed periodic report under the Exchange Act, other than pursuant to the exercise of stock options under the Company's stock incentive plans and the issuance of shares of Common Stock pursuant to the Company's at-the-market sales agreement. No Person has any right of first refusal, preemptive right, right of participation, or any similar right to participate in the transactions contemplated by this Agreement. Except as disclosed on Schedule 3.1(a) and as a result of the purchase and sale of the Shares, there are no outstanding options, warrants, scrip rights to subscribe to, calls or commitments of any character whatsoever relating to, or securities, rights or obligations convertible into or exercisable or exchangeable for, or giving any Person any right to subscribe for or acquire, any shares of Common Stock, or contracts, commitments, understandings or arrangements by which the Company is or may become bound to issue additional shares of Common Stock or Common Stock Equivalents. The issuance and sale of the Shares will not obligate the Company to issue shares of Common Stock or other securities to any Person and will not result in a right of any holder of Company securities to adjust the exercise, conversion, exchange or reset price under any

of such securities. All of the outstanding shares of capital stock of the Company are duly authorized, validly issued, fully paid and nonassessable, have been issued in compliance with all federal and state securities laws, and none of such outstanding shares was issued in violation of any preemptive rights or similar rights to subscribe for or purchase securities. No further approval or authorization of any stockholder, the Board of Directors or others is required for the issuance and sale of the Shares. Except as disclosed on Schedule 3.1(a), there are no stockholders agreements, voting agreements or other similar agreements with respect to the Company's capital stock to which the Company is a party or, to the knowledge of the Company, between or among any of the Company's stockholders. The Common Stock is registered pursuant to Section 12(b) or 12(g) of the Exchange Act, and the Company has taken no action designed to, or which to the Company's knowledge is likely to have the effect of, terminating the registration of the Common Stock under the Exchange Act nor has the Company received any notification that the Commission is contemplating terminating such registration.

(b) Litigation. There are no actions, suits, proceedings or, to the knowledge of the Company, any investigations, pending or currently threatened against the Company or its Subsidiary that question the validity of this Agreement or the issuance of the Shares contemplated hereby or would, if there were an unfavorable decision, have or could reasonably be expected to result in a Material Adverse Effect. As of the date hereof, there is no material action, suit, or proceeding pending or, to the knowledge of the Company, currently threatened against the Company or its Subsidiary. As of the date hereof, there are no material outstanding consents, orders, decrees or judgments of any governmental entity naming the Company or its Subsidiary. Neither the Company, its Subsidiary nor, to the knowledge of the Company, any director or officer thereof, is or has been the subject of any action involving a claim of violation of or liability under federal or state securities laws or a claim of breach of fiduciary duty. There has not been, and to the knowledge of the Company, there is not pending or contemplated, any investigation by the Commission involving the Company, its Subsidiary or any current or former director or officer of the Company or its Subsidiary. The Commission has not issued any stop order or other order suspending the effectiveness of any registration statement filed by the Company under the Exchange Act or the Securities Act.

(c) Organization and Good Standing. The Company is a corporation duly organized, validly existing and in good standing under the laws of the State of Delaware, and its Subsidiary is a corporation duly organized, validly existing and in good standing under the laws of the Commonwealth of Massachusetts. Each of the Company and its Subsidiary has all requisite corporate power and authority to own, lease and operate its properties and carry on its business as now conducted and as proposed to be conducted as described in the SEC Reports. Each of the Company and the Subsidiary is duly qualified and is in good standing as a foreign corporation in each jurisdiction in which the properties owned, leased or operated, or the business conducted, by it requires such qualification except where the failure to be so qualified or in good standing, individually or in the aggregate, would not have a Material Adverse Effect.

(d) Authorization. All corporate actions on the part of the Company, its officers, directors and stockholders necessary for the authorization, execution and

delivery of this Agreement and for the issuance of the Shares have been taken. The Company has the requisite corporate power to enter into this Agreement and to carry out and perform its obligations hereunder. This Agreement has been duly authorized, executed and delivered by the Company and, upon due execution and delivery by Purchaser, will be a valid and binding agreement of the Company, except as enforceability may be limited by bankruptcy, insolvency, reorganization, moratorium or similar laws affecting creditors' rights generally or by equitable principles.

(e) Subsidiary. The Company owns, directly or indirectly, all of the capital stock or other equity interests of the Subsidiary free and clear of any Liens. All of the issued and outstanding shares of capital stock of the Subsidiary are validly issued, fully paid, non-assessable and free of preemptive and similar rights to subscribe for or purchase securities. Other than the Subsidiary, the Company does not currently own or control, directly or indirectly, any interest in any other corporation, partnership, trust, joint venture, limited liability company, association, or other business entity, and the Subsidiary is the only entity the Company is required to disclose pursuant to Item 601(b)(21) of Regulation S-K in an exhibit to its Annual Report on Form 10-K. Except as disclosed in the SEC Reports, the Company is not a participant in any material joint venture, partnership or similar arrangement.

(f) No Conflict With Other Instruments. Neither the execution, delivery nor performance of this Agreement, nor the issuance of the Shares will result in (i) any violation of, be in conflict with, cause any acceleration or any increased payments under, or constitute a default under, with or without the passage of time or the giving of notice: (a) any provision of the Company's certificate of incorporation or bylaws; (b) any provision of any judgment, decree or order to which the Company or its Subsidiary is a party or by which it is bound; (c) any law, rule or regulation applicable to the Company or its Subsidiary; or (d) any note, mortgage, material contract, material agreement, material license, waiver, exemption, order or permit; or (ii) the creation or imposition of any lien, encumbrance, claim, security interest or restriction whatsoever upon any of the material properties or assets of the Company or its Subsidiary or an acceleration of indebtedness pursuant to any obligation, agreement or condition contained in any material bond, debenture, note or any other evidence of indebtedness or any material indenture, mortgage, deed of trust or any other agreement or instrument to which the Company or its Subsidiary is a party or by which it is bound or to which any of the material property or assets of the Company or its Subsidiary is subject.

(g) Disclosure Documents. Since July 6, 2016, the Company has filed, on a timely basis or has received a valid extension as of such time of filing and has thereafter made such filings prior to the expiration of any such extension, all reports, schedules, forms, statements and other documents required to be filed by the Company with the Commission under the Securities Act and the Exchange Act, including pursuant to Section 13(a) or 15(d) thereof (the foregoing materials, including the exhibits thereto and documents incorporated by reference therein, being collectively referred to herein as the "SEC Reports"), and the Company has paid all fees and assessments due and payable in connection with the SEC Reports. As of their respective dates, the SEC Reports complied in all material respects with all statutes and applicable rules and regulations of

the Commission, including the requirements of the Securities Act and the Exchange Act, as applicable, and none of the SEC Reports, when filed, contained any untrue statement of a material fact or omitted to state a material fact required to be stated therein or necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading. Other than the transactions that are the subject of this Agreement and the Collaboration Agreement, no material fact or circumstance exists that would be required to be disclosed in a current report on Form 8-K or in a registration statement filed under the Securities Act, were such a registration statement filed on the date hereof, which has not been disclosed in an SEC Report. The financial statements of the Company included in the SEC Reports comply in all material respects with applicable accounting requirements and the rules and regulations of the Commission with respect thereto as in effect at the time of filing. Such financial statements (i) have been prepared in accordance with United States generally accepted accounting principles ("GAAP"), applied on a consistent basis during the periods involved, except as may be otherwise specified in such financial statements or the notes thereto and except that unaudited financial statements may not contain all footnotes required by GAAP and (ii) fairly present in all material respects the financial position of the Company and its consolidated Subsidiary as of and for the dates thereof and the results of operations and cash flows for the periods then ended, subject, in the case of unaudited statements, to normal, immaterial, year-end audit adjustments.

(h) Absence of Certain Events and Changes . Except as otherwise disclosed in the SEC Reports, since the date of the Company's Quarterly Report on Form 10-Q for the quarter ended on September 30, 2017: (i) each of the Company and its Subsidiary has conducted its business in the ordinary course consistent with past practice, (ii) there has not been any event, change or development which, individually or in the aggregate, has had or could reasonably be expected to have a Material Adverse Effect, (iii) neither the Company nor its Subsidiary has incurred any material liabilities (absolute or accrued, contingent or otherwise) other than expenses incurred in the ordinary course of business consistent with past practice, (iv) neither the Company nor its Subsidiary has altered its method of accounting in any material respect, and (v) the Company has not declared or made any dividend or distribution of cash or other property to its shareholders or purchased, redeemed or made any agreements to purchase or redeem any shares of its capital stock.

(i) Intellectual Property. Except as otherwise disclosed by the Company in writing to Purchaser, the Company owns, or has the right pursuant to a valid, written license agreement to use and exploit, all Intellectual Property used in or necessary for the conduct of the business of the Company and that is material to the business of the Company as conducted as of the date hereof (the "Company Intellectual Property"). The Subsidiary does not own or have the right to use any Intellectual Property, other than shrink wrap licenses for business software used in the ordinary course of the business presently conducted by the Subsidiary. The Company Intellectual Property that is owned by the Company is owned free from any Liens (other than any Liens set forth in any license agreement relating to such Company Intellectual Property), and all of the Company's material licenses are in full force and effect in accordance with their terms, are free of any Liens and neither the Company nor, to the Company's knowledge, any

other party thereto is in material breach of any such material license, and no event has occurred that with notice or lapse of time or both would constitute such a breach or default thereunder or would result in the termination thereof or would cause or permit the acceleration or other change of any right or obligation or the loss of any benefit thereunder by the Company, except for such failures to be in full force and effect, such Liens and such material breaches that would not reasonably be expected, individually or in the aggregate, to have a Material Adverse Effect. To the knowledge of the Company, (i) all issued patents and registered trademarks that are Company Intellectual Property and that are owned by the Company are valid and enforceable and are currently in compliance with formal legal requirements (including without limitation, as applicable, payment of filing, examination and maintenance fees, proofs of work or use, timely post registration filing of affidavits of use and incontestability and renewal applications), and (ii) there is no existing infringement or misappropriation by another Person of any of the Company Intellectual Property that has had or could reasonably be expected to have a Material Adverse Effect. Except as disclosed in the SEC Reports, since July 1, 2016, no claims have been asserted by a third party in writing and there are no proceedings pending (of which the Company has received notice or otherwise has knowledge) or, to the knowledge of the Company, threatened (a) alleging that the conduct of the business of the Company has infringed or misappropriated any Intellectual Property rights of such third party, or (b) challenging the validity or effectiveness of any Company Intellectual Property, and, to the Company's knowledge, there is no valid basis for any such claim. No loss or early expiration of any of the Company Intellectual Property is pending, or, to the Company's knowledge, threatened. The Company has taken reasonable steps in accordance with standard industry practices to protect its rights in the Company Intellectual Property and to maintain the confidentiality of all information used in connection with its business that constitutes or constituted a trade secret of the Company.

(j) Compliance. Each of the Company and its Subsidiary has all material permits, licenses, franchises, authorizations, orders and approvals of (collectively, "Permits"), and has made all filings, applications and registrations with, Governmental Authorities that are required in order to permit the Company or its Subsidiary, as applicable, to own or lease its properties and assets and to carry on its business as presently conducted. Neither the sale of the Shares hereunder nor the performance of the Company's other obligations under this Agreement will result in the suspension, revocation, impairment, forfeiture or nonrenewal of any Permit applicable to the Company or its Subsidiary, their respective businesses or operations or any of their respective assets or properties. Each of the Company and its Subsidiary has complied and is in compliance in all material respects with all Permits, statutes, laws, regulations, rules, judgments, orders and decrees of all Governmental Authorities applicable to it that relate to its business, including but not limited to compliance with the FCPA and any applicable similar laws in foreign jurisdictions in which the Company or its Subsidiary is currently, or has previously, conducted its business. Neither the Company nor its Subsidiary has received any notice alleging noncompliance, and, to the knowledge of the Company, neither the Company nor its Subsidiary is under investigation with respect to, or threatened to be charged with, any material violation of any applicable statutes, laws, regulations, rules, judgments, orders or decrees of any governmental entities. Neither the Company nor its Subsidiary has received any notice of proceedings relating to the

revocation or modification of any Permit. No Permit is subject to termination as a result of the execution of this Agreement or consummation of the transactions contemplated hereby. Except as disclosed in the SEC Reports, since July 1, 2016, neither the Company nor its Subsidiary has entered into or been subject to any judgment, consent decree, compliance order or administrative order with respect to any aspect of the business, affairs, properties or assets of the Company or its Subsidiary or received any formal or informal complaint or claim from any regulatory agency with respect to any aspect of the business, affairs, properties or assets of the Company or its Subsidiary.

(k) Clinical Data and Regulatory Compliance. To the Company's knowledge, (i) the preclinical tests and clinical trials, and other studies (collectively, "studies") that are described in, or the results of which are referred to in, the SEC Reports were and, if still pending, are being conducted in all material respects in accordance with the protocols, procedures and controls designed and approved for such studies pursuant to, where applicable, accepted professional scientific standards; (ii) each description of the results of such studies in the SEC Reports is accurate and complete in all material respects and fairly presents the data derived from such studies; (iii) the Company has no knowledge of any other studies not disclosed in the SEC Reports the results of which are inconsistent in any material respect with, or otherwise call into question, the results described or referred to in the SEC Reports; (iv) the Company has made all such filings and obtained all such approvals as may be required by the Food and Drug Administration of the U.S. Department of Health and Human Services (the "FDA") or comparable federal, state, local or foreign Governmental Authorities (collectively, the "Regulatory Agencies") in order to permit the Company to carry on its business as now conducted and as proposed to be conducted, except where any failures to make or obtain the same would not, individually or in the aggregate, reasonably be expected to have a Material Adverse Effect; (v) except as described in the SEC Reports, the Company has not received any notice of, or correspondence from, any Regulatory Agency requiring the termination, suspension or material modification of any clinical trials that are described or referred to in the SEC Reports; and (vi) the Company has operated and currently is in compliance in all material respects with all applicable rules and regulations of the Regulatory Agencies governing its business.

(l) Clinical Trials. Each Investigational New Drug ("IND") application submitted to the FDA by the Company and, to the knowledge of the Company, each IND submitted by a third party in relation to the Company's product candidates, and related documents and information, has been filed, approved and maintained in compliance in all material respects with applicable statutes, rules, regulations or orders administered or promulgated by the FDA or other Regulatory Agency, and all pre-clinical and clinical studies undertaken to support approval of products for commercialization have been conducted in compliance with all applicable current Good Laboratory Practices and Good Clinical Practices in all material respects. No filing or submission to the FDA or any other Regulatory Agency by the Company and, to the knowledge of the Company, no filing or submission to the FDA or any other Regulatory Agency by a third party that is intended to be the basis for any approval for one of the Company's product candidates, contains any material omission or material false information.

(m) Valid Issuance of Shares . The Shares are duly authorized and, when issued and paid for in accordance with this Agreement, will be duly and validly issued, fully paid and nonassessable, free and clear of all Liens (other than as arising pursuant to this Agreement, as a result of any action by the Purchaser or under federal or state securities laws), and, based in part on the representations of Purchaser in Section 3.2 of this Agreement, will be issued in compliance with all applicable federal and state securities laws. Neither the Company nor any Person acting on behalf of the Company has offered or sold any of the Shares by any form of general solicitation or general advertising. The Company has offered the Shares for sale only to Purchaser.

(n) Governmental Consents. No consent, approval, order or authorization of, or registration, qualification, designation, declaration or filing with, any Governmental Authority on the part of the Company is required in connection with the Company's execution, delivery and performance of this Agreement and the consummation of the transactions contemplated by this Agreement, except such as have been obtained or made by the Company and are in full force and effect and except for notices required or permitted to be filed with certain state and federal securities commissions, which notices will be filed on a timely basis.

(o) No Brokers. No broker, finder or investment banker is entitled to any brokerage, finder's or other fee or commission in connection with the transactions contemplated by this Agreement based on arrangements made by the Company.

(p) No Undisclosed Liabilities. Neither the Company nor its Subsidiary has any liabilities (absolute or accrued, contingent or otherwise), except for (i) liabilities reflected or reserved against in consolidated financial statements of the Company and its Subsidiary (or otherwise disclosed in the accompanying footnotes) included in the SEC Reports filed with the Commission prior to the date of this Agreement, (ii) liabilities incurred in the ordinary course of business or otherwise disclosed in SEC Reports subsequent to the period covered by the Company's Quarterly Report on Form 10-Q for the quarter ended on September 30, 2017 and (iii) liabilities that have not been and would not reasonably be expected, individually or in the aggregate, to be material.

(q) Internal Controls. The Company has implemented and maintains a system of internal control over financial reporting (as required by Rule 13a-15(a) under the Exchange Act) that is designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of consolidated financial statements for external purposes, and, to the knowledge of the Company, such system of internal control over financial reporting is effective. For purposes of this Section 3.1(q), "knowledge of the Company" means the actual knowledge of the Principal Executive Officer and Principal Financial Officer of the Company as of the date hereof. The Company has implemented and maintains disclosure controls and procedures (as required by Rule 13a-15(a) of the Exchange Act) that are designed to ensure that information required to be disclosed by the Company in the reports it files or submits under the Exchange Act is recorded, processed, summarized and reported within the timeframes specified by the Commission's rules and forms (and such disclosure controls and procedures are effective), and has disclosed, based on its most recent evaluation of its system of internal

control over financial reporting prior to the date of this Agreement, to the audit committee of the Board of Directors, (i) any significant deficiencies and material weaknesses known to it in the design or operation of its internal control over financial reporting (as defined in Rule 13a-15(f) of the Exchange Act) that would reasonably be expected to adversely affect the Company's ability to record, process, summarize and report financial information and (ii) any fraud known to it, that involves management or other employees who have a significant role in the Company's internal control over financial reporting.

(r) Company Not An "Investment Company." The Company has been advised of the rules and requirements under the Investment Company Act of 1940, as amended (the "Investment Company Act"). The Company is not, and immediately after receipt of payment for the Shares will not be, an "investment company" or an entity "controlled" by an "investment company" within the meaning of the Investment Company Act.

(s) Solvency. Neither the Company nor its Subsidiary has: (i) made a general assignment for the benefit of creditors; (ii) filed any voluntary petition in bankruptcy or suffered the filing of any involuntary petition by its creditors; (iii) suffered the appointment of a receiver to take possession of all, or substantially all, of its assets; (iv) suffered the attachment or other judicial seizure of all, or substantially all, of its assets; (v) admitted in writing its inability to pay its debts as they come due; or (vi) made an offer of settlement, extension or composition to its creditors generally.

(t) No Integrated Offering. Neither the Company, nor any of its Affiliates, nor any Person acting on its or their behalf has, directly or indirectly, made any offers or sales of any security or solicited any offers to buy any security, under circumstances that would cause this offering of the Shares to be integrated with prior offerings by the Company for purposes of the Securities Act or any applicable shareholder approval provisions, including, without limitation, under the rules and regulations of The NASDAQ Global Select Market.

(u) Whistleblowers. To the knowledge of the Company, as of the date hereof, no employee of the Company or its Subsidiary has provided since July 1, 2016 or is providing information to any law enforcement agency regarding the violation of any applicable law of the type described in Section 806 of the Sarbanes-Oxley Act by the Company or its Subsidiary. Neither the Company nor its Subsidiary have discharged, demoted or suspended an employee of the Company or its Subsidiary in the terms and conditions of employment because of any lawful act of such employee described in Section 806 of the Sarbanes-Oxley Act.

(v) Foreign Corrupt Practices. Neither the Company, its Subsidiary nor, to the knowledge of the Company, any agent or other Person acting on behalf of the Company or its Subsidiary has (i) directly or indirectly, used any corporate funds for unlawful contributions, gifts, entertainment or other unlawful expenses related to foreign or domestic political activity; (ii) made any unlawful payment to foreign or domestic government officials or employees or to any foreign or domestic political parties or

campaigns from corporate funds; (iii) failed to disclose fully any contribution made by the Company or its Subsidiary (or made by any Person acting on behalf of the Company or its Subsidiary of which the Company is aware) which is in material violation of law; or (iv) violated in any material respect any provision of the FCPA or any non-U.S. anti-bribery law applicable to the Company or its Subsidiary.

(w) Regulation M Compliance. The Company has not, and to its knowledge no one acting on its behalf has, (i) taken, directly or indirectly, any action designed to cause or to result in the stabilization or manipulation of the price of any security of the Company to facilitate the sale or resale of any of the Shares; (ii) sold, bid for, purchased, or paid any compensation for soliciting purchases of any of the Shares; or (iii) paid or agreed to pay to any Person any compensation for soliciting another to purchase any other securities of the Company, in each case in violation of Regulation M or to the extent otherwise unlawful.

(x) Office of Foreign Assets Control . Neither the Company, its Subsidiary nor, to the Company's knowledge, any director, officer, agent, employee or affiliate of the Company is currently subject to any U.S. sanctions administered by the Office of Foreign Assets Control of the U.S. Treasury Department.

3.2 Representations and Warranties of Purchaser. Purchaser hereby represents and warrants to the Company as of the date hereof (unless specifically made as of another date, in which case as of such other date) as follows:

(a) Legal Power. Purchaser has the requisite corporate power to enter into this Agreement and to carry out and perform its obligations hereunder.

(b) Due Execution. This Agreement has been duly authorized, executed and delivered by Purchaser, and, upon due execution and delivery by the Company, will constitute a valid and legally binding obligation of Purchaser, enforceable against Purchaser in accordance with its terms, except as may be limited by bankruptcy, insolvency, reorganization, moratorium or similar laws affecting creditors' rights generally or by equitable principles.

(c) Investment Representations. In connection with the offer, purchase and sale of the Shares, Purchaser makes the following representations:

(i) Purchaser is acquiring the Shares for its own account for the purpose of investment and not with a view to or for sale in connection with any distribution thereof, and has no present intention to effect, or any present or contemplated plan, agreement, undertaking, arrangement, obligation, indebtedness, or commitment providing for, any distribution of the Shares.

(ii) Purchaser has carefully reviewed the representations concerning the Company contained in this Agreement and has made detailed inquiry concerning the Company, its business and its personnel.

(iii) Purchaser understands that the Shares have not been registered under the Securities Act or any applicable state securities laws and, consequently, Purchaser may have to bear the risk of owning the Shares for an indefinite period of time because the Shares may not be transferred unless (x) the resale of the Shares is registered pursuant to an effective registration statement under the Securities Act in accordance with the terms and conditions set forth in Section 4.1 hereof; (y) Purchaser has delivered to the Company an opinion of counsel (in form, substance and scope customary for opinions of counsel in comparable transactions) to the effect that the Shares to be sold or transferred may be sold or transferred pursuant to an exemption from such registration; or (z) the Shares are sold or transferred pursuant to Rule 144.

(iv) Purchaser has such knowledge and experience in financial or business matters that it is capable of evaluating the merits and risks of the investment in the Shares to be purchased hereunder.

(v) Purchaser is an "accredited investor" as defined in Rule 501(a) of the rules and regulations promulgated under the Securities Act.

(d) Certain Fees. No broker, finder or investment banker is entitled to any brokerage, finder's or other fee or commission in connection with the transactions contemplated by this Agreement based on arrangements made by Purchaser.

(e) Legends. In connection with the issuance and sale of the Shares, Purchaser understands that each of the Shares, whether certificated or in book-entry form, will be endorsed with the following legend:

"THE SECURITIES REPRESENTED HEREBY HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "ACT"), OR UNDER THE SECURITIES LAWS OF CERTAIN STATES. THESE SECURITIES ARE SUBJECT TO RESTRICTIONS ON TRANSFERABILITY AND RESALE AND MAY NOT BE TRANSFERRED OR RESOLD EXCEPT AS PERMITTED UNDER THE ACT AND ANY APPLICABLE STATE SECURITIES LAWS, PURSUANT TO REGISTRATION OR EXEMPTION THEREFROM OR UNLESS THE COMPANY HAS RECEIVED AN OPINION OF COUNSEL SATISFACTORY TO THE COMPANY AND ITS COUNSEL THAT SUCH REGISTRATION IS NOT REQUIRED."

The Company acknowledges and agrees that the representations contained in Section 3.2 shall not modify, amend or affect Purchaser's right to rely on the Company's representations and warranties contained in this Agreement or any representations and warranties contained in the Collaboration Agreement or any other document or instrument executed and/or delivered in connection with this Agreement or the Collaboration Agreement or the consummation of the transactions contemplated hereby.

ARTICLE IV.
REGISTRATION RIGHTS

4.1 Registration of the Shares. The Company shall file with the Commission, on or before the date that is twenty (20) days after the Closing Date or, in the case of securities sold to the Purchaser pursuant to the participation rights set forth in Section 5.8 hereof, thirty (30) days after the delivery of such securities to the Purchaser, a Registration Statement covering the resale to the public by Purchaser of the Shares or securities sold to the Purchaser pursuant to Section 5.8 hereof. (For purposes of this Article IV, the term "Shares" shall also refer to securities sold to the Purchaser pursuant to Section 5.8.) The Company shall use commercially reasonable efforts to cause the Registration Statement covering the Shares to be declared effective by the Commission by March 30, 2018 or, in the case of securities sold to the Purchaser pursuant to the participation rights set forth in Section 5.8 hereof, within ninety (90) days after the delivery of such securities to the Purchaser. The Company shall cause such Registration Statement to remain effective under the Securities Act until all Shares covered by such Registration Statement have been sold or may be sold without volume restrictions pursuant to Rule 144. The Company shall promptly notify Purchaser of the effectiveness of such Registration Statement after the Company confirms effectiveness with the Commission. The Company hereby covenants and agrees to use reasonable commercial efforts to maintain its eligibility to make filings with the Commission on Form S-3 until one or more Registration Statements covering the resale of all of the Shares shall have been filed with, and declared effective by, the Commission pursuant to the terms and conditions of this Agreement.

4.2 Registration Default. In relation to the Shares sold under this Agreement, in the event that the Registration Statement has not been declared effective by March 30, 2018 (it being acknowledged and agreed that there shall be no cure period for any such breach), the Company shall pay to the Purchaser a fee of one percent (1%) of the Purchase Price (i) within seven (7) days after March 30, 2018 and (ii) for every thirty (30) day period thereafter that the Registration Statement has not been declared Effective (with the initial such thirty (30) day period commencing on March 30, 2018), up to a maximum of six percent (6%) of the Purchase Price for any such fees due to the Purchaser under (i) and (ii), in the aggregate; *provided*, however, that the Company shall not be obligated to pay any such liquidated damages if: (a) the Company has complied with all obligations of the Company set forth in Section 4.1 and has filed responses to any comments from the Commission related to the Registration Statement within ten (10) Business Days of receiving such comments; (b) the Shares that would otherwise be covered by the Registration Statement may be sold without the requirement to be in compliance with Rule 144(c)(1) and otherwise without restriction or limitation pursuant to Rule 144 under the Securities Act; or (c) the Company is unable to fulfill its registration obligations as a result of rules, regulations, positions or releases issued or actions taken by the Commission pursuant to its authority with respect to Rule 415, and the Company registers at such time the maximum number of shares of Common Stock permissible upon consultation with the staff of the Commission; *provided, further*, that if the Purchaser fails to provide the Company with any information that is required to be provided in such Registration Statement with respect to the Purchaser, then the commencement of the first thirty (30) day period described above shall be extended until two (2) Business Days following the date of receipt by the Company of such required information. For the avoidance of doubt, this Section 4.2 shall not apply to any securities sold to the Purchaser pursuant to the participation rights set forth in Section 5.8 hereof.

4 . 3 Registration Covenant. Purchaser covenants and agrees that it will comply with the prospectus delivery requirements of the Securities Act as applicable to it in connection with sales of the Shares pursuant to a Registration Statement. The Company shall comply in all material respects with all applicable rules and regulations of the Commission applicable to the filing of a Registration Statement.

4.4 Registration Procedures.

(a) In connection with the filing by the Company of a Registration Statement covering the Shares, the Company shall furnish to Purchaser (i) a copy of the prospectus, including a preliminary prospectus, in conformity with the requirements of the Securities Act and (ii) such other documents as Purchaser may reasonably request, in order to facilitate the public sale or other disposition of the Shares.

(b) The Company shall use commercially reasonable efforts to register or qualify the Shares covered by a Registration Statement under the securities laws of each state of the United States as Purchaser shall reasonably request; provided, however, that the Company shall not be required in connection with this subsection (b) to qualify as a foreign corporation or execute a general consent to service of process in any jurisdiction.

(c) If the Company has delivered preliminary or final prospectuses to Purchaser and after having done so the prospectus is amended or supplemented to comply with the requirements of the Securities Act, the Company shall promptly notify Purchaser and, if requested by the Company, Purchaser shall immediately cease making offers or sales of the Shares covered by a Registration Statement and return all prospectuses to the Company. The Company shall promptly provide Purchaser with revised or supplemented prospectuses and, following receipt of the revised or supplemented prospectuses, Purchaser shall be free to resume making offers and sales of the Shares under such Registration Statement.

(d) The Company shall be entitled to include in a Registration Statement the shares of Common Stock held by other shareholders of the Company, provided such other shares of Common Stock are excluded first from such Registration Statement in order to comply with any applicable laws or request from any Governmental Authority or The NASDAQ Global Select Market, or in the case of an underwritten offering, in order to comply with a cutback request of any underwriter.

(e) The Company shall pay all expenses incurred in connection with the preparation and filing of such Registration Statement pursuant to this Article IV, including all registration and filing fees and printer, legal and accounting fees related thereto but excluding (i) any brokerage fees, selling commissions or underwriting discounts incurred by Purchaser in connection with sales under any Registration Statement covering the Shares and (ii) the fees and expenses of counsel retained by Purchaser.

(f) The Company shall use commercially reasonable efforts to avoid the issuance of any order suspending the effectiveness of a Registration Statement, or any

suspension of the qualifications (or exemption from qualification) of any of the Shares covered by a Registration Statement for sale in any jurisdiction. The Company shall advise Purchaser promptly after it shall receive notice of any stop order or issuance of any order by the Commission delaying or suspending the effectiveness of a Registration Statement covering the Shares or of the initiation of any proceeding for that purpose, and it will promptly use commercially reasonable efforts to prevent the issuance of any stop order or to obtain its withdrawal at the earliest possible moment if such stop order should be issued.

4 . 5 Registration Confidentiality. Purchaser agrees to treat as confidential (unless otherwise publicly disclosed by the Company or a third party not to the knowledge of Purchaser in breach of an agreement of confidentiality with the Company) any written notice from the Company regarding the Company's plans to file a Registration Statement and shall not disclose such information to any other person, or use such information, except as is necessary to exercise its rights under this Agreement.

4.6 Indemnification.

(a) The Company agrees to indemnify and hold harmless Purchaser and each other person, if any, who controls Purchaser within the meaning of the Securities Act or Exchange Act from and against any losses, claims, damages or liabilities to which Purchaser or controlling person may become subject (under the Securities Act, the Exchange Act, state securities or "Blue Sky" laws or otherwise) insofar as such losses, claims, damages or liabilities (or actions or proceedings in respect thereof) arise out of, or are based upon, (i) any untrue statement or alleged untrue statement of a material fact contained in any Registration Statement covering the Shares or in any preliminary prospectus or final prospectus contained in such Registration Statement, or any amendment or supplement to such Registration Statement, or the omission or alleged omission to state a material fact required to be stated therein or necessary to make the statements therein not misleading, or (ii) any violation by the Company of the Securities Act or the Exchange Act, or any rule or regulation promulgated under the Securities Act or the Exchange Act, applicable to the Company and relating to action or inaction required of the Company in connection with such registration. The Company will reimburse Purchaser or controlling person for any reasonable legal or other expenses reasonably incurred in investigating, defending or preparing to defend any such action, proceeding or claim, or preparing to defend any such action, proceeding or claim; provided, however, that the Company shall not be liable in any such case to the extent that such loss, claim, damage or liability arises out of, or is based upon, an untrue statement made in such Registration Statement, preliminary prospectus or prospectus, or any amendment or supplement in reliance upon and in conformity with written information furnished to the Company by or on behalf of Purchaser or controlling person specifically for use in the preparation thereof.

(b) Purchaser agrees to indemnify and hold harmless the Company and each person, if any, who controls the Company within the meaning of Section 15 of the Securities Act, each officer of the Company who signs the Registration Statement and each director of the Company, from and against any losses, claims, damages or liabilities

to which the Company or any officer, director or controlling person may become subject (under the Securities Act, the Exchange Act, state securities or "Blue Sky" laws or otherwise), insofar as such losses, claims, damages or liabilities (or actions or proceedings in respect thereof) arise out of, or are based upon any untrue statement of a material fact contained in any Registration Statement covering the Shares or in any preliminary prospectus, final prospectus contained in such Registration Statement, or any amendment or supplement to such Registration Statement or the omission or alleged omission to state a material fact required to be stated therein or necessary to make the statements therein not misleading, if such untrue statement or omission was made in reliance upon and in conformity with written information furnished by or on behalf of Purchaser specifically for use in preparation of the Registration Statement, prospectus, amendment or supplement and Purchaser will reimburse the Company, or such officer, director or controlling person, as the case may be, for any legal or other expenses reasonably incurred in investigating, defending or preparing to defend any such action, proceeding or claim; provided, however, that Purchaser's obligation to indemnify the Company shall be limited to the Purchase Price.

(c) Promptly after receipt by any indemnified person of a notice of a claim or the beginning of any action in respect of which indemnity is to be sought against an indemnifying person pursuant to this Section 4.6, such indemnified person shall notify the indemnifying person in writing of such claim or of the commencement of such action, but the omission to so notify the indemnifying party will not relieve it from any liability which it may have to any indemnified party under this Section 4.6 (except to the extent that such omission materially and adversely affects the indemnifying party's ability to defend such action). Subject to the provisions hereinafter stated, in case any such action shall be brought against an indemnified person, the indemnifying person shall be entitled to participate therein, and, to the extent that it shall elect by written notice delivered to the indemnified party promptly after receiving the aforesaid notice from such indemnified party, shall be entitled to assume the defense thereof, with counsel reasonably satisfactory to such indemnified person. After notice from the indemnifying person to such indemnified person of its election to assume the defense thereof, such indemnifying person shall not be liable to such indemnified person for any legal expenses subsequently incurred by such indemnified person in connection with the defense thereof; provided, however, that if there exists or shall exist a conflict of interest that would make it inappropriate, in the opinion of counsel to the indemnified person, for the same counsel to represent both the indemnified person and such indemnifying person or any Affiliate or associate thereof, the indemnified person shall be entitled to retain its own counsel at the expense of such indemnifying person; and provided, further, that no indemnifying person shall be responsible for the fees and expenses of more than one separate counsel (together with appropriate local counsel) for all indemnified parties. In no event shall any indemnifying person be liable in respect of any amounts paid in settlement of any action unless the indemnifying person shall have approved the terms of such settlement; provided, however, that such consent shall not be unreasonably withheld. No indemnifying person shall, without the prior written consent of the indemnified person, effect any settlement of any pending or threatened proceeding in respect of which any indemnified person is or could have been a party and indemnification could have been sought hereunder by such indemnified person, unless such settlement includes an

unconditional release of such indemnified person from all liability on claims that are the subject matter of such proceeding.

(d) If the indemnification provided for in this Section 4.6 is unavailable to or insufficient to hold harmless an indemnified party under subsection (a) or (b) above in respect of any losses, claims, damages or liabilities (or actions or proceedings in respect thereof) referred to therein, then each indemnifying party shall contribute to the amount paid or payable by such indemnified party as a result of such losses, claims, damages or liabilities (or actions in respect thereof) in such proportion as is appropriate to reflect the relative fault of the Company on the one hand and Purchaser on the other hand, in connection with the statements or omissions or other matters which resulted in such losses, claims, damages or liabilities (or actions in respect thereof), as well as any other relevant equitable considerations. The relative fault shall be determined by reference to, among other things, in the case of an untrue statement, whether the untrue statement relates to information supplied by the Company on the one hand or Purchaser on the other hand and the parties' relative intent, knowledge, access to information and opportunity to correct or prevent such untrue statement. The Company and Purchaser agree that it would not be just and equitable if contribution pursuant to this subsection (d) were determined by pro rata allocation or by any other method of allocation which does not take into account the equitable considerations referred to above in this subsection (d). The amount paid or payable by an indemnified party as a result of the losses, claims, damages or liabilities (or actions in respect thereof) referred to above in this subsection (d) shall be deemed to include any legal or other expenses reasonably incurred by such indemnified party in connection with investigating or defending any such action or claim. Notwithstanding the provisions of this subsection (d), Purchaser shall not be required to contribute any amount in excess of the amount by which the net amount received by Purchaser from the sale of the Shares to which such loss relates exceeds the amount of any damages which Purchaser has otherwise been required to pay by reason of such untrue statement. No person guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the Securities Act) shall be entitled to contribution from any person who was not guilty of such fraudulent misrepresentation.

(e) The rights and obligations of the Company and Purchaser under this Section 4.6 shall survive the termination of this Agreement.

ARTICLE V.
COVENANTS AND ADDITIONAL AGREEMENTS

5.1 Stock Ownership Governance.

(a) Lock-Up Period. Excluding any transfers of Shares between Purchaser and any of its Affiliates, during the twelve (12) month period beginning on the date hereof and ending on the first anniversary thereof (the "Lock-Up Period"), Purchaser shall not, and shall not cause any other holder of the Shares to, without the prior written consent of the Company, sell, contract to sell, pledge or otherwise dispose of, directly or indirectly, any Shares or enter into a transaction which would have the same effect. The Purchaser acknowledges that the Company shall impose stop-transfer instructions with

respect to the Shares until the end of the Lock-Up Period in accordance with the transfer restrictions set forth in this Section 5.1(a).

(b) Market Stand-Off Agreement. During the Lock-Up Period, Purchaser agrees that in connection with any registration of the Company's securities that, upon the request of the Company or the underwriters managing any underwritten offering of the Company's securities, Purchaser will not sell, make any short sale of, loan, grant any option for the purchase of, or otherwise dispose of any Shares without the prior written consent of the Company or such underwriters, as the case may be, for such period of time within the Lock-Up Period from the effective date of such registration as the Company or the underwriters may specify.

(c) Remedies. Without prejudice to the rights and remedies otherwise available to the parties, the Company shall be entitled to equitable relief by way of injunction if Purchaser or any other holder of the Shares breaches or threatens to breach any of the provisions of this Section 5.1.

5.2 Non-Public Information. Except as contemplated by the Collaboration Agreement, the Company covenants and agrees that neither it, nor any other Person acting on its behalf will provide Purchaser or its agents or counsel with any information that the Company believes constitutes material non-public information, unless prior thereto Purchaser shall have entered into a written agreement with the Company regarding the confidentiality and use of such information. The Company understands and confirms that Purchaser shall be relying on the foregoing covenant in effecting transactions in securities of the Company.

5.3 Use of Proceeds. The Company shall use the net proceeds from the sale of the Shares hereunder for working capital purposes and shall not use such proceeds: (a) for the redemption of any Common Stock or Common Stock Equivalents, or (b) in violation of FCPA or regulations of the Office of Foreign Assets Control of the U.S. Treasury Department.

5.4 Public Disclosure. The provisions of Sections 7.3 and 7.4 of the Collaboration Agreement shall be applicable, *mutatis mutandis*, with respect to any public disclosures regarding the proposed transactions contemplated by this Agreement or regarding the parties hereto or their affiliates.

5.5 Listing of Common Stock, No Integrated Offerings. The Company shall take no action designed to, or which to the knowledge of the Company is likely to have the effect of, terminating the registration of the Common Stock under the Exchange Act. The Company hereby agrees to use commercially reasonable efforts to maintain the listing of the Common Stock, including the Shares, on The NASDAQ Global Select Market. The Company further agrees, if the Company applies to have the Common Stock traded on any other trading market, it will include in such application all of the Shares, and will take such other action as is necessary to cause all of the Shares to be listed on such other trading market as promptly as possible. The Company will take all action reasonably necessary to continue the listing and trading of its Common Stock, including the Shares, on The NASDAQ Global Select Market and will comply in all material respects with the Company's reporting, filing and other obligations under the bylaws or rules of The NASDAQ Global Select Market. The Company has taken no action

designed to, or which to its knowledge is likely to have the effect of, terminating the registration of the Common Stock under the Exchange Act or delisting the Common Stock from The NASDAQ Global Select Market nor has the Company received in the past twelve (12) months any notification that the Commission or FINRA is contemplating terminating such registration or listing. The Company currently meets the continuing eligibility requirements for listing on The NASDAQ Global Select Market. The Company has not, and to its knowledge no one acting on its behalf has, (i) taken, directly or indirectly, any action designed to cause or to result in the stabilization or manipulation of the price of any security of the Company to facilitate the sale or resale of any of the Shares, (ii) sold, bid for, purchased, or paid any compensation for soliciting purchases of, any of the Shares, or (iii) paid or agreed to pay to any Person any compensation for soliciting another to purchase any other securities of the Company (except in the case of this clause (iii) as disclosed in the SEC Reports in connection with the private placement of shares of the Company's Common Stock in April 2017). The Company agrees to file with the Commission in a timely manner all reports and other filings required of the Company under the Securities Act and the Exchange Act. The Company shall not sell, offer for sale or solicit offers to buy or otherwise negotiate in respect of any security (as defined in Section 2 of the Securities Act) that would be integrated with the offer or sale of the Shares in a manner that would require the registration under the Securities Act of the sale of the Shares to Purchaser or that would be integrated with the offer or sale of the Shares for purposes of the rules and regulations of The NASDAQ Global Select Market.

5.6 Blue Sky Filings. The Company shall take such action as the Company shall reasonably determine is necessary in order to obtain an exemption, or to qualify the Shares, for sale to the Purchaser at the Closing under applicable securities or "Blue Sky" laws of the states of the United States, and shall provide evidence of such actions promptly upon request of the Purchaser.

5.7 Legend Removal.

(a) Certificates evidencing the Shares shall not contain the legend set forth in Section 3.2(e) (i) following a sale of such Shares pursuant to a registration statement covering the resale of such Shares, while such registration statement is effective under the Securities Act; (ii) following any sale of such Shares pursuant to Rule 144; (iii) if such Shares are eligible for sale under Rule 144 without the requirement for the Company to be in compliance with the current public information required under Rule 144 as to such Shares and without volume or manner-of-sale restrictions; or (iv) following the expiration of the Lock-Up Period; provided, however, that any transfer described in clause (i) or (ii) shall be in compliance with all applicable provisions of this Agreement, including, without limitation, Section 5.1(a) hereof.

(b) The Company agrees that at such time as any legend set forth in Section 3.2(e) is no longer required under this Section 5.7, the Company will, no later than three (3) Business Days following the delivery by the Purchaser to the Company or the Transfer Agent of a certificate representing Shares issued with such legend and receipt from the Purchaser by the Company and the Transfer Agent of customary representations and other documentation reasonably acceptable to the Company and the Transfer Agent in connection therewith, deliver or cause to be delivered to the Purchaser

a certificate representing such Shares that is free from such legend or, in the event that such shares are uncertificated, remove any such legend in the Company's stock records.

5.8 Participation in Future Financing.

(a) Subject to compliance with applicable securities laws, from the date hereof until the earlier of (i) the second anniversary of the Closing Date or (ii) expiration of the Term (as such term is defined in the Collaboration Agreement), upon (1) any issuance by the Company of unregistered shares of Common Stock or Common Stock Equivalents (a "Private Offering") or (2) any issuance by the Company of registered shares of Common Stock or Common Stock Equivalents (a "Public Offering" and together with the Private Offering, a " Subsequent Financing"), in each case for cash consideration, indebtedness or a combination thereof, then for a Private Offering the Purchaser shall have the right to participate and with respect to a Public Offering the Purchaser shall have the right to participate by means of a side-by-side private placement including registration rights at least as favorable to the Purchaser as those set forth in Section 4.1 hereof, in an amount of the Subsequent Financing up to the Purchaser's Pro-Rata Share (as defined below). The Purchaser shall have the right to purchase the same securities as are offered in the Subsequent Financing and at the same price as the securities offered in the Subsequent Financing and on the same other terms (except for reasonable modifications in the terms of a Public Offering to adjust for a side-by-side private placement with registration rights at least as favorable to the Purchaser as those set forth in Section 4.1 hereof of any securities sold to the Purchaser) as such securities are offered to other investors in the Subsequent Financing. For purposes of this Agreement, the Purchaser's "Pro-Rata Share" shall be equal to the lesser of (x) the number of shares of Common Stock deemed to be beneficially owned by the Purchaser immediately prior to the closing of the Subsequent Financing (based upon documentation or written representation reasonably satisfactory to the Company), divided by the total number of shares of Common Stock outstanding (including any shares of Common Stock issuable upon conversion or exercise of outstanding Common Stock Equivalents deemed to be beneficially owned by the Purchaser and included in the numerator) immediately prior to the closing of the Subsequent Financing or (y) the number of shares of Common Stock that would result in Purchaser beneficially owning 15.0% of the outstanding shares of Common Stock of the Company immediately prior to the closing of the Subsequent Financing.

(b) At least five (5) Trading Days prior to the closing of a Public Offering or a Private Offering, as applicable, the Company shall deliver to the Purchaser a confidential notice of its intention to effect a Subsequent Financing (the "Subsequent Financing Notice"). In the event of a Private Offering, the Subsequent Financing Notice shall be written and describe in reasonable detail the proposed terms of such Subsequent Financing, the amount of proceeds intended to be raised thereunder and the name and contact information of the placement agent(s) for such Private Offering and shall include a copy of any term sheet or similar document (if any) that has been prepared for potential investors in such offering as an attachment. In the event of a Public Offering, the Subsequent Financing Notice shall describe in reasonable detail the class of security being offered, the proposed amount of proceeds intended to be raised in such Public

Offering, and the estimated date and time at which the Company expects to enter into an underwriting agreement with the underwriters for the Public Offering (the "Pricing Time").

(c) If the Purchaser desires to participate in a Private Offering or undertake a side-by-side private placement at the time of a Public Offering, then the Purchaser must provide a written notice to the Company by not later than 5:30 p.m. (New York City time) on the third (3rd) Trading Day after Purchaser has received a Subsequent Financing Notice and, in the case of a Public Offering, no later than the Pricing Time (provided that the Subsequent Financing Notice is delivered to the Purchaser at least two (2) Trading Days prior to the Pricing Time, in addition to in accordance with Section 5.8(b) hereof), stating the amount of the Purchaser's elected participation. If the Company receives no such notice from the Purchaser in the applicable time periods, the Purchaser shall be deemed to have notified the Company that it does not elect to participate in the Subsequent Financing or side-by-side private placement. In the event that the Purchaser elects, or is deemed to have elected, not to purchase its full Pro Rata Share in the Subsequent Financing, the Purchaser will thereafter have no further right to participate in any future Subsequent Financing.

(d) Notwithstanding anything to the contrary in this Section 5.8 and unless otherwise agreed by the Purchaser, in the event the Company determines to abandon a Subsequent Financing, the Company shall, or shall cause the managing underwriter(s) or placement agent(s), as the case may be, to confirm such abandonment to the Purchaser in the same manner and on the same day as such abandonment is communicated to other potential investors. If, by the twentieth (20th) day following delivery of the Subsequent Financing Notice, no public disclosure regarding a transaction with respect to the Subsequent Financing has been made, such Subsequent Financing shall be deemed to have been abandoned and the Purchaser shall be deemed to not be in possession of any material, non-public information with respect to the proposed Subsequent Financing by the Company, unless the Company advises the Purchaser that the Subsequent Financing has not been abandoned. The Company understands and confirms that the Purchaser may rely on this Section 5.8(d) when effecting transactions in securities of the Company.

(e) Notwithstanding the foregoing, this Section 5.8 shall not apply in respect of an Exempt Issuance.

(f) Purchaser further agrees to execute such other documents and agreements as may reasonably be requested of Purchaser by the Company or placement agent(s), as the case may be, in connection with a Subsequent Financing.

ARTICLE VI.
MISCELLANEOUS

6 . 1 Termination. This Agreement and the obligations of the parties hereunder may be terminated by the Company and the Purchaser, by providing mutual written consent to terminate.

6.2 Fees and Expenses. Each party shall pay the fees and expenses of its advisers, counsel, accountants and other experts, if any, and all other expenses incurred by such party incident to the negotiation, preparation, execution, delivery and performance of this Agreement. The Company shall pay all Transfer Agent fees (including, without limitation, any fees required for same-day processing of any instruction letter delivered by the Company and any exercise notice delivered by Purchaser), stamp taxes and other taxes and duties levied in connection with the delivery of any Shares to Purchaser, and the Company shall pay all fees and expenses related to preparation and filing of any Registration Statement filed hereunder as contemplated by Article IV.

6.3 Entire Agreement. This Agreement, together with the exhibits and schedules hereto, contains the entire understanding of the parties with respect to the subject matter hereof and supersedes all prior agreements and understandings, oral or written, with respect to such matters, which the parties acknowledge have been merged into this Agreement.

6.4 Notices. Any and all notices or other communications or deliveries required or permitted to be provided hereunder shall be in writing and shall be deemed given and effective on the earliest of: (a) the date of transmission, if such notice or communication is delivered via facsimile at the facsimile number set forth below at or prior to 5:30 p.m. (New York City time) on a Trading Day, (b) the next Trading Day after the date of transmission, if such notice or communication is delivered via facsimile at the facsimile number set forth below on a day that is not a Trading Day or later than 5:30 p.m. (New York City time) on any Trading Day, (c) the second (2nd) Trading Day following the date of mailing, if sent by U.S. nationally recognized overnight courier service or (d) upon actual receipt by the party to whom such notice is required to be given. The address for such notices and communications shall be as set forth below:

If to the Company:

Syros Pharmaceuticals, Inc.
620 Memorial Drive, Suite 300
Cambridge, MA 02139
Attention: Chief Legal Officer
Facsimile: (617) 744-1377

with a copy to:

WilmerHale
60 State Street
Boston, Massachusetts 02109, USA
Attention: Steven D. Singer, Esq.
Facsimile: (617) 526-5000

If to Purchaser:

Incyte Corporation
1801 Augustine Cut-Off
Wilmington, Delaware 19803, USA

Attention: General Counsel
Facsimile: (302) 425-2707

with a copy to:

King & Spalding LLP
101 Second Street, Suite 2300
San Francisco, California 94105, USA
Attention: Thomas E. Duley, Esq.
Facsimile: (415) 318-1300

6.5 Amendments; Waivers. No provision of this Agreement may be waived, modified, supplemented or amended except in a written instrument signed by the Company and Purchaser. No waiver of any default with respect to any provision, condition or requirement of this Agreement shall be deemed to be a continuing waiver in the future or a waiver of any subsequent default or a waiver of any other provision, condition or requirement hereof, nor shall any delay or omission of any party to exercise any right hereunder in any manner impair the exercise of any such right.

6.6 Headings. The headings herein are for convenience only, do not constitute a part of this Agreement and shall not be deemed to limit or affect any of the provisions hereof.

6.7 Successors and Assigns. This Agreement shall be binding upon and inure to the benefit of the parties and their successors and permitted assigns. The Company may not assign this Agreement or any rights or obligations hereunder without the prior written consent of Purchaser (other than by merger). Purchaser may assign any or all of its rights under this Agreement to any Person to whom Purchaser assigns or transfers any Shares, provided that such transferee agrees in writing to be bound, with respect to the transferred Shares, by the provisions of this Agreement that apply to "Purchaser."

6.8 No Third-Party Beneficiaries. This Agreement is intended for the benefit of the parties hereto and their respective successors and permitted assigns and is not for the benefit of, nor may any provision hereof be enforced by, any other Person, except as otherwise set forth in Section 4.6.

6.9 Governing Law. This Agreement shall in all respects be governed by and construed in accordance with the laws of the State of Delaware, USA, including all matters of construction, validity and performance, in each case without reference to any conflict of law rules that might lead to the application of the laws of any other jurisdiction.

6.10 Survival of Representation and Warranties. The representations and warranties contained herein shall survive the Closing and the delivery of the Shares for the applicable statute of limitations.

6.11 Execution in Counterparts. This Agreement may be executed in two or more counterparts, all of which when taken together shall be considered one and the same agreement and shall become effective when counterparts have been signed by each party and delivered to

each other party, it being understood that the parties need not sign the same counterpart. In the event that any signature is delivered by facsimile transmission or by e-mail delivery of a ".pdf" format data file, such signature shall create a valid and binding obligation of the party executing (or on whose behalf such signature is executed) with the same force and effect as if such facsimile or ".pdf" signature page were an original thereof.

6.12 Severability. If any term, provision, covenant or restriction of this Agreement is held by a court of competent jurisdiction to be invalid, illegal, void or unenforceable, the remainder of the terms, provisions, covenants and restrictions set forth herein shall remain in full force and effect and shall in no way be affected, impaired or invalidated, and the parties hereto shall use their commercially reasonable efforts to find and employ an alternative means to achieve the same or substantially the same result as that contemplated by such term, provision, covenant or restriction. It is hereby stipulated and declared to be the intention of the parties that they would have executed the remaining terms, provisions, covenants and restrictions without including any of such that may be hereafter declared invalid, illegal, void or unenforceable.

6.13 Replacement of Securities. If any certificate or instrument evidencing any of the Shares is mutilated, lost, stolen or destroyed, the Company shall issue or cause to be issued in exchange and substitution for and upon cancellation thereof (in the case of mutilation), or in lieu of and substitution therefor, a new certificate or instrument, but only upon receipt of evidence reasonably satisfactory to the Company of such loss, theft or destruction. The applicant for a new certificate or instrument under such circumstances shall also pay any reasonable third-party costs (including customary indemnity) associated with the issuance of such replacement Shares.

6.14 Remedies. In addition to being entitled to exercise all rights provided herein or granted by law, including recovery of damages, Purchaser and the Company will be entitled to specific performance under this Agreement. The parties agree that monetary damages may not be adequate compensation for any loss incurred by reason of any breach of obligations contained in this Agreement and hereby agree to waive and not to assert in any action for specific performance of any such obligation the defense that a remedy at law would be adequate.

6.15 Construction. The parties agree that each of them and/or their respective counsel have reviewed and had an opportunity to revise this Agreement and, therefore, the normal rule of construction to the effect that any ambiguities are to be resolved against the drafting party shall not be employed in the interpretation of this Agreement or any amendments hereto. In addition, each and every reference to share prices and shares of Common Stock in this Agreement shall be subject to adjustment for reverse and forward stock splits, stock dividends, stock combinations and other similar transactions of the Common Stock that occur after the date of this Agreement.

6.16 **WAIVER OF JURY TRIAL. IN ANY ACTION, SUIT, OR PROCEEDING IN ANY JURISDICTION BROUGHT BY ANY PARTY AGAINST ANY OTHER PARTY, THE PARTIES EACH KNOWINGLY AND INTENTIONALLY, TO THE GREATEST EXTENT PERMITTED BY APPLICABLE LAW, HEREBY ABSOLUTELY, UNCONDITIONALLY, IRREVOCABLY AND EXPRESSLY WAIVE FOREVER TRIAL BY JURY.**

(Signature Pages Follow)

IN WITNESS WHEREOF, the parties hereto have caused this Stock Purchase Agreement to be duly executed by their respective authorized signatories as of the date first indicated above.

SYROS PHARMACEUTICALS, INC.

By:/s/ Nancy Simonian
Name:Nancy Simonian, M.D.
Title: Chief Executive Officer

INCYTE CORPORATION

By:/s/ Hervé Hoppenot
Name:Hervé Hoppenot
Title: President and Chief Executive Officer

AMENDMENT NO. 1 TO STOCK PURCHASE AGREEMENT

This Amendment No. 1 to Stock Purchase Agreement (this " Amendment") is dated as of January 31, 2018 (the "Amendment Date"), between Syros Pharmaceuticals, Inc., a Delaware corporation (the "Company"), and Incyte Corporation, a Delaware corporation (" Purchaser"), to amend that certain Stock Purchase Agreement, dated as of January 8, 2018, between the Company and Purchaser (the "Agreement"). Capitalized terms used and not otherwise defined herein shall have the meanings ascribed to such terms in the Agreement.

WHEREAS, in Section 5.8 of the Agreement, the Company granted to Purchaser the right to purchase up to Purchaser's Pro-Rata Share in the event of a Subsequent Financing;

WHEREAS, the Company intends to undertake a Public Offering, subject to market and other conditions (the "2018 Public Offering"); and

WHEREAS, Purchaser, pursuant to the terms and conditions of the Agreement (as amended by this Amendment), desires to undertake a side-by-side private placement at the same time as the 2018 Public Offering, in an amount equal to Purchaser's Pro-Rata Share and at a price per share equal to the public offering price per share that the Common Stock is sold to the public in the 2018 Public Offering (the "Public Offering Price").

NOW, THEREFORE, IN CONSIDERATION of the mutual covenants contained herein, and for other good and valuable consideration the receipt and adequacy of which are hereby acknowledged, the Company and Purchaser agree as follows:

1. Amendment of Section 2.1 . Section 2.1 of the Agreement is hereby deleted in its entirety and the following is inserted in lieu thereof:

> "Subject to the terms and conditions of this Agreement, the Company agrees to sell to Purchaser at the Initial Closing, free and clear of all Liens, and Purchaser agrees to purchase from the Company at the Initial Closing, 793,021 shares of Common Stock (the "Initial Shares") at a price per share of $12.61 for an aggregate purchase price of $9,999,994.81 (the "Initial Purchase Price"). Subject to the satisfaction or waiver of the conditions set forth in Section 2.4, the Initial Closing shall take place remotely via the exchange of documents and signatures at 10:00 a.m. Eastern Time on January 8, 2018, or at such other time and location as the Company and Purchaser shall mutually agree (which time and location are designated as the "Initial Closing" and the date thereof as the "Initial Closing Date"). Subject to the terms and conditions of this Agreement, the Company agrees to sell to Purchaser at the Additional Closing, free and clear of all Liens, and Purchaser agrees to purchase from the Company at the Additional Closing, 121,995 shares of Common Stock ("Additional Shares") at a price per share of $9.55 for an aggregate purchase price of $1,165,052.25 (the "Additional Purchase Price"). Upon satisfaction or waiver of the conditions set forth in Section 2.4, the Additional Closing shall take place remotely via the exchange of documents and signatures concurrently with the closing of the 2018 Public Offering, which the Company and Purchaser anticipate will be on or about two (2) Business Days following the Amendment Date, or at such other time and location as the Company and Purchaser shall mutually agree (which time

and location are designated as the "Additional Closing" and the date thereof as the "Additional Closing Date"). The shares of Common Stock issued to Purchaser pursuant to this Agreement (including the Initial Shares and any Additional Shares) shall be referred to in this Agreement as the "Shares," unless otherwise specified. Similarly, in the event there is more than one closing, the term "Closing" shall apply to each such closing, as applicable; the term "Closing Date" shall apply to the date of each such closing, as applicable; and the term "Purchase Price" shall apply to the Initial Purchase Price or the Additional Purchase Price, as applicable, in each case, unless otherwise specified."

2. Amendment of Section 2.4. Section 2.4 of the Agreement is hereby amended by:

(a) Deleting the phrase "the date hereof" where it appears therein and inserting in lieu thereof "the date hereof, as of the Amendment Date and as of each Closing Date."

(b) Inserting the following as new Section 2.4(a)(v) and new Section 2.4(b)(x):

"Solely with respect to the Additional Closing, any of J.P. Morgan Securities LLC, Cowen and Company, LLC or Piper Jaffray & Co., the representatives of the several underwriters for the 2018 Public Offering (the "Underwriters"), shall have purchased, concurrent with the purchase of the Additional Shares by Purchaser hereunder, the Underwritten Shares (as defined in the Underwriting Agreement to effect the 2018 Public Offering (the "Underwriting Agreement")) at the Public Offering Price (less any underwriting discounts or commissions)."

3. Amendment of Sections 3.1 and 3.2. The first sentence of each of Sections 3.1 and 3.2 of the Agreement is hereby amended by deleting the phrase "the date hereof" where it appears therein and inserting in lieu thereof "the date hereof and as of the Amendment Date."

4. Amendment of Section 3.1(a). The second sentence of Section 3.1(a) of the Agreement is hereby deleted in its entirety and the following is inserted in lieu thereof:

"The Company has not issued any capital stock since its most recently filed periodic report under the Exchange Act, other than pursuant to this Agreement and the 2018 Public Offering, pursuant to the exercise of stock options under the Company's stock incentive plans and the issuance of shares of Common Stock pursuant to the Company's at-the-market sales agreement."

5. Amendment of Section 5.1. Section 5.1 of the Agreement is hereby deleted in its entirety and the following is inserted in lieu thereof:

"5.1 Stock Ownership Governance.

(a) Lock-Up Period. Excluding any transfers of Initial Shares between Purchaser and any of its Affiliates, during the twelve (12) month period beginning on the Initial Closing Date and ending on the first anniversary thereof (the "Lock-Up Period"), Purchaser shall not, and shall not cause any other holder of the Initial Shares to, without the prior written consent of the Company, sell, contract to sell, pledge or otherwise

dispose of, directly or indirectly, any Initial Shares or enter into a transaction which would have the same effect. The Purchaser acknowledges that the Company shall impose stop-transfer instructions with respect to the Initial Shares until the end of the Lock-Up Period in accordance with the transfer restrictions set forth in this Section 5.1(a).

(b) Market Stand-Off Agreement. During the Lock-Up Period, Purchaser agrees that in connection with any registration of the Company's securities that, upon the request of the Company or the underwriters managing any underwritten offering of the Company's securities, Purchaser will not sell, make any short sale of, loan, grant any option for the purchase of, or otherwise dispose of any Initial Shares without the prior written consent of the Company or such underwriters, as the case may be, for such period of time within the Lock-Up Period from the effective date of such registration as the Company or the underwriters may specify.

(c) Remedies. Without prejudice to the rights and remedies otherwise available to the parties, the Company shall be entitled to equitable relief by way of injunction if Purchaser or any other holder of the Initial Shares breaches or threatens to breach any of the provisions of this Section 5.1."

6. Amendment of Section 5.7(a). Clause (iv) of Section 5.7(a) of the Agreement is hereby deleted in its entirety and the following is inserted in lieu thereof: "(iv) following the expiration of the Lock-Up Period (solely as to the Initial Shares);".

7. Amendment of Section 5.8(a). The first sentence of Section 5.8(a) of the Agreement is hereby amended by deleting the phrase "Closing Date" where it appears therein and inserting in lieu thereof "Initial Closing Date."

8. Underwriters Exercise of Overallotment.

8.1 Purchase and Sale of Option Shares; Option Closings. In the event that the Underwriters exercise, in full or in part, their right under the Underwriting Agreement to purchase additional shares of Common Stock to cover overallotments, if any, the Company shall provide written notice to Purchaser of such exercise in accordance with Section 5.8 of the Agreement (as amended by this Amendment). In the event that Purchaser elects, pursuant to Section 5.8 of the Agreement (as amended by this Amendment), to purchase its Pro-Rata Share of shares of Common Stock in relation to any such exercise ("Option Shares"), subject to the terms and conditions of the Agreement (as amended by this Amendment), the Company shall sell to Purchaser at an Option Closing (as defined below), free and clear of all Liens, and Purchaser agrees to purchase from the Company at such Option Closing, the applicable Option Shares at a price per share of $9.55 for an aggregate purchase price equal to the price per share multiplied by the number of Option Shares purchased in such Option Closing (for each Option Closing, if any, the "Option Purchase Price"). Upon satisfaction or waiver of the conditions set forth in Section 2.4 of the Agreement (as amended by this Amendment), any Option Closing shall take place remotely via the exchange of documents and signatures concurrently with the closing of the Underwriters' purchase of shares of Common Stock upon exercise of their overallotment option, or at such other time and location as the Company and Purchaser shall mutually agree (each such

time and location are designated as an "Option Closing" and the date thereof as an "Option Closing Date").

8.2. Amendment of Section 2.1 for an Option Closing. In the event of an Option Closing, the last two sentences of Section 2.1 of the Agreement (as amended herein) shall be deleted in their entirety and the following inserted in lieu thereof:

> "The shares of Common Stock issued to Purchaser pursuant to this Agreement (including the Initial Shares, the Additional Shares and any Option Shares) shall be referred to in this Agreement as the "Shares," unless otherwise specified. Similarly, in the event there is more than one closing, the term "Closing" shall apply to each such closing, as applicable; the term "Closing Date" shall apply to the date of each such closing, as applicable; and the term "Purchase Price" shall apply to the Initial Purchase Price, the Additional Purchase Price or an Option Purchase Price, as applicable, in each case, unless otherwise specified."

8.3. Amendment of Section 2.4 for an Option Closing. In the event of an Option Closing, Section 2.4 of the Agreement shall be amended by inserting the following as new Section 2.4(a)(vi) and new Section 2.4(b)(xi):

> "Solely with respect to an Option Closing, the Underwriters shall have purchased, concurrent with the purchase of the Option Shares by Purchaser hereunder, the Option Shares (for purposes of this clause, as defined in the Underwriting Agreement) at the Public Offering Price (less any underwriting discounts or commissions)."

9. Termination of Amendment. This Amendment and the obligations, representations and warranties of the parties under the Agreement (as amended by this Amendment) with respect to the purchase of Additional Shares shall automatically terminate and be of no further force and effect upon the earliest to occur, if any, of: (a) either the Company, on the one hand, or the Underwriters, on the other hand, advising the other in writing, prior to the execution of the Underwriting Agreement, that they have determined not to proceed with the 2018 Public Offering, (b) termination of the Underwriting Agreement (other than the provisions thereof which survive termination) prior to the sale of any of the Common Stock to the Underwriters, or (c) the Underwriting Agreement has not become effective by March 31, 2018.

10. Entire Agreement. The Agreement, as supplemented and modified by this Amendment, together with the exhibits and schedules thereto, contains the entire understanding of the parties with respect to the subject matter hereof and supersedes all prior agreements and understandings, oral or written, with respect to such matters, which the parties acknowledge have been merged into the Agreement.

11. Governing Law. This Amendment shall in all respects be governed by and construed in accordance with the laws of the State of Delaware, USA, including all matters of construction, validity and performance, in each case without reference to any conflict of law rules that might lead to the application of the laws of any other jurisdiction.

12. Execution in Counterparts. This Amendment may be executed in two or more counterparts, all of which when taken together shall be considered one and the same agreement and shall become effective when counterparts have been signed by each party and delivered to each other party, it being understood that the parties need not sign the same counterpart. In the event that any signature is delivered by facsimile transmission or by e-mail delivery of a ".pdf" format data file, such signature shall create a valid and binding obligation of the party executing (or on whose behalf such signature is executed) with the same force and effect as if such facsimile or ".pdf" signature page were an original thereof.

13. Remaining Provisions of the Agreement. Except as provided herein, each of the other provisions of the Agreement shall remain in full force and effect.

14. References. Upon the effectiveness of this Amendment, on and after the date hereof, each reference in the Agreement to "this Agreement," "hereunder," "hereof," "herein" or words of like import shall mean and be a reference to the Agreement, as amended hereby.

(Signature Pages Follow)

IN WITNESS WHEREOF, the parties hereto have caused this Amendment No. 1 to Stock Purchase Agreement to be duly executed by their respective authorized signatories as of the date first indicated above.

SYROS PHARMACEUTICALS, INC.

By:/s/ Nancy Simonian
Name:Nancy Simonian, M.D.
Title: Chief Executive Officer

INCYTE CORPORATION

By:/s/ Hervé Hoppenot
Name:Hervé Hoppenot
Title: President and Chief Executive Officer

Exhibit 10.13

620 Memorial Drive, Suite 300
Cambridge, Ma 02139
Syros.com

November 6, 2017

Jeremy Springhorn
Via e-mail

Dear Jeremy:

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 Business Officer effective November 13, 2017. As Chief Business Officer, you will report to Nancy Simonian, the Company's President and Chief Executive Officer, and be responsible for leading all aspects of the Company's business development initiatives, playing a key role in the Company's strategic planning process, and such other duties as may from time to time be reasonably assigned to you by the Company.

2. Your salary will be $390,000 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. You will receive performance reviews in accordance with the Company's standard practice for executive officers.

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 bonus of up to 40% of your base salary in your first full year of employment with the Company, as approved by the Board of Directors. Future bonus eligibility will be approved by the Board of Directors. Any bonus made pursuant to this paragraph will be paid no later than March 15th of the year immediately following the year to which the applicable annual bonus relates.

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 dental and vision 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, or its successor, 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 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, without limitation, a release of all releasable claims and non-disparagement and cooperation obligations with Company paying reasonable expenses incurred by you in connection with such cooperation, but not including restrictive covenants with respect to non-competition or non-solicitation greater than those contained in the Ancillary Agreements). For clarity, the foregoing release will not affect your rights to indemnification or defense, vested benefits under benefit or equity plans, or under ERISA or COBRA. 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. If you die after you execute the release of claims and before you receive the severance payments you are entitled to, the remaining payments will be paid to your spouse. If she is not alive at the time, the payments will be made to your estate.

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 or breach 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. Subject to the approval of the Board of Directors of the Company (the "**Board**"), the Company will grant to you an option (a "**Time-Based Option**") under the Company's 2016 Stock Incentive Plan (the "**Plan**") for the purchase of 150,000 shares of common stock of the Company

("**Common Stock**"), at a price per share equal to the closing price of the Common Stock on the date 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 underlying the option on the one-year anniversary of your first day of employment, and (ii) as to the remaining shares underlying the option in equal monthly installments for the next 36 months thereafter, becoming fully vested on the fourth anniversary of your first day of employment, provided that you remain employed by us on the applicable vesting date. Subject to the approval of the Board, you shall also be granted an option (a "**Performance-Based Option**") under the Plan to purchase an additional 50,000 shares of Common Stock of the Company, at a price per share equal to the closing price of the Common Stock on the date of Board approval, which option shall be granted within 30 days of your first day of employment and vest six years from your first day of employment, subject to accelerated vesting according to the following schedule: (i) 33% upon the earlier of (A) achievement of clinical proof of concept with a molecule beyond SY-1425 or (B) the start of the first pivotal trial; and (ii) 67% upon signing by the Company of a business development, collaboration or partnership agreement around the Company's platform or one of its product candidates other than the transaction previously disclosed to you, in each cased based on parameters approved by the Board, and provided that the Participant remains employed by the Company on the applicable vesting date.

Each of the Time-Based Option and the Performance-Based Option shall be subject to all terms herein, including the acceleration of vesting under the circumstances set forth in paragraph 4 above, and other provisions set forth in the Plan and in a separate option agreement.

You will be eligible to receive such future long-term incentive awards as the Board shall deem appropriate.

6. 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**"). Upon your appointment by the Board of Directors as an "executive officer" of the Company, the Company will enter into an Indemnification Agreement with you in the form currently approved by the Board of Directors.

7. 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.

8. 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.

9. 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.

10. This letter is intended to provide payments that are exempt from or compliant with Section 409A (as defined in Attachment A), and should be interpreted consistent with that intent.

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 Lisa Roberts at lroberts@syros.com. If you do not accept this offer by November 8, 2017, this offer will be revoked.

Very truly yours,

/s/ Nancy Simonian
Name:Nancy Simonian
Title: President & Chief Executive Officer

The foregoing correctly sets forth the terms of my employment by Syros Pharmaceuticals, Inc.

/s/ Jeremy Springhorn Date: 11/9/17
Jeremy Springhorn

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 l.409A-l (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 l.409A-l (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 A

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 Jeremy Springhorn (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:

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.

Proprietary and Confidential Information.

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.

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.

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.

Notwithstanding the provisions of (a)-(c) above, nothing in this Agreement prohibits the Employee from communicating with government agencies about possible violations of federal, state, or local laws or otherwise providing information to government agencies or participating in government agency investigations or proceedings. The Employee is not required to notify the Company of any such communications; *provided, however*, that nothing herein authorizes the disclosure of information the Employee obtained through a communication that was subject to the attorney-client privilege. Further, notwithstanding the Employee's confidentiality and nondisclosure obligations, the Employee is hereby advised as follows pursuant to the Defend Trade Secrets Act: "An individual shall not be held criminally or civilly liable under any Federal or State trade secret law for the disclosure of a trade secret that (A) is made (i) in confidence to a Federal, State, or local government official, either directly or indirectly, or to an attorney; and (ii) solely for the purpose of reporting or investigating a suspected violation of law; or (B) is made in a complaint or other document filed in a lawsuit or other proceeding, if such filing is made under seal. An individual who files a lawsuit for retaliation by an employer for reporting a suspected violation of law may disclose the trade secret to the attorney of the individual and use the trade secret information in the court proceeding, if the individual (A) files any document containing the trade secret under seal; and (B) does not disclose the trade secret, except pursuant to court order."

Developments.

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").

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.

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.

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.

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.

Miscellaneous.

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.

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.

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.

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.

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.

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.

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.

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.

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.

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:

SYROS PHARMACEUTICALS, INC.

Date: _____

By: /s/ Nancy Simonian
Name: Nancy Simonian
Title: Chief Executive Officer

Date: 11/9/17

/s/ Jeremy Springhorn
Jeremy Springhorn

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 Jeremy Springhorn (the "Employee").

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 or (ii) hire, or recruit or attempt to hire, or engage or attempt to engage 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 recruitment or hiring or other engagement of any individual whose employment or other

engagement with the Company was terminated by the Company or the individual has resigned from the Company 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.

SYROS PHARMACEUTICALS, INC.

Date: _____

By: /s/ Nancy Simonian
Name: Nancy Simonian
Title: Chief Executive Officer

Date: 11/9/17

/s/ Jeremy Springhorn
Jeremy Springhorn

Confidential Materials omitted and filed separately with the

Securities and Exchange Commission. Double asterisks denote omissions.

Exhibit 10.22

TARGET DISCOVERY, RESEARCH COLLABORATION AND OPTION AGREEMENT

between

SYROS PHARMACEUTICALS, INC.

and

INCYTE CORPORATION

Dated as of January 8, 2018

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TARGET DISCOVERY, RESEARCH COLLABORATION AND OPTION AGREEMENT

This Target Discovery, Research Collaboration and Option Agreement (this " Agreement") is made effective as of January 8, 2018 (the "Effective Date") by and between Syros Pharmaceuticals, Inc., a Delaware corporation having its principal place of business at 620 Memorial Drive, Suite 300, Cambridge, Massachusetts 02139 ("Syros") and Incyte Corporation, a Delaware corporation having its principal place of business at 1801 Augustine Cut-Off, Wilmington, Delaware 19803 ("Incyte"). Syros and Incyte are each referred to herein by name or as a "Party" or, collectively, as " Parties".

RECITALS

WHEREAS, Syros owns or controls proprietary technology for the discovery of novel therapeutic targets involved in human disease, based on an understanding of transcriptional networks and their roles in defining cell state;

WHEREAS, Incyte is engaged in the research, development and commercialization of pharmaceutical products;

WHEREAS, Syros and Incyte desire to engage in a collaborative research program using Syros' proprietary platform technology to identify therapeutic targets relevant to the MPN Field (as defined below) and to validate such therapeutic targets in preclinical validation studies;

WHEREAS, Incyte desires to further validate such therapeutic targets and develop and commercialize pharmaceutical products containing compounds directed to certain targets selected by Incyte as Validated Targets (as defined below) in accordance with the terms of this Agreement;

WHEREAS, each Party desires to maintain the right to Exploit (as defined below) targets and pharmaceutical products containing compounds directed to targets (including Program Targets (as defined below)) outside of this collaboration, whether alone or with one or more third parties, and thus the rights granted under this Agreement to select and reserve targets are non-exclusive (including with respect to Reserved Targets (as defined below)), subject in the case of Syros to the exclusive license grants by Syros to Incyte with respect to Program IP (as defined below) (and any Option (as defined below) with respect thereto).

NOW, THEREFORE, in consideration of the premises and mutual covenants and conditions set forth below, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties, intending to be legally bound, hereby agree as follows:

ARTICLE 1 - DEFINITIONS

The following terms shall have the following meanings as used in this Agreement:

1.1 "Affiliate" means, with respect to a Party, any Person that directly, or indirectly through one (1) or more intermediaries, controls, is controlled by or is under common control with such Party. For purposes of this definition, "control" and, with correlative meanings, the terms "controlled by" and "under common control with," means (a) the possession, directly or indirectly,

of the power to direct the management or policies of a business entity, whether through the ownership of voting securities, by contract relating to voting rights or corporate governance or otherwise or (b) the ownership, directly or indirectly, of more than fifty percent (50%) of the voting securities or other ownership interest of a business entity (or, with respect to a limited partnership or other similar entity, its general partner or controlling entity).

1.2 "Alliance Manager" has the meaning provided in Section 2.2.2.

1.3 "All Uses Field" means the prevention or treatment of any disease or condition in humans or animals. For clarity, the "All Uses Field" includes the "MPN Field".

1.4 "All Uses Field Patentability Criteria " means, with respect to a Definitive Research Target and the Program Data related to such Definitive Research Target, the criteria established by the JPC for determining whether such Program Data are sufficient to support the filing of a Program Patent that Covers the Exploitation of such Definitive Research Target in the All Uses Field.

1.5 "AML" means acute myeloid leukemia.

1.6 "Antitrust Approval" means any consent, approval or other authorization required under the applicable Antitrust Laws from the applicable Antitrust Authority.

1.7 "Antitrust Authority" means any applicable Governmental Authority with respect to any Antitrust Laws.

1.8 "Antitrust Condition" means that (a) the waiting period (and any extension thereof) applicable to Incyte's selection of any Initial Research Target, Definitive Research Target or Extended Research Target as a Validated Target pursuant to Section 3.1.1, 3.1.2 or 3.1.3, as applicable, under any and all applicable Antitrust Laws, shall have expired or been terminated, and (b) if applicable, any applicable Antitrust Approval for designation of such Initial Research Target, Definitive Research Target or Extended Research Target as a Validated Target, as applicable, under such Antitrust Laws has been received.

1.9 "Antitrust Filing" means a filing or filings by the Parties with the applicable Antitrust Authority as required by the Antitrust Laws with respect to Incyte's selection of an Initial Research Target, Definitive Research Target or Extended Research Target as a Validated Target pursuant to Section 3.1.1, 3.1.2 or 3.1.3, as applicable, together with all required documentary attachments thereto.

1.10 "Antitrust Laws" means any Applicable Law governing competition, monopolies or restrictive trade practices, including the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, and the rules and regulations promulgated thereunder.

1.11 "Applicable Law" means applicable laws, rules and regulations, including any rules, regulations, guidance or other requirements of Regulatory Authorities, that may be in effect from time to time and applicable to a particular activity hereunder, and shall be deemed to include the applicable regulations and guidance of the applicable Regulatory Authorities that constitute good

laboratory practices, good manufacturing practices and good clinical practices (and, if and as appropriate under the circumstances, International Conference on Harmonization (ICH) guidance).

1.12 "Associated Compound" means, with respect to a Program Target, a compound the primary activity of which is Modulation of such Program Target, including any such compound that is a small molecule or biologic; *provided* that Associated Compound shall exclude any such compound owned or controlled by Incyte, any of its Affiliates or its or their (sub)licensees that is not Exploited in whole or in part by Incyte, or any of its Affiliates or its or their (sub)licensees (a) in the conduct of activities (i) under the Research Plan, (ii) supporting a program initiated under the Research Plan or (iii) enabled under any license granted to Incyte in Section 3.3.1, or (b) relying on or using any Syros Confidential Information or Program Know-How. For clarity, an Associated Compound with respect to a Program Target is intended, and shall be construed, to include any nucleic acid-based therapy whose primary activity is Modulation of such Program Target (such as a gene therapy, RNA interference therapy or antisense therapy) unless such nucleic acid-based therapy is excluded pursuant to the proviso in the first sentence of this definition.

1.13 "Associated Licensed Field" means, with respect to each Validated Target, the Field in which Incyte is granted license rights under Syros' interest in Program IP and Syros Existing Background Target IP to Exploit Associated Compounds and Associated Products with respect to such Validated Target, pursuant to Section 3.3.1(b)(i) or Section 3.3.1(b)(ii) as applicable.

1.14 "Associated Optioned Field(s)" means, with respect to each Program Target and point in time, the Field(s) in which Incyte retains an unexercised Option, at such point in time.

1.15 "Associated Product" means, with respect to a Program Target, a product containing an Associated Compound with respect to such Program Target.

1.16 "Biological Target" means (a) a biological molecule, as identified by its ENSEMBL ID and (b) any variants of such biological molecule that are also identified by such ENSEMBL ID, including, in the case of this clause (b), any naturally occurring mutant or allelic variants of such biological molecule, such as (i) transcriptional or post-transcriptional isoforms (e.g., alternative splice variants), (ii) post-translational modification variants (e.g., protein processing, maturation and glycosylation variants), or (iii) truncated forms (including fragments).

1.17 "Biosimilar Application" means an application for Regulatory Approval of a product claimed to be biosimilar to or interchangeable with (as those terms are defined in Section 351(i) of the PHSA) any Associated Product owned or controlled by Incyte or any of its Affiliates or Sublicensees that Modulates a Validated Target.

1.18 "Breaching Party" has the meaning provided in Section 10.2.1.

1.19 "Breakthrough Therapy Designation" means the designation of a drug as (a) a breakthrough therapy by the FDA pursuant to Section 506(a) of the FFDCA (21 U.S.C. §356(a)), as amended by Section 902 of the Food and Drug Administration Safety and Innovation Act, or (b) a priority medicine by the EMA pursuant to the EMA's PRIME scheme.

1.20 "Budget" means the Initial Budget, as amended in accordance with the terms of this Agreement.

1.21 "Business Day" means a day other than a Saturday or Sunday or a day on which banking institutions in New York, New York are permitted or required to be closed.

1.22 "Calendar Quarter" means each successive period of three calendar months commencing on January 1, April 1, July 1 and October 1, except that the first Calendar Quarter of the Term shall commence on the Effective Date and end on the day immediately prior to the first to occur of January 1, April 1, July 1 or October 1 after the Effective Date and the last Calendar Quarter shall end on the last day of the Term.

1.23 "Calendar Year" means each successive period of twelve calendar months commencing on January 1 and ending on December 31, except that the first Calendar Year of the Term shall commence on the Effective Date and end on December 31 of the year in which the Effective Date occurs and the last Calendar Year of the Term shall commence on January 1 of the year in which the Term ends and end on the last day of the Term.

1.24 "Change of Control" means, with respect to a Party, a transaction or series of related transactions occurring after the Effective Date in which: (a) such Party sells, conveys or otherwise disposes of (including via an exclusive license) all or substantially all of its assets to which this Agreement relates; (b) any "person" or "group" (within the meaning of Section 13(d) and 14(d) of the Securities Exchange Act of 1934, as amended) becomes the "beneficial owner" (as defined in Rule 13d-3 under the Securities Exchange Act of 1934, as amended), directly or indirectly, of more than 50% of the outstanding voting securities of such Party having the right to vote for the election of members of the board of directors or equivalent; or (c) such Party consummates a business combination (including a reorganization, merger or consolidation) such that the stockholders of such Party immediately prior to such business combination, in the aggregate, no longer beneficially own, directly or indirectly, more than fifty percent (50%) of the outstanding voting securities or capital stock of the surviving entity or the ultimate parent of the surviving entity immediately following the closing of such reorganization, merger, consolidation, other transaction or series of related transactions.

1.25 "Circuitry Map Data" means [**].

1.26 "Combination Product" means a Royalty Product that is comprised of or contains an Associated Compound as an active ingredient together with one (1) or more other active ingredients and is sold either as a fixed dose/unit or as separate doses/units in a single package.

1.27 "Commercially Reasonable Efforts" means, with respect to a Party and a Program Target or its Associated Compound(s) or Associated Product(s), such efforts that are consistent with the efforts and resources that a company in the pharmaceutical industry would typically apply to targets, compounds or products of similar market potential at a similar stage in development or product life, taking into account all scientific, commercial and other factors that such company would typically take into account with respect to such targets, compounds or products, including, (a) with respect to Syros, the amount of funding provided by Incyte with respect to the Research

Program and the resources enabled by such funding during the Research Term, and (b) with respect to Incyte, pricing and reimbursement status achieved or likely to be achieved, amounts payable to licensors of patent or other intellectual property rights, and other products in Incyte's pipeline.

1.28 "Commercialization" means any and all activities directed to the preparation for sale, offering for sale or sale of a product, including activities related to marketing, promoting, distributing, importing and commercial manufacturing, and interacting with Regulatory Authorities regarding any of the foregoing. When used as a verb, "Commercialize" means to engage in Commercialization.

1.29 "Confidential Information" has the meaning provided in Section 7.1.

1.30 "Confidentiality Agreement" means that certain Mutual Confidential Disclosure Agreement entered into between the Parties as of October 28, 2016.

1.31 "Control" means, with respect to any information, material, compound, product, Patent, Know-How or other intellectual property right, and subject to Section 11.2.2, the possession of the right, whether directly or indirectly and whether by ownership, license or otherwise (other than by operation of the licenses and other grants in Article 3), to grant a license, sublicense or other right to or under such information, material, compound, product, Patent, Know-How or other intellectual property right as provided herein without violating the terms of any agreement with any Third Party.

1.32 "Controlled Affiliate" means, with respect to Syros, any Person that directly, or indirectly through one (1) or more intermediaries, is controlled by Syros. For purposes of this definition, "controlled by" has the meaning provided in the definition of "Affiliate".

1.33 "Cover" means, with respect to a Patent and any Know-How, compound, product, platform or other subject matter, that such patent (a) discloses such Know-How, compound, product, platform or other subject matter; (b) claims the Exploitation of such Know-How, compound, product, platform or other subject matter; or (c) claims such Know-How, compound, product, platform or other subject matter as a composition of matter.

1.34 "Defending Party" means, with respect to any Invalidity or Unenforceability Action, the Party that has the right to defend such Invalidity or Unenforceability Action under Section 6.4.

1.35 "Definitive Research Target" means an Original Target, Preliminary Target or Initial Research Target selected by Incyte and designated as a "definitive research target" in accordance with Section 2.8.6 or Section 3.4.

1.36 "Definitive Research Target Payment" has the meaning provided in Section 5.3.1.

1.37 "Definitive Research Target Selection Date" means the earlier of (a) the date that Incyte designates the final Definitive Research Target pursuant to Section 2.8.6 and (b) the expiration of the Definitive Research Target Selection Period.

1.38 "Definitive Research Target Selection Period" has the meaning provided in Section 2.8.6.

1.39 "Definitive Research Target Validation Data" means that portion of the Program Data generated by or on behalf of Incyte or its Affiliates and resulting from the conduct of the Definitive Validation Studies.

1.40 "Definitive Validation Studies" has the meaning provided in Section 2.8.7.

1.41 "Delivery Date" has the meaning provided in Section 2.8.1(c).

1.42 "Development" means any and all activities related to research, pre-clinical and other non-clinical testing, test method development and stability testing, toxicology, formulation, process development, qualification and validation, quality assurance/quality control, clinical studies, statistical analysis and report writing, manufacturing activities with respect to any of the foregoing, regulatory affairs with respect to the foregoing and all other activities necessary or reasonably useful or otherwise requested or required by a Regulatory Authority as a condition or in support of obtaining or maintaining a Regulatory Approval. When used as a verb, "Develop" means to engage in Development.

1.43 "Development Milestone Event" has the meaning provided in Section 5.4.

1.44 "Development Milestone Payment" has the meaning provided in Section 5.4.

1.45 "Dispute" has the meaning provided in Section 11.4.1.

1.46 "Dollars" or "$" means United States Dollars.

1.47 "Drug Approval" means with respect to any Validated Target and any country, approval by a Regulatory Authority of a Drug Approval Application with respect to an Associated Product and, where applicable in any country other than the United States, Pricing and Reimbursement Approval.

1.48 "Drug Approval Application" means (a) a new drug application or abbreviated new drug application submitted under Section 505 of the FFDCA, including any amendment or supplement to such application; (b) a biologics license application submitted to the FDA under Section 351 of the PHSA, including any amendment or supplement to such application; or (c) any corresponding foreign application, amendment or supplement including, (i) with respect to the European Union, a marketing authorization application filed with the EMA pursuant to the centralized approval procedure or with the applicable Regulatory Authority of a country in the European Union with respect to the mutual recognition or any other national approval procedure and (ii) with respect to Japan, a marketing authorization application filed with the PMDA.

1.49 "Drug Discovery and Development Activities" means any and all activities related to drug discovery and development, including activities related to compound structure discovery, drug discovery screening, compound chemistry, structure-activity relationships, in vitro or in vivo pharmacology, pharmacodynamics, toxicology, biomarkers, clinical research and Manufacturing.

1.50 "Drug Discovery and Development Know-How" means Know-How to the extent relating to drug discovery and development, including Know-How to the extent relating to compound structure discovery, drug discovery screening, compound chemistry, structure-activity relationships, in vitro or in vivo pharmacology, pharmacodynamics, toxicology, biomarkers, clinical research or Manufacturing.

1.51 "EMA" means the European Medicines Agency and any successor entity thereto.

1.52 "End of Original Research Term" means the effective date of termination or expiration of the original Research Term, without regard to any extensions.

1.53 "Enforcing Party" means, with respect to the Infringement of any Patent or Know-How, the Party that has the right to prosecute such Infringement and to defend any Invalidity or Unenforceability Action initiated as a defense or counterclaim to the prosecution of such Infringement.

1.54 "ENSEMBL ID" means, with respect to a biological molecule, the ENSEMBL gene identification number for such biological molecule.

1.55 "EU Major Market" means France, Germany, Italy and Spain.

1.56 "European Union" or "EU" means the economic, scientific and political organization of member states of the European Union as it is constituted as of the Effective Date, together with any countries that become member states after the Effective Date.

1.57 "Executive Resolution Period" has the meaning provided in Section 11.4.1.

1.58 "Exploit" means to make, have made, import, use, sell or offer for sale, including to research, Develop, Commercialize, register, Manufacture, have Manufactured, hold or keep (whether for disposal or otherwise), have used, export, transport, distribute, promote, market, have sold, otherwise dispose of, or otherwise exploit. "Exploitation" means the act of Exploiting. For clarity, "Exploitation" of a Program Target includes the identification of Associated Compounds or Associated Products with respect to such Program Target and the selection of patients for treatment with such an Associated Product.

1.59 "Extended Research Target" means Definitive Research Target selected by Incyte and designated as an "extended research target" in accordance with Section 2.8.8 or Section 3.4.

1.60 "Extended Research Target Selection Date" means the earlier of (a) the date that Incyte designates the final Extended Research Target pursuant to Section 2.8.8 and (b) the expiration of the Extended Research Target Selection Period.

1.61 "Extended Research Target Selection Period" has the meaning provided in Section 2.8.8.

1.62 "FDA" means the United States Food and Drug Administration and any successor entity thereto.

1.63 "FFDCA" means the United States Federal Food, Drug, and Cosmetic Act, as amended from time to time, together with any rules, regulations and requirements promulgated thereunder (including all additions, supplements, extensions and modifications thereto).

1.64 "Field" means, as applicable, the All Uses Field or the MPN Field.

1.65 "First Commercial Sale" means, with respect to a Royalty Product and a country, the first arms-length sale for monetary value of such Royalty Product to the end user in such country after Regulatory Approval for such Royalty Product has been obtained in such country. For clarity, sales or transfers (a) to an Affiliate or sublicensee or (b) of reasonable quantities of Royalty Product for clinical trial purposes, or for a bona fide charitable purpose or an early access program or for a compassionate use or similar use shall not be considered a First Commercial Sale.

1.66 "FTE" means the equivalent of the work of one employee full time for one Calendar Year containing twelve calendar months (consisting of a total of at least [**] hours of scientific or technical work directly related to the applicable activity described hereunder. Any person who devotes less than [**] hours during a Calendar Year to the applicable activity shall be treated as an FTE on a *pro rata* basis.

1.67 "GAAP" means United States generally accepted accounting principles.

1.68 "Gatekeeper" has the meaning provided in Section 2.7.1.

1.69 "Generic Product" means, with respect to a Royalty Product, any pharmaceutical or biological product that is distributed by a Third Party under a Drug Approval Application approved by a Regulatory Authority that references or otherwise relies, in whole or in part, on the prior approval (or on safety or efficacy data submitted in support of the prior approval) of such Royalty Product, including any product authorized for sale: (a) in the U.S. pursuant to (i) Section 505(b)(2) or Section 505(j) of the FFDCA (21 U.S.C. §355(b)(2) and 21 U.S.C. §355(j), respectively) or (ii) Section 351(k) of the PHSA (42 U.S.C. §262(k)) as interchangeable with such Royalty Product in accordance with Section 351(k)(4) of the PHSA (42 U.S.C. §262(k)(4)); (b) in the EU pursuant to a provision of Articles 10, 10a or 10b of Parliament and Council Directive 2001/83/EC as amended (including an application under Article 6.1 of Parliament and Council Regulation (EC) No 726/2004 that relies for its content on any such provision); or (c) in any other country or jurisdiction pursuant to an equivalent of such provisions.

1.70 "Governmental Authority" means any applicable government authority, court, tribunal, arbitrator, agency, department, legislative body, commission or other instrumentality of (a) any government of any country or territory; (b) any nation, state, province, county, city or other political subdivision thereof; or (c) any supranational body.

1.71 "ICD10" has the meaning provided in the definition of "Indication".

1.72 "Incyte Excluded Target" means an Incyte Internal Target that is designated by Incyte as an Incyte Excluded Target in accordance with Section 2.7.4.

1.73 "Incyte Excluded Target List" means a list identifying each Incyte Excluded Target by ENSEMBL ID and name, as generated and supplemented by Incyte from time to time in accordance with Section 2.7.4 and maintained by the Gatekeeper.

1.74 "Incyte Independent Program" has the meaning provided in Section 2.14.1.

1.75 "Incyte Internal Target" means a Biological Target that is the subject of an Internal Incyte Program.

1.76 "Incyte Restricted Personnel" has the meaning provided in Section 2.14.1.

1.77 "Indemnification Claim Notice" has the meaning provided in Section 9.3.

1.78 "Indemnified Party" has the meaning provided in Section 9.3.

1.79 "Indemnifying Party" has the meaning provided in Section 9.3.

1.80 "Indication" means, with respect to any Associated Product with respect to a Validated Target, a separate and distinct disease or medical condition in humans that such Associated Product is intended to treat, cure or prevent, subject to Section 5.4, as defined by reference to the World Health Organization International Classification of Diseases, version 10 (as in effect on the Effective Date, "ICD10").

1.81 "IND" means (a) an investigational new drug application filed with the FDA for authorization to commence clinical studies or any corresponding or similar application in other countries or regulatory jurisdictions and (b) all supplements and amendments that may be filed with respect to the foregoing.

1.82 "IND Clearance" means, with respect to an IND and the FDA, the earlier of (a) the date the FDA has notified the applicant for such IND that one or more clinical studies may commence under such IND and (b) the date that one or more clinical studies may commence under such IND in the absence of the notice described in clause (a). By way of example, the conditions of clause (b) would be fulfilled if the FDA (i) does not impose a clinical hold within [**] after filing of an applicable IND and (ii) does not provide the notice described in clause (a).

1.83 "Infringement" has the meaning provided in Section 6.3.1.

1.84 "Initial Budget" has the meaning provided in Section 2.6.3(b).

1.85 "Initial Research Plan" means (a) the initial plan for carrying out the research activities of Syros and its Affiliates during the Research Term and (b) a high-level summary of the research activities of Incyte and its Affiliates during and after the Research Term, in relation to any Program Target other than a Validated Target, including, in each case, ((a) and (b)): [**]. The Initial Research Plan is attached hereto as Schedule 1.85.

1.86 "Initial Research Target" means an Original Target or Preliminary Target selected by Incyte and designated as an "initial research target" in accordance with Section 2.8.4 or Section 3.4.

1.87 "Initial Research Target Selection Date" means the earlier of (a) the date that Incyte designates the final Initial Research Target pursuant to Section 2.8.4 and (b) the expiration of the Initial Research Target Selection Period.

1.88 "Initial Research Target Selection Period" has the meaning provided in Section 2.8.4.

1.89 "Initial Research Target Validation Data" means that portion of the Program Data generated by or on behalf of either Party or its Affiliates, solely or jointly, and resulting from the conduct of the Initial Validation Studies.

1.90 "Initial Validated Targets" means each of the [**] of the Initial Research Targets, Definitive Research Targets or Extended Research Targets selected by Incyte and designated as a "validated target" in accordance with Section 3.1.

1.91 "Initial Validation Studies" has the meaning provided in Section 2.8.5.

1.92 "Initial Validation Study Data Package" has the meaning provided in Section 2.8.5.

1.93 "Internal Incyte Program" means, with respect to a Biological Target, a bona fide internal Incyte program where Incyte or any of its Affiliates has conducted or is conducting activities directed to (a) [**] or (b) a compound with respect to which any Drug Discovery and Development Activities have been conducted and wherein such compound directly binds to and activates, inhibits, agonizes, antagonizes or otherwise modulates such Biological Target. For clarity, an "internal Incyte program" shall include a program as described in this Section 1.93 with respect to which Incyte or any of its Affiliates engages a Third Party academic or other not-for-profit collaborator to conduct any activities on behalf of or in collaboration with Incyte or any of its Affiliates.

1.94 "Internal Syros Program" means, with respect to a Biological Target other than a Premium Target, a bona fide internal Syros program where Syros or any of its Affiliates has conducted or is conducting activities directed to (a) [**] or (b) a compound with respect to which any Drug Discovery and Development Activities have been conducted and wherein such compound directly binds to and activates, inhibits, agonizes, antagonizes or otherwise modulates such Biological Target. For clarity, an "internal Syros program" shall include a program as described in this Section 1.94 with respect to which Syros or any of its Affiliates engages a Third Party academic or other not-for-profit collaborator to conduct any activities on behalf of or in collaboration with Syros or any of its Affiliates.

1.95 "Invalidity or Unenforceability Action" means, with respect to a Patent, any alleged or threatened assertion of invalidity or unenforceability of such Patent that is made outside of a proceeding recited in clause (b) of the definition of "Prosecution Activities".

1.96 "Joint Patent Committee" or "JPC" has the meaning provided in Section 2.2.3(a).

1.97 "Joint Program IP" has the meaning provided in Section 6.1.2.

1.98 "Joint Research Committee" or "JRC" has the meaning provided in Section 2.2.

1.99 "Know-How" means any and all technical, scientific and other know-how, inventions, trade secrets, technology, methods, processes, formulae, instructions, techniques, procedures, designs, drawings, apparatuses, specifications, data, results of the analysis of data, and other material, including: biological, chemical, pharmacological, toxicological, pharmaceutical, physical and analytical, pre-clinical, clinical, safety, manufacturing and quality control data; in each case (whether or not confidential, proprietary, patented or patentable) in written, electronic or any other form now known or hereafter developed.

1.100 "Legal Requirements" has the meaning provided in Section 2.12.2.

1.101 "Losses" has the meaning provided in Section 9.1.

1.102 "Manufacture" means any and all activities related to the production, manufacture, processing, filling, finishing, packaging, labeling, shipping, and holding of a compound or product, or any intermediate thereof, including process development, process qualification and validation, scale-up, manufacture and analytic development, product characterization, stability testing, quality assurance, and quality control.

1.103 "Modulate" means, with respect to a compound and a Program Target, that such compound (a) directly binds to such Program Target and (b) activates, inhibits, agonizes, antagonizes or otherwise modulates such Program Target.

1.104 "MPN Exclusivity Period" means the period commencing on the Effective Date and ending on [**].

1.105 "MPN Field" or "Myeloproliferative Neoplasm Field" means the prevention or treatment of any of the following diseases or conditions in humans or animals: (a) myelofibrosis (MF); (b) chronic neutrophilic leukemia (CNL); (c) polycythemia vera (PV); (d) primary myelofibrosis, including prefibrotic, early stage or overt fibrotic stage (PMF); (e) essential thrombocythemia (ET); (f) chronic eosinophilic leukemia, not otherwise specified (NOS); (g) myeloproliferative neoplasms (unclassifiable); (h) 8p11 myeloproliferative syndrome; (i) mastocytosis; (j) chronic myelomonocytic leukemia (CMML); (k) juvenile myelomonocytic leukemia (JMML); (l) myelodysplastic syndrome / myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T); and (m) myelodysplastic syndrome / myeloproliferative neoplasm (unclassifiable), in each case ((a)-(m)), as defined by reference to ICD10. The MPN Field shall be deemed to exclude the following indications: (i) acute myeloid leukemia (AML); (ii) chronic myeloid leukemia (CML); and (iii) myelodysplastic syndromes (MDS).

1.106 "MPN Field Patentability Criteria" means, with respect to a Definitive Research Target and the Program Data related to such Definitive Research Target, the criteria established by the JPC for determining whether such Program Data are sufficient to support the filing of a Program Patent that Covers the Exploitation of such Definitive Research Target in the MPN Field.

1.107 "Net Sales" means the gross amount invoiced for the sale of any Royalty Product by or on behalf of Incyte, any of its Affiliates, its or their direct or indirect successors (whether as a

successor-in-interest with respect to any of the foregoing Persons or such Royalty Product by way of product acquisition or otherwise) or any licensee or sublicensee of any of the foregoing to a Third Party (the "Invoiced Sales"), less reasonable and customary deductions for: (a) trade, cash, quantity and prompt settlement discounts (including chargebacks and allowances) actually allowed; (b) amounts repaid or credited by reason of rejection, return or recall of goods, rebates or bona fide price reductions; (c) freight, postage, shipping, transportation and insurance expenses to the extent that such items are included in the gross amount invoiced; (d) customs and excise duties, value added, sales and use, excise and other taxes or duties related to the sales to the extent that such items are included in the gross amount invoiced; (e) rebates and similar compulsory payments made with respect to sales paid for by any governmental or Regulatory Authority such as Federal or state Medicaid, Medicare or similar state programs or equivalent foreign governmental programs; (f) [**]; and (g) [**]. Subject to the limitations with respect to permitted deductions that may be taken as set forth above, Net Sales shall be calculated in accordance with GAAP, consistently applied.

In the event that a Royalty Product is sold in any country in the form of a Combination Product, Net Sales of such Royalty Product shall be determined by multiplying actual Net Sales of such Combination Product in such country calculated pursuant to the foregoing definition of "Net Sales" by the fraction A/(A+B), where A is the volume-weighted average sale price in such country of any Royalty Product that contains the same Associated Compound(s) as such Combination Product as its sole active ingredient(s), if sold separately in such country and B is the volume-weighted average sale price in such country of each product that contains active ingredient(s) other than the Associated Compound(s) contained in such Combination Product as its sole active ingredient(s) if sold separately in such country; *provided* that the sale price in a country for each Royalty Product that contains only the Associated Compound(s) and each product that contains solely active ingredient(s) other than the Associated Compound(s) included in the Combination Product shall be for a quantity comparable to that used in such Combination Product and of substantially the same class, purity and potency or functionality, as applicable. If [**], the Parties shall negotiate in good faith a reasonable adjustment to Net Sales in such country that takes into account [**].

1.108 "Nexus" has the meaning provided in Section 3.4.2(b).

1.109 "Non-Breaching Party" has the meaning provided in Section 10.2.1.

1.110 "Non-Validated Target Patent" has the meaning provided in Section 6.2.2.

1.111 "Non-Validated Target Program IP" has the meaning provided in Section 6.3.2.

1.112 "Notice of Conditional Exercise" has the meaning provided in Section 3.1.4(a).

1.113 "Notice Period" has the meaning provided in Section 10.2.1.

1.114 "Option" means an option granted to Incyte pursuant to Section 3.1 to select an Initial Research Target, Definitive Research Target or Extended Research Target, as applicable, as a Validated Target in accordance with Section 3.1 in order to obtain the applicable (a) exclusive license under Program IP pursuant Section 3.3.1(b)(i)(A) or 3.3.1(b)(ii)(A), and (b) non-exclusive

license under Syros Existing Background Target IP pursuant Section 3.3.1(b)(i)(B) or 3.3.1(b)(ii)(B), in each case ((a) and (b)), to Exploit the applicable Associated Compounds and Associated Products with respect to a Validated Target.

1.115 "Orange Book" means the FDA publication "Approved Drug Products with Therapeutic Equivalence Evaluations".

1.116 "Original Target" has the meaning provided in Section 2.8.1(b).

1.117 "Original Target List" has the meaning provided in Section 2.8.1(b).

1.118 "Patent Challenge" has the meaning provided in Section 10.2.5.

1.119 "Patents" means (a) all national, regional and international patents and patent applications, including provisional patent applications; (b) all patent applications filed either from such patents, patent applications or provisional applications or from an application claiming priority from any of these, including divisionals, continuations, continuations-in-part, provisionals, converted provisionals and continued prosecution applications; (c) any and all patents that have issued or in the future issue from the foregoing patent applications ((a) and (b)), including utility models, petty patents, innovation patents and design patents and certificates of invention; (d) any and all extensions or restorations by existing or future extension or restoration mechanisms, including revalidations, reissues, re-examinations and extensions (including any supplementary protection certificates and the like) of the foregoing patents or patent applications ((a), (b) and (c)); and (e) any similar rights, including so-called pipeline protection or any importation, revalidation, confirmation or introduction patent or registration patent or patent of additions to any of such foregoing patent applications and patents.

1.120 "Payment" has the meaning provided in Section 5.8.

1.121 "Permitted Overrun Costs" has the meaning provided in Section 2.6.3(d).

1.122 "Person" means an individual, sole proprietorship, partnership, limited partnership, limited liability partnership, corporation, limited liability company, business trust, joint stock company, trust, unincorporated association, joint venture or other similar entity or organization, including a government or political subdivision, department or agency of a government.

1.123 "PHSA" means the Public Health Service Act as set forth at 42 U.S.C. Chapter 6A, as may be amended from time to time, together with any rules, regulations and requirements promulgated thereunder (including all additions, supplements, extensions and modifications thereto).

1.124 "Pilot Samples" has the meaning provided in Section 2.8.1(a).

1.125 "Pilot Target" has the meaning provided in Section 2.8.1(a).

1.126 "Pilot Target List" has the meaning provided in Section 2.8.1(a).

1.127 "Pivotal Trial" means a human clinical trial of a product that is on a sufficient number of subjects that, prior to commencement of the trial, satisfies both of the following ((a) and (b)):

(a) such trial, together with other available evidence from prior clinical trials, is prospectively designed to establish that such product has an acceptable safety and efficacy profile for its intended use, and to determine warnings, precautions, and adverse reactions that are associated with such product in the dosage range to be prescribed, which trial is intended to support Regulatory Approval of such product in the United States, the European Union or Japan and will provide substantial evidence of safety and effectiveness for reliance by Regulatory Authorities in granting Regulatory Approval; and

(b) such trial is prospectively designed to be a registration trial sufficient, together with other available evidence from prior clinical trials, for submitting an application for Regulatory Approval for such product in the United States, the European Union or Japan, as evidenced by (i) an agreement with or statement from the FDA, EMA or PMDA on a special protocol assessment or equivalent, or (ii) other guidance or minutes issued by the FDA, EMA or PMDA, for such registration trial.

1.128 "PMDA" means the Pharmaceuticals and Medical Devices Agency in Japan and any successor entity thereto.

1.129 "Preliminary Target" means an Original Target selected by Incyte and designated as a "preliminary target" in accordance with Section 2.8.2.

1.130 "Preliminary Target Selection Date" means the earlier of (a) the date that Incyte designates the final Preliminary Target pursuant to Section 2.8.2 and (b) the expiration of the Preliminary Target Selection Period.

1.131 "Preliminary Target Selection Period" has the meaning provided in Section 2.8.2.

1.132 "Premium Targets" means [**] Biological Targets identified by or on behalf of Syros or its Affiliates, prior to the Effective Date, as potentially relevant to [**] as supported by Premium Target Data that show a rationale sufficient to demonstrate that each of such Biological Targets is directly relevant to [**] and that are each designated as a "premium target" to the Gatekeeper in accordance with Section 2.7.2.

1.133 "Premium Target Confirmation Period" has the meaning provided in Section 2.8.4(c).

1.134 "Premium Target Data" means, with respect to a Premium Target, internal research data and results, together with the results of analyses thereof, that are or have been generated with respect to such Premium Target by or on behalf of Syros from [**].

1.135 "Premium Target List" has the meaning provided in Section 2.7.2.

1.136 "Prepaid Research Amount" has the meaning provided in Section 5.1.

1.137 "Pricing and Reimbursement Approval" means the approval, agreement, determination or decision from a Regulatory Authority establishing the price and/or reimbursement for an Associated Product for sale in a given country or regulatory jurisdiction, if and as required by Applicable Law in such country or other regulatory jurisdiction prior to or subsequent to the marketing and sale of an Associated Product in such country or regulatory jurisdiction.

1.138 "Program Data" means that portion of the Program Know-How consisting of data, together with the results of analyses thereof.

1.139 "Program IP" means the Program Know-How, Program Patents and any intellectual property rights with respect to the Program Know-How other than Program Patents.

1.140 "Program Know-How" means any Know-How conceived, discovered, generated or otherwise made by or on behalf of (a) either Party or its Affiliates, solely or jointly, and resulting from the conduct of activities under the Research Plan; or (b) Incyte or its Affiliates, solely or jointly, and (i) resulting from the conduct of activities (A) in support of a program initiated under the Research Plan or (B) under the license granted to Incyte in Section 3.3.1(a), (ii) resulting from reliance on or use of any Syros Confidential Information, or (iii) resulting from reliance on or use of any Know-How covered by clause (a), (b)(i) or (b)(ii); excluding, in each case ((a) and (b)), any Know-How (1) within the Syros Platform Improvements and (2) to the extent consisting of Drug Discovery and Development Know-How.

1.141 "Program Patent" means any Patent that Covers any Program Know-How and that does not Cover any Know-How within the Syros Platform Improvements.

1.142 "Program Target" means, as applicable, an Original Target that is not also an Incyte Excluded Target, Supplemental Target that is not also an Incyte Excluded Target, Preliminary Target, Initial Research Target, Definitive Research Target, Extended Research Target or Validated Target.

1.143 "Progress Reports" has the meaning provided in Section 4.2.

1.144 "Prosecuting Party" means, with respect to a Patent, the Party that has the right to conduct the Prosecution Activities with respect to such Patent.

1.145 "Prosecution Activities" means, with respect to a Patent, (a) the preparation, filing, prosecution and maintenance of such Patent and (b) any activities conducted in relation to any interference proceeding, re-issuance proceeding, re-examination proceeding, review proceeding, opposition proceeding or patent term extension with respect to such Patent.

1.146 "Purple Book" means the FDA publication "Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations".

1.147 "Regulatory Approval" means all clearances, approvals (including Pricing and Reimbursement Approval), licenses, registrations or authorizations of any Regulatory Authority necessary to commercially distribute, sell and market a product in a country or territory under this Agreement.

1.148 "Regulatory Authority" means any applicable supra-national, federal, national, regional, state, provincial or local regulatory agencies, departments, bureaus, commissions, councils or other government entities regulating or otherwise exercising authority with respect to the Exploitation of any Associated Compound or Associated Product with respect to any Program Target, including (a) the FDA in the United States, (b) the EMA in the European Union and (c) the PMDA in Japan.

1.149 "Regulatory Exclusivity Period" means, with respect to each Royalty Product in any country, a period of exclusivity (other than Patent exclusivity) granted or afforded by Applicable Law or by a Regulatory Authority in such country that confers exclusive marketing rights with respect to such Royalty Product in such country or prevents another party from using or otherwise relying on any data supporting Regulatory Approval of such Royalty Product without the prior written consent of the holder of the Drug Approval Application, such as new chemical entity exclusivity, new use or indication exclusivity, new formulation exclusivity, orphan drug exclusivity, non-patent related pediatric exclusivity, reference product exclusivity or any other applicable marketing or data exclusivity, including any such periods listed in the FDA's Orange Book or Purple Book, or any such periods under Article 14(11) of Parliament and Council Regulation (EC) No. 726/2004, Parliament and Council Regulation (EC) No. 141/2000 on orphan medicines, Parliament and Council Regulation (EC) No. 1901/2006 on medicinal products for pediatric use and under national implementations in the European Union of Article 10 of Parliament and Council Directive 2001/83/EC, and all international equivalents of any of the foregoing.

1.150 "Research Documentation" has the meaning provided in Section 2.11.

1.151 "Research Plan" means the Initial Research Plan, as amended in accordance with the terms of this Agreement, including the anticipated average number of FTEs for each Party, the deliverables, and timelines, in each case that are described therein.

1.152 "Research Program" means the research activities performed by the Parties pursuant to the Research Plan and in accordance with the terms of this Agreement.

1.153 "Research Term" means the period commencing on the Effective Date and, unless extended pursuant to Section 2.9, ending on the earlier of (a) [**] and (b) [**].

1.154 "Reserved Targets" means, subject to Section 3.4, (a) all Original Targets until the Preliminary Target Selection Date, upon which all Original Targets (i) selected as Preliminary Targets shall continue to be Reserved Targets unless and until such Preliminary Targets subsequently become Unreserved Targets and (ii) not selected as Preliminary Targets shall become Unreserved Targets; (b) all Preliminary Targets until the Initial Research Target Selection Date, upon which all Preliminary Targets (i) selected as Initial Research Targets shall continue to be Reserved Targets unless and until such Initial Research Targets subsequently become Unreserved Targets and (ii) not selected as Initial Research Targets shall become Unreserved Targets; (c) all Initial Research Targets until the expiration of the option under Section 3.1.1(b), upon which all Initial Research Targets (i) selected as Definitive Research Targets or Validated Targets shall continue to be Reserved Targets unless and until such Definitive Research Targets subsequently become Unreserved Targets and (ii) not selected as Definitive Research Targets or Validated Targets

shall become Unreserved Targets; (d) all Definitive Research Targets until the expiration of the option under Section 3.1.2(b), upon which all Definitive Research Targets (i) selected as Extended Research Targets or Validated Targets shall continue to be Reserved Targets unless and until such Extended Research Targets subsequently become Unreserved Targets and (ii) not selected as Extended Research Targets or Validated Targets shall become Unreserved Targets; (e) all Extended Research Targets until the expiration of the option under Section 3.1.3(b), upon which all Extended Research Targets (i) selected as Validated Targets shall continue to be Reserved Targets and (ii) not selected as Validated Targets shall become Unreserved Targets; and (f) all Validated Targets.

1.155 "Reverted Target Data" has the meaning provided in Section 6.2.2(c)(iii)(B).

1.156 "Reverted Target Patent" has the meaning provided in Section 6.2.2(c)(iii)(A).

1.157 "Royalty Product" means an Associated Product with respect to a Validated Target that is sold or invoiced for sale by or on behalf of Incyte, any of its Affiliates, its or their direct or indirect successors (whether as a successor-in-interest with respect to any of the foregoing Persons or such Associated Product by way of product acquisition or otherwise) or any licensee or sublicensee of any of the foregoing.

1.158 "Royalty Term" means, with respect to each Royalty Product and country, the period commencing on the date of the First Commercial Sale of such Royalty Product in such country and ending on the latest to occur of: (a) the expiration of the last-to-expire Program Patent or Syros Existing Background Target Patent in such country that contains a Valid Claim that claims (i) (A) the applicable Validated Target or (B) any nucleic acid sequence encoding such Validated Target, in each case ((A) or (B)), as a composition of matter; (ii) the Exploitation of such Validated Target with respect to any compound or product, including any method of treatment related to the Modulation of such Validated Target; or (iii) any compound whose primary activity is Modulation of such Validated Target, as a composition of matter; *provided* that, in each case ((i)-(iii)), the Exploitation of such Royalty Product would infringe such Valid Claim (or, in the case of a pending Valid Claim, would infringe such pending Valid Claim if it issued) but for ownership of the Patent in which such Valid Claim is listed or but for the licenses granted to Incyte under Section 3.3.1(b); (b) the expiration of Regulatory Exclusivity Period in such country for such Royalty Product; and (c) the tenth (10th) anniversary of such First Commercial Sale.

1.159 "Sales Milestone Event" has the meaning provided in Section 5.5.

1.160 "Sales Milestone Payment" has the meaning provided in Section 5.5.

1.161 "Sample Specifications" has the meaning provided in Section 2.12.1.

1.162 "Samples" has the meaning provided in Section 2.6.2.

1.163 "SEC" means the United States Securities and Exchange Commission.

1.164 "Selection Window" means the period commencing on the Effective Date and ending on the earlier of (a) [**] or (b) [**].

1.165 "Senior Executive" means, with respect to Syros, Syros' Chief Executive Officer (CEO) or the CEO's designee and with respect to Incyte, Incyte's Chief Scientific Officer (CSO) or the CSO's designee.

1.166 "Stock Purchase Agreement" means that certain Stock Purchase Agreement between the Parties, effective as of the Effective Date.

1.167 "Sublicensee" means a Third Party that is granted a sublicense by Incyte or its Affiliate under the license grants in Section 3.3.1(b).

1.168 "Super-Enhancer Data" means [**]. For clarity, the Super-Enhancer Data is not intended, and shall not be construed, to include any Circuitry Map Data.

1.169 "Supplemental Samples" has the meaning provided in Section 2.8.3(a).

1.170 "Supplemental Target" has the meaning provided in Section 2.8.3(a).

1.171 "Supplemental Target Data Package" has the meaning provided in Section 2.8.3(c).

1.172 "Supplemental Target List" has the meaning provided in Section 2.8.3(a).

1.173 "Supplemental Validated Target" means each of the [**] of the Initial Research Targets, Definitive Research Targets or Extended Research Targets selected by Incyte and designated as a "validated target" in accordance with Section 3.1.

1.174 "Syros Excluded Target List" means a list identifying each Syros Excluded Target by ENSEMBL ID and name, as generated and supplemented by Syros from time to time in accordance with Section 2.7.3 and maintained by the Gatekeeper.

1.175 "Syros Excluded Targets" means the (a) Syros Initial Excluded Targets; (b) Syros Internal Excluded Targets; (c) Syros Third Party Excluded Targets; and (d) any Premium Target not (i) selected by Incyte as an Initial Research Target within the Initial Research Target Selection Period or (ii) confirmed by Incyte as an Initial Research Target within the Premium Target Confirmation Period.

1.176 "Syros Existing Background Target IP" means the Syros Existing Background Target Know-How and Syros Existing Background Target Patents.

1.177 "Syros Existing Background Target Know-How" means, with respect to a Program Target, any Know-How Controlled by Syros or any of its Controlled Affiliates as of the Effective Date, to the extent specifically relating to such Program Target, excluding any (a) Program Know-How, (b) Know-How to the extent relating to the Syros Platform and (c) Drug Discovery and Development Know-How (including any Know How relating to any Syros Therapeutic).

1.178 "Syros Existing Background Target Patent" means, with respect to a Program Target, any Patent Controlled by Syros or any of its Controlled Affiliates as of the Effective Date that Covers any Syros Existing Background Target Know-How specifically relating to such Program

Target, excluding any (a) Program Patent, (b) Patent Covering the Syros Platform and (c) Patent Covering any Drug Discovery and Development Know-How (including any Patent Covering any Syros Therapeutic).

1.179 "Syros FTE Rate" means [**] Dollars ($[**]) per FTE.

1.180 "Syros Independent Program" has the meaning provided in Section 2.14.2.

1.181 "Syros Initial Excluded Targets" means [**].

1.182 "Syros Internal Excluded Target" means a Syros Internal Target that is designated by Syros as a Syros Internal Excluded Target in accordance with Section 2.7.3(b).

1.183 "Syros Internal Target" means a Biological Target that is the subject of an Internal Syros Program.

1.184 "Syros Platform" means the proprietary gene expression (including differential gene expression) and control platform that enables the identification of therapeutic targets based on an understanding of disease-causing alterations in gene expression, including instruments, analytical methods, algorithms, databases of regulatory genomes, procedures, reagents, techniques, software and platforms, in each case, controlled by Syros or any of its Controlled Affiliates as of the Effective Date or at any time during the Term, excluding, in each case, any aspect of the Syros Platform excluded pursuant to Section 11.2.2(b).

1.185 "Syros Platform Improvements" means (a) any Know-How, to the extent relating to the Syros Platform or relating to any improvement thereto, conceived, discovered, generated or otherwise made by or on behalf of either Party or its Affiliates, solely or jointly, during the Term; (b) any Patent that Covers any Know-How of clause (a); or (c) any intellectual property rights with respect to the Know-How of clause (a), other than the Patents of clause (b). For clarity, the Circuitry Map Data and Super-Enhancer Data are not intended, and shall not be construed, to be included in the Syros Platform Improvements.

1.186 "Syros Restricted Personnel" has the meaning provided in Section 2.14.2.

1.187 "Syros Therapeutic" means any compound or product researched, Developed, Commercialized, owned or Controlled by Syros or any of its Affiliates (a) as of the Effective Date or (b) after the Effective Date, during the Term and outside of the Research Program, including SY-1425 and SY-1365, and any improvements to any of the foregoing.

1.188 "Syros Third Party Excluded Target" means a Syros Third Party Target that is designated by Syros as a Syros Third Party Excluded Target in accordance with Section 2.7.3(c).

1.189 "Syros Third Party Target" means a Biological Target that is the subject of a Third Party Collaboration Agreement.

1.190 "Target" means each Biological Target identified in accordance with the Research Plan during the Research Term by Syros' use of the Syros Platform to analyze the Samples.

1.191 "Term" has the meaning provided in Section 10.1.

1.192 "Termination Notice" has the meaning provided in Section 10.2.1.

1.193 "Third Party" means any Person other than a Party or its Affiliates.

1.194 "Third Party Claims" has the meaning provided in Section 9.1.

1.195 "Third Party Collaboration Agreement" means, with respect to a Biological Target, an executed agreement with a Third Party under which Syros has granted or grants such Third Party any ownership interest or license, or an option to obtain any ownership interest or license, in or to any intellectual property rights with respect to (a) such Biological Target or (b) any compound directed to or that activates, inhibits, agonizes, antagonizes or otherwise modulates such Biological Target.

1.196 "Third Party Infringement Claim" has the meaning provided in Section 6.5.1.

1.197 "Third Party Platform Rights" has the meaning provided in Section 6.6.1(b).

1.198 "Unreserved Targets" means any Program Target that is not a Reserved Target.

1.199 "Valid Claim" means any claim of (a) an issued and unexpired Patent that has not been held unenforceable, unpatentable or invalid by a decision of a court or other governmental agency of competent jurisdiction, unappealable or unappealed within the time allowed for appeal, and which has not been admitted to be invalid or unenforceable through disclaimer or otherwise; or (b) a pending Patent application that was filed and is being prosecuted in good faith and has not been abandoned or finally disallowed without the possibility of appeal or re-filing of such application and that has been pending for less than seven (7) years from the filing date of the Patent from which such Patent application claims its earliest priority date.

1.200 "Validated Target" means an Initial Research Target, a Definitive Research Target or an Extended Research Target selected by Incyte and designated as a "validated target" in accordance with Section 3.1. For clarity, the Validated Targets include the Initial Validated Targets and the Supplemental Validated Targets.

1.201 "Validated Target Patent" has the meaning provided in Section 6.2.3.

1.202 "Validated Target Payment" has the meaning provided in Section 5.3.2.

1.203 "Validated Target Program IP" has the meaning provided in Section 6.3.2.

1.204 "[**]" has the meaning provided in Section 3.3.4.

1.205 "[**]" has the meaning provided in Section 3.3.4.

ARTICLE 2 - RESEARCH PROGRAM; IDENTIFICATION AND SELECTION OF ORIGINAL TARGETS, PRELIMINARY TARGETS, INITIAL RESEARCH TARGETS, DEFINITIVE RESEARCH TARGETS AND EXTENDED RESEARCH TARGETS

2.1 Overview. The principal goal of the Research Program shall be to identify, validate and select Validated Targets as set forth below.

2.2 Joint Research Committee. The Parties shall establish a joint research committee (the "Joint Research Committee" or "JRC") promptly and no later than [**] after the Effective Date. The JRC shall consist of three (3) representatives from each of the Parties, each of which shall be employees of the applicable Party or an Affiliate thereof with the requisite experience and seniority to enable such representative to represent the applicable Party with respect to the responsibilities set forth in Section 2.2.1. From time to time, each Party may substitute one or more of its representatives to the JRC upon written notice to the other Party.

2.2.1 Responsibilities of the JRC. The JRC shall oversee the Research Program and, in particular, shall:

(a) facilitate communications between the Parties with respect to the Research Program and coordinate the activities of the Parties under the Research Plan;

(b) oversee the progress of the Research Program, and review and discuss the results of the activities under the Research Plan;

(c) review the Research Plan on an as-needed basis, determine whether to propose amendments based on such review, and propose and recommend any such amendments for approval pursuant to Section 2.4.4;

(d) determine the actual number of Supplemental Samples to be provided in accordance with Section 2.8.3(a), based on the power calculation included in the Original Target Data Package;

(e) as applicable, determine the prioritization and acceleration (but not selection) of Preliminary Targets, Initial Research Targets, Definitive Research Targets, Extended Research Targets or Validated Targets under the Research Program;

(f) review and discuss (but not select) the:

(i) Original Targets under consideration by Incyte for selection as (A) Preliminary Targets in accordance with Section 2.8.2, (B) Initial Research Targets in accordance with Section 2.8.4 or Section 3.4, (C) Definitive Research Targets selected in accordance with Section 2.8.6 or Section 3.4, or (D) Extended Research Targets in accordance with Section 2.8.8 or Section 3.4;

(ii) Preliminary Targets under consideration by Incyte for selection as Initial Research Targets in accordance with Section 2.8.4(a);

(iii) Initial Research Targets under consideration by Incyte for selection as (A) Definitive Research Targets in accordance with Section 2.8.6(a) or (B) Validated Targets in accordance with Section 3.1.1;

(iv) Definitive Research Targets under consideration by Incyte for selection as (A) Extended Research Targets in accordance with Section 2.8.8 or (B) Validated Targets in accordance with Section 3.1.2; and

(v) Extended Research Targets under consideration by Incyte for selection as Validated Targets in accordance with Section 3.1.3;

(g) determine when no further Definitive Validation Studies will be conducted with respect to any Definitive Research Target;

(h) review the list of Original Targets;

(i) review the Initial Validation Study Data Package; and

(j) establish and oversee the JPC in accordance with Section 2.2.3.

2.2.2 Alliance Managers. Each Party shall appoint one of its representatives to the JRC to oversee contact between the Parties for all matters between meetings of the JRC and to have such other responsibilities as the Parties may agree in writing after the Effective Date (each of such representatives, an "Alliance Manager"). The Alliance Managers shall work together to manage and facilitate the communication between the Parties under this Agreement. From time to time, each Party may substitute its Alliance Manager upon written notice to the other Party. Notwithstanding any termination of the JRC pursuant to Section 2.5, following the Research Term, the Parties' Alliance Managers shall continue to manage and facilitate the communication between the Parties under this Agreement with respect to any activities conducted by or on behalf of Incyte or its Affiliates with respect to any Program Target(s) for which Incyte retains an unexercised Option.

2.2.3 Joint Patent Committee.

(a) Establishment. Within [**] after either Party requests to enter into a common interest agreement with respect to certain information to be shared by the Parties hereunder and provides an initial draft of such common interest agreement to the other Party, the Parties shall negotiate in good faith and enter into a common interest agreement to protect attorney-client privilege. Within [**] after entering into such common interest agreement the Parties shall establish a joint patent committee (the "Joint Patent Committee" or "JPC") as more fully described in this Section 2.2.3. Neither Party shall file any Program Patent until after the JPC has been established under this Section 2.2.3 and after the All Uses Field Patentability Criteria and MPN Field Patentability Criteria have been determined by the JPC. The JPC shall facilitate the discussion and coordination of Prosecution Activities with respect to Program Patents.

(b) Membership. The JPC shall be comprised of at least one (1) representative (or such other number of representatives as the Parties may mutually agree) from each of Incyte and Syros. Each Party may replace any or all of its representatives on the JPC at any time

upon written notice to the other Party. Each Party shall be free to appoint outside patent counsel as a representative of such Party to the JPC.

(c) Responsibilities. The JPC shall perform the following functions: (i) determine the All Uses Field Patentability Criteria and MPN Field Patentability Criteria within a reasonable amount of time after the establishment of the JPC; (ii) facilitate the discussion and coordination of the Parties' activities under Section 6.2; (iii) without limitation to clause (ii), serve as a forum for exchanging information and facilitating discussions regarding patentability and freedom to operate assessments; and (iv) perform such other patent-related responsibilities as may be mutually agreed by the Parties from time to time. Notwithstanding the foregoing, the JPC shall not have any decision-making authority beyond establishing the All Uses Field Patentability Criteria and MPN Field Patentability Criteria, and in particular shall not have any power to amend, modify, interpret or waive the terms of this Agreement, or to alter, increase, expand or waive compliance by a Party with its obligations under this Agreement.

(d) Decisions. The All Uses Field Patentability Criteria and MPN Field Patentability Criteria shall be determined by consensus of the JPC, with each Party having one (1) vote. If the JPC cannot agree on such criteria, then either Party may refer such disagreement to the JRC (if still in effect) or the Parties (if the JRC has been terminated) for further discussions; *provided* that the JRC shall not have final decision-making authority over such criteria, which shall only be determined by consensus of the JPC or by mutual agreement of the Parties.

2.3 JRC Meetings. Unless otherwise agreed by the Parties, the JRC shall meet at least quarterly, or more frequently if otherwise agreed by the JRC. Such meetings may be held in-person or by teleconference or videoconference or similar means in which each participant can hear what is said by, and be heard by, the other participants. The location of such in-person meetings shall be mutually agreed by the JRC. If the JRC is unable to agree upon the location of such in-person meetings, then the location of such meetings shall alternate between Cambridge, Massachusetts and Wilmington, Delaware. Each Party shall be responsible for all travel and related expenses incurred by its representatives in connection with JRC meetings. Each Party may invite non-voting observers from the JPC or relevant internal functional areas to attend JRC meetings when appropriate to address matters that are the subject of a meeting; *provided* that such observers (a) are subject to commercially reasonable written obligations of confidentiality and non-use with respect to Confidential Information, except in the case of outside patent counsel serving in a representative capacity on the JPC, and (b) are subject to assignment obligations as necessary to fully effect the ownership of intellectual property as provided for in Section 6.1. The JRC shall have the right to adopt standing rules as necessary or useful for carrying out its responsibilities; *provided* that such rules shall not be inconsistent with the terms of this Agreement.

2.4 Decision-Making.

2.4.1 Generally. Except with respect to the responsibilities set forth in [**], for which the JRC shall have decision-making authority, the JRC shall serve only as an advisory body and shall not have any decision making authority. The authority of the JRC, and the decision-making principles outlined in this Section 2.4, are not intended, and shall not be construed, to extend

to the day-to-day conduct of any activities carried out by either Party with respect to the activities for which such Party is allocated responsibility under the Research Plan.

2.4.2 Process. Except as otherwise set forth in Section 2.4.3(a), the matters subject to the JRC's decision-making authority shall be made by unanimous vote. Incyte's representatives to the JRC shall collectively have one (1) vote and Syros' representatives to the JRC shall collectively have one (1) vote on such matters. No decision shall be made without a quorum of at least two (2) representatives from each Party present. Notwithstanding the foregoing, decisions may be made between meetings of the JRC; *provided* that such decisions are in writing and signed by at least two (2) representatives from each Party to the JRC. Each Party's representatives to the JRC shall use good faith, reasonable efforts to achieve unanimity on all issues.

2.4.3 Dispute Resolution.

(a) If the JRC cannot, or does not, reach consensus on any matter within the JRC's decision-making authority [**] shall have final decision-making authority over such matter and such decision shall be final upon [**] provision of a written, signed document outlining the decision to [**].

(b) Notwithstanding Section 2.4.3(a), [**] may not exercise its final decision-making authority pursuant to Section 2.4.3(a) in a manner that would (i) require [**] with respect to the Research Program in excess of the resources or amounts set forth in the Initial Research Plan, including with respect to any stage of research set forth therein; (ii) result in the transfer to [**] (in whole or in part); (iii) result in [**] infringing or misappropriating any intellectual property owned or controlled by a Third Party or violating any term or condition of any agreement between [**] and a Third Party; or (iv) waive compliance with this Agreement, or amend or otherwise modify any term or condition of this Agreement or the Research Plan. Each Party shall retain the rights, powers, and discretion granted to it under this Agreement and no such rights, powers, or discretion shall be delegated to or vested in the JRC unless such delegation or vesting of rights is expressly provided for in this Agreement or the Parties otherwise agree in writing.

2.4.4 Amendments and Waivers. The JRC shall not have the power to waive compliance with the terms of this Agreement, or to amend or otherwise modify such terms or to amend or modify the Research Plan, and any such amendment to the terms of this Agreement (or the Research Plan) shall be made only pursuant to Section 11.7; [**] thereunder following completion of the Initial Validation Studies. Without limiting the foregoing, and subject to the terms and conditions of this Agreement (including, for clarity Section 2.6.3), [**] shall not unreasonably withhold its consent to proposed amendments to the Research Plan with respect to matters relating to the activities being conducted by [**]; *provided* that such proposed amendments would not (a) require [**] with respect to the Research Program in excess of the resources or amounts set forth in the Initial Research Plan (including by increasing such resources or amounts with respect to any stage of research); (b) result in the transfer to [**] (in whole or in part); (c) result in [**] infringing or misappropriating any intellectual property owned or controlled by a Third Party or violating any term or condition of any agreement between [**] and a Third Party; or (d) result in a change of scope with respect to the nature of the Samples or analyses conducted by Syros with respect to the Samples, or the data generated therefrom.

2.5 Termination of the JRC. Following expiration of the Research Term, if Syros or its Affiliates are not then providing ongoing research, development or other support to Incyte or its Affiliates in connection with this Agreement, then either Party may terminate the JRC, but not the JPC, upon [**] written notice to the other Party.

2.6 Research Plan.

2.6.1 Diligence. Subject to Section 2.8.1(d) and Section 2.8.3(d), Syros shall (a) perform the activities and analyses assigned to Syros under the Research Plan with respect to the Samples in accordance with the terms of the Research Plan and (b) use Commercially Reasonable Efforts to (i) perform such activities and analyses within the timeframes described in the Research Plan, including by allocating an appropriate number of FTEs to the work to be conducted by or on behalf of Syros under the Research Plan at any time during the Research Term and (ii) provide deliverables that meet any applicable minimum criteria for such deliverables as set forth in the Research Plan. Incyte shall (x) perform the activities and analyses assigned to Incyte under the Research Plan in accordance with the terms of the Research Plan and (y) use Commercially Reasonable Efforts to (i) perform such activities and analyses within the timeframes described in the Research Plan and (ii) provide deliverables that meet any applicable minimum criteria for such deliverables as set forth in the Research Plan.

2.6.2 Research Plan Responsibilities. Unless otherwise agreed in writing by the Parties or expressly provided in the Research Plan, the allocation of responsibilities and obligations under the Research Plan shall be as follows: (a) Incyte shall solely have the obligation for (i) providing all samples from, or derived from, human subjects or cell lines that are necessary to perform the Research Program (collectively, "Samples"), including patient samples and control samples, in accordance with Section 2.12 and the Research Plan; (ii) performing the Definitive Validation Studies in accordance with Section 2.8.7 and the Research Plan; and (iii) performing any other research activities at Incyte's election during or following the Research Term in relation to any Program Target with respect to which Incyte retains an unexercised Option, in accordance with the Research Plan; and (b) Syros, subject to Incyte's rights and obligations under clause (a) and Section 2.8.5(a), under the oversight of the JRC, shall solely have the obligation for (i) analyzing the Pilot Samples in accordance with Section 2.8.1 and the Research Plan; (ii) analyzing the Supplemental Samples in accordance with Section 2.8.3 and the Research Plan; and (iii) performing the Initial Validation Studies in accordance with Section 2.8.5 and the Research Plan; in each case ((a) and (b)), subject to and in accordance with the terms of this Agreement. Notwithstanding anything to the contrary in this Agreement or the Research Plan, Syros shall not use any Syros Therapeutic in performing its obligations under this Agreement, including in performing its activities under the Research Plan. Without limiting the foregoing, Incyte shall have the right to use Program IP and Syros Existing Background Target IP to conduct validation activities and preclinical research on Program Targets pursuant to the license granted in Section 3.3.1(a).

2.6.3 Costs and Expenses.

(a) Generally. The Parties intend that Incyte shall fund all costs and expenses incurred by or on behalf of Syros or its Affiliates in performing its or their activities under the Research Program in accordance with the Research Plan, including with respect to FTEs (at the

Syros FTE Rate) and reasonable and documented out-of-pocket costs and expenses; *provided* that Incyte shall have no obligation to pay Syros or its Affiliates more than Seven Million Five-Hundred Thousand Dollars ($7,500,000) in the aggregate for such costs and expenses incurred during the Research Term, except to the extent Incyte has an obligation to pay Syros such excess costs and expenses pursuant to Section 2.6.3(c), Section 2.6.3(d) or Section 2.8.5(b)(iii), or to the extent otherwise agreed to in writing in advance by Incyte.

(b) Initial Budget. The Initial Research Plan includes an initial budget that represents Syros' good faith estimate of its costs and expenses, including with respect to FTEs (at the Syros FTE Rate) and out-of-pocket costs and expenses, for conducting its activities during the Research Term (the "Initial Budget").

(c) Amendments to the Research Plan and Budget. If the Parties agree to amend the Research Plan in a manner that would increase the costs and expenses of, or resources committed by, Syros or any of its Affiliates beyond those set forth in the then-current Budget or Research Plan, including with respect to any stage of research set forth in such Research Plan, then (i) the Parties shall mutually agree upon an amendment to such Budget to account for such increase (including, for clarity, any increased out-of-pocket costs and expenses and additional FTEs of Syros at the applicable Syros FTE Rate) and (ii) Incyte shall pay to Syros any additional amounts agreed to by the Parties in accordance with the terms of such amendment or Section 2.6.3(e). If the Parties are unable to agree upon any such amendment to such Budget, then Syros shall have no obligation to perform any such activities that would increase Syros' costs and expenses, or resources committed, beyond those set forth in the then-existing Research Plan (and Budget), including with respect to any stage of research.

(d) Cost Overruns. Syros shall promptly inform Incyte upon Syros' determining that it is likely to overspend the amounts set forth in the then-current Budget, in the aggregate or with respect to any stage of research. If Syros exceeds the budgeted amounts, including with respect to any stage of research, then Syros shall provide Incyte with an explanation regarding the excess over such budgeted amounts. Subject to the last sentence of this Section 2.6.3(d), any such overspend shall be deemed "Permitted Overrun Costs" to the extent that such overspend (i) (A) did not result from the failure of Syros or any of its Affiliates to adequately supervise a subcontractor or from other negligence or intentional misconduct on the part of Syros or any of its Affiliates or subcontractors with respect to the excess over such budgeted amounts and (B) that Syros has promptly notified Incyte of such overspend and used reasonable efforts to mitigate the size of such overspend; (ii) has been approved by Incyte in writing; or (iii) resulted from the failure of Incyte to perform its obligations in accordance with this Agreement, including the Research Plan. With respect to any portion of Permitted Overrun Costs that exceed [**] percent ([**]%) of the amounts set forth in the then-current Budget, in the aggregate or with respect to any stage of research, Incyte shall only be responsible for such portion in excess of [**] percent ([**]%) to the extent that Syros can establish a reasonable scientific basis for such portion of the overspend.

(e) Payments. Syros agrees to issue no later than [**] after the end of each Calendar Quarter an invoice for (i) Incyte's portion of any Permitted Overrun Costs incurred with respect to such Calendar Quarter and (ii) except as otherwise agreed in an applicable amendment to the Budget, any Permitted Overrun Costs incurred in connection with an amendment

to the Research Plan. Each of such invoices shall provide reasonable detail to permit Incyte to identify the activities conducted by Syros and the related costs and expenses incurred by Syros. Incyte shall pay Syros any undisputed amounts due under such invoices within [**] after receipt and any remaining amounts due within [**] after resolution of any dispute with respect thereto.

2.7 Gatekeeping.

2.7.1 Appointment of Gatekeeper. Within [**] after the Effective Date, the Parties shall cooperate to qualify and select, and Syros shall use reasonable efforts to engage, an independent Third Party gatekeeper reasonably acceptable to both Parties (the "Gatekeeper"). If required to do so by the Gatekeeper in order to engage the Gatekeeper, each Party agrees to indemnify and hold the Gatekeeper harmless from liabilities arising from the performance of the Gatekeeper's responsibilities in connection with this Agreement.

2.7.2 Premium Targets. Within [**] after the Gatekeeper is engaged in accordance with Section 2.7.1, Syros shall submit to the Gatekeeper a list identifying, by ENSEMBL ID and name, each Premium Target (the "Premium Target List").

2.7.3 Syros Excluded Targets.

(a) [**]. As of the Effective Date, the Parties agree that [**] are deemed to be Syros Initial Excluded Targets and shall be included on the Syros Excluded Target List.

(b) Syros Internal Excluded Targets.

(i) Following Appointment of the Gatekeeper. Syros shall have the right, within [**] after the Gatekeeper is engaged in accordance with Section 2.7.1, to designate up to [**] Syros Internal Targets as Syros Internal Excluded Targets, which Syros Internal Targets shall become Syros Internal Excluded Targets, and be added to the Syros Excluded Target List, upon Syros' written notice to the Gatekeeper identifying each of such Syros Internal Targets by ENSEMBL ID and name.

(ii) Otherwise During the Selection Window. Except as set forth in Section 2.7.3(b)(i), Syros shall not have any right to designate any Syros Internal Target as a Syros Excluded Target during the Selection Window.

(iii) Following the Selection Window. Following the Selection Window, Syros shall have the right to designate any number of Syros Internal Targets that are Unreserved Targets as Syros Internal Excluded Targets, which Syros Internal Targets shall become Syros Internal Excluded Targets, and be added to the Syros Excluded Target List, upon Syros' written notice to the Gatekeeper identifying each of such Syros Internal Targets by ENSEMBL ID and name.

(c) Syros Third Party Excluded Targets.

(i) [**] of the Selection Window. During any portion of the Selection Window commencing on the Effective Date and ending on [**], Syros shall not have any right to designate any Syros Third Party Target as a Syros Excluded Target.

(ii) [**] of the Selection Window.

(A) Fresh Pilot Samples. If Syros determines that fresh Pilot Samples must be used in the Research Program, then, during any portion of the Selection Window commencing on [**] and ending [**], Syros shall not have the right to designate any Syros Third Party Target as a Syros Excluded Target.

(B) Frozen Pilot Samples. If Syros determines that frozen Pilot Samples can be used in the Research Program, then, during any portion of the Selection Window commencing on [**] and ending [**], Syros shall have the right to designate up to [**] Syros Third Party Targets that are Unreserved Targets as Syros Third Party Excluded Targets, which Syros Third Party Targets shall become Syros Third Party Excluded Targets, and be added to the Syros Excluded Target List, upon Syros' written notice to the Gatekeeper identifying each of such Syros Third Party Targets by ENSEMBL ID and name.

(iii) Following the Selection Window. Following the Selection Window, Syros shall have the right to designate any number of Syros Third Party Targets that are Unreserved Targets as Syros Third Party Excluded Targets, which Syros Third Party Targets shall become Syros Third Party Excluded Targets, and be added to the Syros Excluded Target List, upon Syros' written notice to the Gatekeeper identifying each of such Syros Third Party Targets by ENSEMBL ID and name.

2.7.4 Incyte Excluded Targets. Incyte shall have the right, during the period commencing on the date that the Gatekeeper is engaged in accordance with Section 2.7.1 and ending on the Delivery Date, to designate up to [**] Incyte Internal Targets as Incyte Excluded Targets, which Incyte Internal Targets shall become Incyte Excluded Targets, and be added to the Incyte Excluded Target List, upon Incyte's written notice to the Gatekeeper identifying each of such Incyte Internal Targets by ENSEMBL ID and name.

2.7.5 Responsibilities of the Gatekeeper. The Gatekeeper shall be responsible for:

(a) maintaining the Premium Target List;

(b) maintaining the Syros Excluded Target List, and updating the Syros Excluded Target List as of the date that Syros designates any (i) Syros Internal Target as a Syros Internal Excluded Target in accordance with Section 2.7.3(b) or (ii) Syros Third Party Target as a Syros Third Party Excluded Target in accordance with Section 2.7.3(c);

(c) maintaining the Incyte Excluded Target List, and updating the Incyte Excluded Target List as of the date that Incyte designates any Incyte Internal Target as an Incyte Excluded Target in accordance with Section 2.7.4;

(d) updating the Syros Excluded Target List to add any Premium Target not (i) selected by Incyte as an Initial Research Target within the Initial Research Target Selection Period or (ii) confirmed by Incyte as an Initial Research Target within the Premium Target Confirmation Period; and

(e) conducting the activities designated to be performed by the Gatekeeper in Section 2.8.1(b), Section 2.8.2, Section 2.8.3(b), Section 2.8.4(a), Section 2.8.4(b), Section 2.8.6(b) and Section 3.4.2(c) of this Agreement.

2.7.6 Disclosure of Premium Targets and Excluded Targets by the Gatekeeper . Except as expressly required by Section 2.8.4(a) or Section 2.8.4(b), the Gatekeeper shall not be permitted to disclose the identity of any Premium Target to Incyte. Except as expressly required by Section 2.8.4(b), Section 2.8.6(b) or Section 3.4.2(c), the Gatekeeper shall not be permitted to disclose the identity of any Syros Excluded Target to Incyte. The Gatekeeper shall not be permitted to disclose the identity of any Incyte Excluded Target to Syros. Notwithstanding the foregoing, the Gatekeeper shall be permitted to disclose the identity of (a) Syros Excluded Targets to Incyte or (b) Incyte Excluded Targets to Syros, in each case ((a) or (b)), if and to the extent required by Applicable Law or as otherwise agreed by the Parties in writing.

2.7.7 Costs and Expenses. The costs and expenses of the Gatekeeper, to the extent reasonably allocable to this Agreement or the Parties' activities hereunder, shall be [**].

2.8 Identification and Selection of Original Targets, Preliminary Targets, Initial Research Targets, Definitive Research Targets and Extended Research Targets.

2.8.1 Pilot Study.

(a) Analyses. Within [**] following the Effective Date (if Syros confirms that frozen Samples will be suitable for it to perform the activities assigned to it under the Research Plan) or within [**] following the Effective Date (if Syros confirms that fresh Samples will be required for it to perform the activities assigned to it under the Research Plan), Incyte shall deliver, or cause another Person to deliver, to Syros blood Samples obtained from subjects diagnosed with myeloproliferative neoplasms and control subjects, in each case, of a nature and in quantities set forth in the Research Plan (the "Pilot Samples"), which Pilot Samples shall meet the applicable Sample Specifications set forth in the Research Plan. Following receipt by Syros of the requisite Samples, Syros shall (i) (A) perform the activities and analyses assigned to Syros under the Research Plan with respect to the Pilot Samples in accordance with the terms of the Research Plan and (B) use Commercially Reasonable Efforts (1) to perform such activities and analyses within the timeframes described in the Research Plan, including by allocating an appropriate number of FTEs to the work to be conducted by or on behalf of Syros under the Research Plan at any time during the Research

Term and (ii) by analyzing the Pilot Samples using the Syros Platform, identify a list of Targets in accordance with the Research Plan provisions with respect to activities using Pilot Samples (each of such Targets a "Pilot Target" and collectively, the "Pilot Targets"; and such list, the "Pilot Target List"), and their corresponding ENSEMBL IDs and names.

(b) Gatekeeping. No later than [**] following Syros' completion of the analyses under Section 2.8.1(a), Syros shall submit the Pilot Target List to the Gatekeeper in writing. Following receipt of the Pilot Target List, the Gatekeeper shall be required to (i) prepare a list of Targets consisting of the Pilot Targets but excluding any Pilot Targets included on the Syros Excluded Target List (such list of Targets prepared by the Gatekeeper, the "Original Target List" and each Target included on the Original Target List an "Original Target") and (ii) deliver to both Parties in writing the Original Target List.

(c) Original Target Data Package. Within [**] after the delivery of the Original Target List by the Gatekeeper to both Parties pursuant to Section 2.8.1(b), Syros shall provide to Incyte a data package containing: (i) for each Original Target, the applicable data specified in the Research Plan with respect to Original Targets, including all Super-Enhancer Data with respect thereto; and (ii) [**] (such data package, the "Original Target Data Package" and the date of delivery of the Original Target Data Package, the "Delivery Date").

(d) Conditions. Syros' obligations under this Section 2.8.1 shall be conditioned upon Incyte's provision of sufficient quality and quantities of Pilot Samples to Syros, in accordance with the Research Plan and Section 2.12, to enable Syros to perform the activities assigned to it under the Research Plan with respect to the Pilot Samples.

2.8.2 Selection of Preliminary Targets. Subject to Section 2.8.9, during the period commencing on the date that the first Original Target is disclosed to Incyte and ending [**] after the Delivery Date (the "Preliminary Target Selection Period"), Incyte shall have the right to select up to [**] Original Targets as Preliminary Targets by providing written notice to (a) the Gatekeeper, designating each Preliminary Target by its ENSEMBL ID and name and (b) Syros, informing Syros that the notice in clause (a) has been submitted to the Gatekeeper. Within [**] after delivery of Incyte's notice to the Gatekeeper, the Gatekeeper shall be required to notify (i) Incyte in writing if any Original Target selected by Incyte as a Preliminary Target is an Incyte Excluded Target, and the identity of such Incyte Excluded Target, and such Incyte Excluded Target shall not become a Preliminary Target; (ii) Syros in writing if any Original Target selected by Incyte as a Preliminary Target is an Incyte Excluded Target, but not the identity of such Incyte Excluded Target; and (iii) the Parties in writing which Original Targets selected by Incyte as Preliminary Targets are not Incyte Excluded Targets. Each Original Target selected as a Preliminary Target in accordance with this Section 2.8.2 shall become a Preliminary Target as of the date that the Gatekeeper notifies the Parties that such Original Target is not an Incyte Excluded Target pursuant to clause (b)(iii). If any Original Target selected by Incyte as a Preliminary Target during the Preliminary Target Selection Period is an Incyte Excluded Target, then Incyte shall have the right to select a different Original Target as a Preliminary Target, in accordance with this Section 2.8.2, until the later of (A) expiration or termination of the Preliminary Target Selection Period and (B) [**] after delivery of the Gatekeeper's notice to Incyte informing Incyte that such Original Target is an Incyte Excluded Target.

2.8.3 Supplemental Study.

(a) Analyses. On or before the later of (i) the Delivery Date and (ii) [**], Incyte shall deliver, or cause another Person to deliver, to Syros additional blood Samples obtained from subjects diagnosed with myeloproliferative neoplasms and control subjects, in each case, of a nature set forth in the Research Plan, and in quantities determined by the JRC based on the power calculation included in the Original Target Data Package (the "Supplemental Samples"), which Supplemental Samples shall meet the applicable Sample Specifications set forth in the Research Plan. Following receipt by Syros of the requisite Samples, Syros shall (A) (1) perform the activities and analyses assigned to Syros under the Research Plan with respect to the Supplemental Samples in accordance with the terms of the Research Plan and (2) use Commercially Reasonable Efforts (I) to perform such activities and analyses within the timeframes described in the Research Plan, including by allocating an appropriate number of FTEs to the work to be conducted by or on behalf of Syros under the Research Plan at any time during the Research Term and (II) by analyzing the Supplemental Samples using the Syros Platform, identify a list of Targets in accordance with the Research Plan provisions with respect to activities using Supplemental Samples (each of such Targets a "Supplemental Target" and collectively, the "Supplemental Targets"; and such list, the " Supplemental Target List"), and their corresponding ENSEMBL IDs and names.

(b) Gatekeeping. No later than [**] following Syros' completion of the analyses under Section 2.8.3(a), Syros shall submit the Supplemental Target List to the Gatekeeper in writing and shall notify Incyte in writing that such list has been submitted to the Gatekeeper. Within [**] after receipt of the Supplemental Target List, the Gatekeeper shall be required to (i) update the Original Target List to add any Supplemental Targets that are not Syros Excluded Targets and (ii) deliver to both Parties in writing the updated Original Target List. Upon the Gatekeeper updating the Original Target List in accordance with this Section 2.8.3(b), each Supplemental Target that is not a Syros Excluded Target shall be deemed to be an Original Target.

(c) Supplemental Target Data Package. Within [**] after the delivery of the updated Original Target List by the Gatekeeper to both Parties pursuant to Section 2.8.3(b), Syros shall provide to Incyte a data package containing: (i) for each Supplemental Target that has become an Original Target, the applicable data specified in the Research Plan with respect to Original Targets, including all Circuitry Map Data and Super-Enhancer Data with respect thereto; and (ii) for each Syros Excluded Target that (A) is not a Syros Third Party Excluded Target and (B) is included on the Supplemental Target List, the protein class and Super-Enhancer Data for, but not ENSEMBL ID for, name of, or other identifying information for, such Syros Excluded Target (such data package, the "Supplemental Target Data Package").

(d) Conditions. Syros' obligations under Section 2.8.3(a) shall be conditioned upon Incyte's provision of sufficient quality and quantities of Supplemental Samples to Syros, in accordance with the Research Plan and Section 2.12, to enable Syros to perform the activities assigned to it under the Research Plan with respect to the Supplemental Samples.

2.8.4 Selection of Initial Research Targets. Subject to Section 2.8.9, during the period commencing on the date that the first Original Target is disclosed to Incyte and ending on [**] (the "Initial Research Target Selection Period"), Incyte shall have the right to select [**]

Original Targets as Initial Research Targets by providing written notice to Syros and the Gatekeeper in accordance with this Section 2.8.4. For clarity, and without limitation to Section 3.4, Incyte may only select [**] Initial Research Targets, in the aggregate, pursuant to this Section 2.8.4.

(a) Selection of Preliminary Targets. Incyte shall have the right to select any Preliminary Target as an Initial Research Target upon delivery of written notice to Syros and the Gatekeeper designating each Initial Research Target by its ENSEMBL ID and name. Following delivery of such notice, the Gatekeeper shall be required to notify the Parties in writing whether any such Initial Research Target is a Premium Target and, if such Initial Research Target is a Premium Target, then Section 2.8.4(c) shall apply. Each Preliminary Target selected as an Initial Research Target in accordance with this Section 2.8.4(a) shall become an Initial Research Target as of the date of Incyte's notice under this Section 2.8.4(a).

(b) Selection of Original Targets that are not Preliminary Targets. Subject to Section 2.8.9, if Incyte wishes to select any Original Target that is not a Preliminary Target as an Initial Research Target, then Incyte shall propose selection of such Original Target as an Initial Research Target by written notice to (i) the Gatekeeper, designating each Original Target by its ENSEMBL ID and name and (ii) Syros, informing Syros that the notice in clause (i) has been submitted to the Gatekeeper. Within [**] after delivery of Incyte's notice to the Gatekeeper, the Gatekeeper shall be required to notify (A) Incyte in writing if any Original Target selected by Incyte as an Initial Research Target is an Incyte Excluded Target, and the identity of such Incyte Excluded Target; (B) Syros in writing if any Original Target selected by Incyte as an Initial Research Target is an Incyte Excluded Target, but not the identity of such Incyte Excluded Target; and (C) the Parties in writing if any Original Target selected by Incyte as an Initial Research Target is (1) a Syros Excluded Target, (2) a Premium Target, or (3) neither an Incyte Excluded Target nor a Syros Excluded Target. If such Original Target is a Syros Excluded Target or an Incyte Excluded Target, then such Original Target shall not become an Initial Research Target. If such Original Target is not a Syros Excluded Target or an Incyte Excluded Target, then such Original Target shall be deemed to be an Initial Research Target as of the date of the Gatekeeper's notice thereof in accordance with this Section 2.8.4(b). If such Initial Research Target is a Premium Target, then Section 2.8.4(c) shall apply.

(c) Premium Targets. If any Initial Research Target selected by Incyte in accordance with Section 2.8.4(a) or Section 2.8.4(b) is a Premium Target, then, during the period commencing on the date of the Gatekeeper's notice pursuant to Section 2.8.4(a) or Section 2.8.4(b) and ending on the later to occur of (x) the expiration of the Initial Research Target Selection Period and (y) [**] after such notice (the "Premium Target Confirmation Period"), Incyte shall have the right to elect, by written notice to Syros, to either:

(i) confirm such Premium Target as an Initial Research Target and receive access to the Premium Target Data for such Premium Target, in which case Syros shall deliver to Incyte a copy of such Premium Target Data for such Premium Target promptly after delivery of such written notice to Syros; or

(ii) select a different Original Target than such Premium Target as an Initial Research Target, in accordance with this Section 2.8.4, in which case (A) Incyte shall not

have any right to receive access to any Premium Target Data for such Premium Target and (B) such Premium Target shall thereafter be deemed a Syros Excluded Target and not an Initial Research Target. If Incyte does not make an election under this Section 2.8.4(c) within the Premium Target Confirmation Period, then the applicable Initial Research Target selected pursuant to Section 2.8.4(a) or Section 2.8.4(b) shall be deemed a Syros Excluded Target and not an Initial Research Target.

2.8.5 Initial Validation Studies.

(a) Generally. Promptly following selection of the Initial Research Targets, Incyte in its sole discretion shall have the right to provide to Syros any tool compounds designated in the Research Plan to be provided to Syros by Incyte to be used by Syros in accordance with the Research Plan as a component of performing the Initial Validation Studies. During the Research Term, and in accordance with the Research Plan, Syros shall conduct the initial validation studies as set forth in the Research Plan (the "Initial Validation Studies") on the Initial Research Targets and provide to Incyte a data package with respect to such Initial Validation Studies, containing the applicable data specified in the Research Plan (the "Initial Validation Study Data Package"). Notwithstanding the foregoing, the Parties acknowledge and agree that, in some cases, Incyte may be able to more efficiently perform certain Initial Validation Studies. In the event that the Parties agree that Incyte is able to more efficiently perform any Initial Validation Study, then the JRC shall discuss and determine in good faith whether such Initial Validation Study will be performed by Syros or Incyte. For clarity, any results generated by Incyte while performing any Initial Validation Studies shall be subject to the reporting obligations under Section 2.10.

(b) Syros' Obligations to Conduct Initial Validation Studies.

(i) General Limitation on Initial Validation Studies. Except as expressly provided in 2.8.5(b)(iii), Syros shall not have any obligation to conduct Initial Validation Studies on [**] Program Targets.

(ii) Initial Validation Studies on Later-Selected Initial Research Targets. If Incyte (A) selects any Original Target as a Definitive Research Target in accordance with Section 2.8.6(b) or (B) substitutes any Initial Research Target, Definitive Research Target or Extended Research Target with an Original Target in accordance with Section 3.4, then, in each case ((A) and ((B)), solely (1) during the Research Term and (2) subject to Section 2.8.5(b)(iii), to the extent that Initial Validation Studies have not already been conducted on [**] Program Targets, Syros shall, at Incyte's request, perform Initial Validation Studies on such Original Target. By way of example, if Initial Validation Studies have been conducted on [**] Program Targets and Incyte substitutes [**] Initial Research Targets with Original Targets in accordance with Section 3.4, then, at Incyte's request, Syros shall perform Initial Validation Studies on up to [**] of such Original Targets. By way of further example, if Initial Validation Studies have been conducted on [**] Program Targets and Incyte substitutes [**] Initial Research Targets with Original Targets in accordance with Section 3.4, then, at Incyte's request, Syros shall perform Initial Validation Studies on [**] of such Original Targets.

(iii) Additional Initial Validation Studies. Solely during the Research Term, and at Incyte's request, cost and expense, Syros shall conduct Initial Validation Studies on up to [**] additional Program Targets [**] that (A) are selected as Definitive Research Targets in accordance with Section 2.8.6(b) or (B) are substituted for Initial Research Targets, Definitive Research Targets or Extended Research Targets in accordance with Section 3.4; *provided* that Incyte shall be responsible for the costs and expenses with respect to such Initial Validation Studies to the extent that such costs and expenses, when added to all other costs and expenses incurred or anticipated to be incurred by Syros or its Affiliates in connection with the Research Program, in the aggregate, exceed or are reasonably anticipated to exceed the Prepaid Research Amount. Syros shall have the right to be reimbursed therefor and, no later than [**] after the end of each Calendar Quarter, shall issue an invoice for Incyte's portion of any Initial Validation Studies conducted pursuant to this Section 2.8.5(b)(iii). Each of such invoices shall provide reasonable detail to permit Incyte to identify the activities conducted by Syros and the related costs and expenses incurred by Syros. Incyte shall pay Syros any undisputed amounts due under such invoices within [**] after receipt and any remaining amounts due within [**] after resolution of any dispute with respect thereto. For clarity, Syros shall not have any obligation to conduct Initial Validation Studies on more than [**] Program Targets, in the aggregate, pursuant this Section 2.8.5 or any other provision of this Agreement.

2.8.6 Selection of Definitive Research Targets. Subject to Section 2.8.9, during the period commencing on the date that the first Original Target is disclosed to Incyte and ending on the [**] (the "Definitive Research Target Selection Period"), Incyte shall have the right to select up to [**] Original Targets as Definitive Research Targets by providing written notice to Syros and the Gatekeeper in accordance with this Section 2.8.6. For clarity, and without limitation to Section 3.4, Incyte may only select up to [**] Definitive Research Targets, in the aggregate, pursuant to this Section 2.8.6.

(a) Selection of Initial Research Targets. Incyte shall have the right to select any Initial Research Target as a Definitive Research Target upon written notice to Syros designating each Definitive Research Target by its ENSEMBL ID and name and payment to Syros of a Definitive Research Target Payment with respect to such Definitive Research Target in accordance with Section 5.3.1. Each Initial Research Target selected as a Definitive Research Target in accordance with this Section 2.8.6(a) shall become a Definitive Research Target as of the first date on which both (i) Incyte has provided notice under this Section 2.8.6(a) and (ii) Syros has received the applicable Definitive Research Target Payment.

(b) Selection of Original Targets that are not Initial Research Targets. Subject to Section 2.8.9, if Incyte wishes to select any Original Target that is not an Initial Research Target as a Definitive Research Target, then Incyte shall propose selection of such Original Target as a Definitive Research Target by written notice to (i) the Gatekeeper, designating each Original Target by its ENSEMBL ID and name and (ii) Syros, informing Syros that the notice in clause (i) has been submitted to the Gatekeeper. Within [**] after delivery of Incyte's notice to the Gatekeeper, the Gatekeeper shall be required to notify (A) Incyte in writing if any Original Target selected by Incyte as a Definitive Research Target is an Incyte

Excluded Target, and the identity of such Incyte Excluded Target; (B) Syros in writing if any Original Target selected by Incyte as a Definitive Research Target is an Incyte Excluded Target, but not the identity of such Incyte Excluded Target; and (C) the Parties in writing if any Original Target selected by Incyte as a Definitive Research Target is (1) a Syros Excluded Target or (2) neither an Incyte Excluded Target nor a Syros Excluded Target. If such Original Target is a Syros Excluded Target or an Incyte Excluded Target, then such Original Target shall not become a Definitive Research Target. If such Original Target is not a Syros Excluded Target or an Incyte Excluded Target, then such Original Target shall be deemed to be a Definitive Research Target as of the first date on which both (I) the Gatekeeper has provided notice thereof in accordance with this Section 2.8.6(b) and (II) Syros has received the applicable Definitive Research Target Payment.

2.8.7 Definitive Validation Studies. Incyte shall have the right to conduct the definitive validation studies set forth in the Research Plan (the "Definitive Validation Studies") on the Definitive Research Targets, in accordance with the Research Plan (including any timelines set forth therein) and the terms of this Agreement.

2.8.8 Selection of Extended Research Targets. During the period commencing on the date that the first Definitive Research Target is selected by Incyte in accordance with Section 2.8.6 and ending on the [**] (the "Extended Research Target Selection Period"), Incyte shall have the right to select up to [**] Definitive Research Targets as Extended Research Targets by providing written notice to Syros designating each Extended Research Target by its ENSEMBL ID and name. Each Definitive Research Target selected as an Extended Research Target in accordance with this Section 2.8.8 shall become an Extended Research Target as of the date of Incyte's notice under this Section 2.8.8.

2.8.9 Incyte Covenants and Gatekeeper Responsibilities Regarding Incyte Excluded Targets. Incyte covenants to Syros that it shall not designate any Original Target that is also an Incyte Excluded Target as (a) a Preliminary Target pursuant to Section 2.8.2; (b) an Initial Research Target pursuant to Section 2.8.4 or Section 3.4; (c) a Definitive Research Target pursuant to Section 2.8.6 or Section 3.4; (d) an Extended Research Target pursuant to Section 2.8.8 or Section 3.4; or (e) a Validated Target pursuant to Section 3.1. The Parties acknowledge and agree that the agreement with the Gatekeeper will prohibit the Gatekeeper from allowing Incyte to designate any Original Target in violation of Incyte's covenants in this Section 2.8.9.

2.9 Extension of Research Term. The Research Term may be extended only by mutual written agreement of the Parties. The Parties acknowledge and agree that, during any extension of the Research Term: (a) the Research Program shall be limited to research and development activities directed to Program Targets for which Incyte retains an unexercised Option, and not (i) any other Program Targets or (ii) the identification of any Targets that are not Program Targets and (b) all costs and expenses of Syros and its Affiliates, including with respect to FTEs (at the Syros FTE Rate) and out-of-pocket costs and expenses, for conducting its activities during such extension shall be funded by Incyte if in excess of the Prepaid Research Amount, in each case ((a) and (b)), unless otherwise mutually agreed by the Parties. For clarity, the Option exercise periods set forth in Section 3.1.1, Section 3.1.2 and Section 3.1.3 shall not be extended by any extension of the Research Term.

2.10 Reports to the JRC and Syros Alliance Manager. During the Research Term each Party will provide to the

JRC, at least once per Calendar Quarter, a written summary of the research activities conducted and results generated by or on behalf of such Party or its Affiliates under the Research Program; *provided, however,* that Incyte shall not have any obligation to provide to the JRC any [**]. Following the Research Term, Incyte will provide to the Syros Alliance Manager (with copy to the Syros Chief Business Officer), at least once per Calendar Quarter, a written summary of the research activities conducted, and activities planned, by or on behalf of Incyte or its Affiliates with respect to any Program Target(s) for which Incyte retains an unexercised Option; *provided, however,* that (a) Incyte shall not have any obligation to provide any [**] and (b) prior to the first IND filing with respect to any Associated Product with respect to a Program Target that becomes a Validated Target, Incyte shall have the right to redact [**].

2.11 Recordkeeping. During the Research Term and for the longest of (a) three (3) years after the completion of activities under the Research Plan or, if later in the case of Incyte, the completion of activities under the license granted to Incyte in Section 3.3.1(a); (b) the period required by the applicable Party's own record retention policies; and (c) the period required by Applicable Law, each Party shall (and shall cause its respective Affiliates to) (i) maintain records regarding data generated and results obtained under the Research Program and, in the case of Incyte, in the conduct of activities under the license granted in Section 3.3.1(a) ("Research Documentation"); (ii) retain and maintain all such Research Documentation in a secure area reasonably protected from theft and destruction and with no less than that degree of protection as such Party would use with its proprietary valuable materials and data generally; and (iii) ensure that such Research Documentation fully and accurately reflects results obtained in the performance of the Research Program and, in the case of Incyte, the conduct of activities under the license granted in Section 3.3.1(a), in sufficient detail and in good scientific manner.

2.12 Samples.

2.12.1 Delivery of Samples. Incyte shall deliver, or cause another Person to deliver, to Syros any Samples specified in Section 2.8.1(a), Section 2.8.3(a) or the Research Plan, free of charge. Each Party shall comply with all applicable requirements set forth in the Research Plan (or as the Parties may mutually agree in writing from time to time) with respect to the identity, nature, supply, use, handling, and storage of Samples ("Sample Specifications"). If Syros determines that any Samples do not conform to their descriptions or are not suitable for the activities under the Research Plan, then Incyte shall provide new or replacement Samples or, if it is not possible to do so, discuss with Syros in good faith an alternative approach reasonably acceptable to Syros.

2.12.2 Legal Requirements. Incyte shall ensure that all Samples provided to Syros under this Agreement have been collected, stored, handled, transported, and delivered in a manner appropriate to ensure compliance with Applicable Law and applicable ethical standards, including privacy and patient confidentiality laws, in connection with the collection and use of the Samples (collectively, "Legal Requirements"). With respect to any Samples provided to Syros hereunder, Incyte shall follow its documented policies and procedures with respect to the protection of the autonomy and confidentiality of the human subjects from whom the Samples were collected in compliance with the Legal Requirements. If collection of the Samples was subject to informed consent or required authorization, Incyte shall ensure that the scope of such

informed consent or authorization is consistent with the transfer of and Syros' permitted use of the Samples (and any accompanying data) as permitted by this Agreement and the Research Plan without any obligation of compensation to the subjects from whom the Samples were obtained. At Syros' request, with respect to any Sample supplied hereunder, Incyte shall provide Syros with (a) a copy of any necessary institutional review board or other ethics committee approvals and form of informed consent with respect to such Sample; (b) a certification that all necessary approvals and informed consents have been obtained with respect to such Sample; and (c) copies such approvals or informed consents; in each case ((a) - (c)), redacted for confidential information. All Samples delivered under this Agreement shall be labelled clearly as required by any Legal Requirements.

2.12.3 Identifiable Healthcare Information. Incyte shall not, without first obtaining Syros' prior written consent, deliver to Syros, or its Affiliates, any personally identifiable healthcare information or data relating to patients or subjects, in connection with the Samples or otherwise.

2.13 Compliance with Applicable Law. Each Party shall perform its obligations with respect to the Research Program in good scientific manner, and in compliance with Applicable Law.

2.14 Firewalls.

2.14.1 Incyte Firewall. No later than the date on which Syros is obligated to deliver to Incyte the Original Target Data Package, and with respect to each Program Target, Incyte shall adopt reasonable procedures to prevent use of Program Know-How for any use other than (a) exercising the rights granted under Section 3.3.1(a) or Section 3.3.1(b); or (b) exercising the rights granted, and performing obligations required, under and in accordance with Article 6, including preventing use of Program Know-How in connection with the Development or Commercialization by Incyte or its Affiliates, alone or with a Third Party, of any compound or product (other than an Associated Compound or Associated Product Exploited in connection with this Agreement) directed to any Program Target (any such activities not conducted in connection with this Agreement, an "Incyte Independent Program"). At Syros' request, Incyte shall provide Syros with a summary of such procedures. Further, Incyte agrees that as a part of such procedures, it shall take reasonable steps to preclude employees [**] ("Incyte Restricted Personnel") from [**]. Notwithstanding the foregoing, Incyte Restricted Personnel shall not include any of the following: [**].

2.14.2 Syros Firewall. No later than the date on which Syros is obligated to deliver to Incyte the Original Target Data Package, and with respect to each Program Target, Syros shall adopt reasonable procedures to prevent use of Program Know-How for any use other than the performance of the Research Plan or the exercise of rights or performance of obligations under and in accordance with Article 6, including preventing use of Program Know-How in connection with a Syros Independent Program; *provided* that Syros shall have the right to use Program Know-How to maintain gatekeeping procedures. For purposes of this Agreement, "Syros Independent Program" means any Internal Syros Program or program conducted in connection with any Third Party Collaboration Agreement. At Incyte's request, Syros shall provide Incyte with a summary of such procedures. Further, Syros agrees that as a part of such procedures, it shall take reasonable steps to preclude employees [**] ("Syros Restricted Personnel") from working on any of the following activities with respect to a Syros Independent Program directed to such a Program Target:

[**]. Notwithstanding the foregoing, Syros Restricted Personnel shall not include any of the following: [**].

ARTICLE 3 - GRANTS OF RIGHTS AND RESTRICTIVE COVENANTS

3.1 Options to Select Validated Targets.

3.1.1 Options to Select Initial Research Targets as Validated Targets.

(a) All Uses Field. Subject to Section 3.1.4 and Section 3.2.1, Syros hereby grants to Incyte, for the period commencing on the date that a Program Target becomes an Initial Research Target in accordance with Section 2.8.4 or Section 3.4 and ending [**], an option in the All Uses Field to select any Initial Research Target as a Validated Target and obtain the rights set forth in Section 3.3.1(b)(i) with respect to such Validated Target, by (i) providing written notice to Syros designating the applicable Validated Target by its ENSEMBL ID and name, and (ii) paying to Syros a Definitive Research Target Payment in accordance with Section 5.3.1 and a Validated Target Payment in accordance with Section 5.3.2, which option is exclusive with respect to the right to obtain the applicable exclusive license under Program IP pursuant Section 3.3.1(b)(i)(A).

(b) MPN Field. Subject to Section 3.1.4 and Section 3.2.1, Syros hereby grants to Incyte, for the period commencing on the date that a Program Target becomes an Initial Research Target in accordance with Section 2.8.4 or Section 3.4 and ending [**], an option solely in the MPN Field to select any Initial Research Target as a Validated Target and obtain the rights set forth in Section 3.3.1(b)(ii) with respect to such Validated Target, by (i) providing written notice to Syros designating the applicable Validated Target by its ENSEMBL ID and name, and (ii) paying to Syros a Definitive Research Target Payment in accordance with Section 5.3.1 and a Validated Target Payment in accordance with Section 5.3.2, which option is exclusive with respect to the right to obtain the applicable exclusive license under Program IP pursuant 3.3.1(b)(ii)(A).

3.1.2 Options to Select Definitive Research Targets as Validated Targets.

(a) All Uses Field. Subject to Section 3.1.4 and Section 3.2.1, Syros hereby grants to Incyte, for the period commencing on the date that a Program Target becomes a Definitive Research Target in accordance with Section 2.8.6 or Section 3.4 and ending [**], an option in the All Uses Field to select any Definitive Research Target as a Validated Target and obtain the rights set forth in Section 3.3.1(b)(i) with respect to such Validated Target, by (i) providing written notice to Syros designating the applicable Validated Target by its ENSEMBL ID and name, and (ii) paying to Syros a Validated Target Payment in accordance with Section 5.3.2, which option is exclusive with respect to the right to obtain the applicable exclusive license under Program IP pursuant Section 3.3.1(b)(i)(A).

(b) MPN Field. Subject to Section 3.1.4 and Section 3.2.1, Syros hereby grants to Incyte, for the period commencing on the date that a Program Target becomes a Definitive Research Target in accordance with Section 2.8.6 or Section 3.4 and ending [**], an option solely in the MPN Field to select any Definitive Research Target as a Validated Target and obtain the rights

set forth in Section 3.3.1(b)(ii) with respect to such Validated Target, by (i) providing written notice to Syros designating the applicable Validated Target by its ENSEMBL ID and name, and (ii) paying to Syros a Validated Target Payment in accordance with Section 5.3.2, which option is exclusive with respect to the right to obtain the applicable exclusive license under Program IP pursuant Section 3.3.1(b)(ii)(A).

3.1.3 Options to Select Extended Research Targets as Validated Targets .

(a) All Uses Field. Subject to Section 3.1.4 and Section 3.2.1, Syros hereby grants to Incyte, for the period commencing on the date that a Program Target becomes an Extended Research Target in accordance with Section 2.8.8 or Section 3.4 and ending [**], an option in the All Uses Field to select any Extended Research Target as a Validated Target and obtain the rights set forth in Section 3.3.1(b)(i) with respect to such Validated Target, by (i) providing written notice to Syros designating the applicable Validated Target by its ENSEMBL ID and name, and (ii) paying to Syros a Validated Target Payment in accordance with Section 5.3.2, which option is exclusive with respect to the right to obtain the applicable exclusive license under Program IP pursuant Section 3.3.1(b)(i)(A).

(b) MPN Field. Subject to Section 3.1.4 and Section 3.2.1, Syros hereby grants to Incyte, for the period commencing on the date that a Program Target becomes an Extended Research Target in accordance with Section 2.8.8 or Section 3.4 and ending [**], an option solely in the MPN Field to select any Extended Research Target as a Validated Target and obtain the rights set forth in Section 3.3.1(b)(ii) with respect to such Validated Target, by (i) providing written notice to Syros designating the applicable Validated Target by its ENSEMBL ID and name, and (ii) paying to Syros a Validated Target Payment in accordance with Section 5.3.2, which option is exclusive with respect to the right to obtain the applicable exclusive license under Program IP pursuant Section 3.3.1(b)(ii)(A). For clarity, the rights set forth in this Section 3.1.3(b) are a subset of the rights granted under Section 3.1.2(b), given that each Extended Research Target is also a Definitive Research Target.

3.1.4 Antitrust Filings.

(a) If Incyte desires to exercise any Option, Incyte shall reasonably determine in good faith prior to exercise of any such Option whether the transactions to be consummated upon the exercise of such Option require any Antitrust Filings. If Incyte determines in good faith that any Antitrust Filing(s) is required in connection with Incyte's exercise of any Option and Incyte desires to exercise such Option, then Incyte shall deliver to Syros a notice of intent to exercise such Option within the period set forth in Section 3.1, 3.1.2 or 3.1.3 for such Option exercise, as applicable, which notice shall identify any required Antitrust Filings and include Incyte's irrevocable binding commitment to complete the exercise of such Option, subject only to satisfaction of the Antitrust Conditions and the terms of this Section 3.1.4 (any such notice, a "Notice of Conditional Exercise"), whereupon the relevant Option exercise period shall be tolled with respect to the applicable Initial Research Target, Definitive Research Target or Extended Research Target for so long as is necessary for Incyte to satisfy applicable Antitrust Conditions, but subject to Incyte's compliance with the requirements of Section 3.1.4(b) and Section 3.1.4(d). For clarity, the Initial Research Target, Definitive Research Target or Extended Research Target will not

become a Validated Target and Incyte shall not obtain the rights set forth in Section 3.3.1(b) with respect to such Initial Research Target, Definitive Research Target or Extended Research Target unless and until the Parties have obtained satisfaction of any applicable Antitrust Condition for the applicable Antitrust Filing filed pursuant to this Section 3.1.4 and complied with the requirements of this Section 3.1.4.

(b) If Incyte delivers a Notice of Conditional Exercise with respect to any Initial Research Target, Definitive Research Target or Extended Research Target in accordance with this Section 3.1.4, each of Incyte and Syros shall cooperate to prepare and make any necessary Antitrust Filings as promptly as is practicable and advisable, with the goal of filing Antitrust Filings within [**] after the date upon which Incyte delivers the applicable notice, as applicable (or such later time as may be agreed to in writing by the Parties). Incyte will be responsible for both Parties' reasonable costs and expenses (including attorneys' fees and filing fees) associated with any Antitrust Filing. Neither Party, or any of its respective Affiliates, will be required to: (i) sell, divest (including through a license), hold separate, transfer or dispose of any assets, operations, rights, product lines, businesses or interests therein (or consent to any of the foregoing actions), or (ii) litigate or otherwise formally oppose any determination (whether judicial or administrative in nature) by a Governmental Authority seeking to impose any of the restrictions referenced in clause (i) above.

(c) Subject to Section 3.1.4(b), within [**] after the Parties obtaining satisfaction of any applicable Antitrust Condition for any applicable Antitrust Filing with respect to any Initial Research Target, Definitive Research Target or Extended Research Target, Incyte shall deliver to Syros a notice designating the applicable Validated Target by its ENSEMBL ID and name, and Syros shall invoice Incyte within [**] thereafter and Incyte shall make the payment(s) required pursuant to Section 3.1.1, 3.1.2 or 3.1.3, as applicable, resulting in such Initial Research Target, Definitive Research Target or Extended Research Target becoming a Validated Target.

(d) Notwithstanding the foregoing, unless otherwise agreed by the Parties in writing, if satisfaction of any applicable Antitrust Condition has not occurred within [**] after such time as both Parties have made the necessary Antitrust Filings, then, unless mutually agreed to by the Parties in writing, such proposed Initial Research Target, Definitive Research Target or Extended Research Target shall no longer be eligible for Option exercise by Incyte and all Option exercise periods as provided in Section 3.1, 3.1.2 or 3.1.3, as applicable, shall automatically be deemed to expire with respect to such Initial Research Target, Definitive Research Target or Extended Research Target.

3.1.5 Amendment of Schedule. On or after the date on which any Initial Research Target, Definitive Research Target or Extended Research Target becomes a Validated Target pursuant to this Section 3.1, the Parties shall amend Schedule 3.1.5 to add such Validated Target to such Schedule.

3.2 Limitations on Numbers of Program Targets.

3.2.1 Validated Targets. Incyte shall have the right to select up to [**] Initial Validated Targets and up to [**] Supplemental Validated Targets, for a total of up to seven (7) Validated Targets, in the aggregate, in accordance with Section 3.1. Upon selection of seven (7) Validated Targets, in the aggregate, in accordance with Section 3.1, the Option rights granted to Incyte in Section 3.1 shall be deemed to have been exhausted and no further Option rights shall remain in effect (for clarity, regardless of the periods for which Option rights were granted).

3.2.2 Other Program Targets. At no point in time shall [**] in the aggregate and with respect to any and all Program Target selection or substitution rights under this Agreement. For clarity, this Section 3.2.2 is not intended, and shall not be construed, to establish or suggest that any minimum number of Program Targets (i) can or will be identified by Syros or (ii) will be selected by Incyte, in each case ((i) and (ii)), in relation to each of the foregoing categories.

3.2.3 Target Progression. For clarity, and notwithstanding anything to the contrary in this Agreement: (a) each Validated Target shall also be deemed to be an Extended Research Target, a Definitive Research Target, an Initial Research Target, a Preliminary Target and an Original Target; (b) each Extended Research Target shall also be deemed to be a Definitive Research Target, an Initial Research Target, a Preliminary Target and an Original Target; (c) each Definitive Research Target shall also be deemed to be an Initial Research Target, a Preliminary Target and an Original Target; (d) each Initial Research Target shall also be deemed to be a Preliminary Target and an Original Target; and (e) each Preliminary Target shall also be deemed to be an Original Target. Any Initial Research Target, Definitive Research Target or Extended Research Target that is substituted with an Original Target in accordance with Section 3.4 shall no longer be considered an Initial Research Target, Definitive Research Target or Extended Research Target, as applicable, and shall instead be considered an Unreserved Target.

3.3 License Grants.

3.3.1 Grants to Incyte.

(a) Research License. Subject to the terms and conditions of this Agreement, Syros hereby grants to Incyte a non-exclusive, worldwide, royalty-free license under (i) Syros' interest in the Program IP (including Syros' rights under the Super-Enhancer Data and Circuitry Map Data) and (ii) the Syros Existing Background Target IP, in each case ((i) and (ii)), as necessary and solely for (A) conducting Incyte's research and validation activities during the Research Term and in accordance with the Research Plan, and (B) evaluating Program Targets to select such Program Targets as Validated Targets (including by performing internal research studies on such Program Targets) during the period that Incyte retains an unexercised Option. The license granted under this Section 3.3.1(a) shall terminate automatically upon the later of (1) expiration or termination of the Research Term or (2) expiration or termination of all Options.

(b) Validated Target Licenses.

(i) All Uses Field License(s).

(A) Exclusive All Uses Field License(s) Under Program IP. Subject to the terms and conditions of this Agreement, including Section 3.3.4, upon a Program Target becoming a Validated Target in accordance with Section 3.1.1(a), Section 3.1.2(a) or Section 3.1.3(a), as applicable, Syros shall, and does hereby, grant to Incyte, during the remainder of the Term, a worldwide, royalty-bearing exclusive (including as to Syros and its Affiliates) license in the All Uses Field, with the right to grant sublicenses solely in accordance with Section 3.3.3, under Syros' interest in the Program IP as necessary and for the sole purpose of Exploiting Associated Compounds and Associated Products with respect to such Validated Target in the All Uses Field, including (1) conducting a drug discovery program to identify Associated Compounds whose primary activity is Modulation of such Validated Target, (2) Developing such Associated Compounds and Associated Products containing such Associated Compounds, and (3) Commercializing such Associated Compounds and Associated Products, in each case ((1)-(3)), in the All Uses Field.

(B) Non-Exclusive All Uses Field License(s) Under Syros Existing Background Target IP. Subject to the terms and conditions of this Agreement, including Section 3.3.4, upon a Program Target becoming a Validated Target in accordance with Section 3.1.1(a), Section 3.1.2(a) or Section 3.1.3(a), as applicable, Syros shall, and does hereby, grant to Incyte, during the remainder of the Term, a worldwide, royalty-bearing non-exclusive license in the All Uses Field, with the right to grant sublicenses solely in accordance with Section 3.3.3, under Syros Existing Background Target IP as necessary and for the sole purpose of Exploiting in the All Uses Field Associated Compounds and Associated Products with respect to such Validated Target owned or controlled by Incyte or any of its Affiliates, including (1) conducting a drug discovery program to identify Associated Compounds owned or controlled by Incyte or any of its Affiliates whose primary activity is Modulation of such Validated Target, (2) Developing such Associated Compounds and Associated Products owned or controlled by Incyte or any of its Affiliates containing such Associated Compounds, and (3) Commercializing such Associated Compounds and Associated Products, in each case ((1)-(3)), in the All Uses Field.

(ii) MPN Field License(s).

(A) Exclusive MPN Field License(s) Under Program IP. Subject to the terms and conditions of this Agreement, including Section 3.3.4, upon a Program Target becoming a Validated Target in accordance with Section 3.1.1(b), Section 3.1.2(b) or Section 3.1.3(b), as applicable, Syros shall, and does hereby, grant to Incyte, during the remainder of the Term, a worldwide, royalty-bearing exclusive (including as to Syros and its Affiliates) license solely in the MPN Field, with the right to grant sublicenses solely in accordance with Section 3.3.3, under Syros' interest in the Program IP as necessary and for the sole purpose of Exploiting Associated Compounds and Associated Products with respect to such Validated Target in the MPN Field, including (1) conducting a drug discovery program to identify Associated Compounds whose primary activity is Modulation of such Validated Target, (2) Developing such Associated Compounds and Associated Products containing such Associated Compounds, and (3) Commercializing such Associated Compounds and Associated Products, in each case ((1)-(3)), in the MPN Field.

(B) Non-Exclusive MPN Field License(s) Under Syros Existing Background Target IP. Subject to the terms and conditions of this Agreement, including Section 3.3.4, upon a Program Target becoming a Validated Target in accordance with Section 3.1.1(b), Section 3.1.2(b) or Section 3.1.3(b), as applicable, Syros shall, and does hereby, grant to Incyte, during the remainder of the Term, a worldwide, royalty-bearing non-exclusive license solely in the MPN Field, with the right to grant sublicenses solely in accordance with Section 3.3.3, under Syros Existing Background Target IP as necessary and for the sole purpose of Exploiting in the MPN Field Associated Compounds and Associated Products with respect to such Validated Target owned or controlled by Incyte or any of its Affiliates, including (1) conducting a drug discovery program to identify Associated Compounds owned or controlled by Incyte or any of its Affiliates whose primary activity is Modulation of such Validated Target, (2) Developing such Associated Compounds and Associated Products owned or controlled by Incyte or any of its Affiliates containing such Associated Compounds, and (3) Commercializing such Associated Compounds and Associated Products, in each case ((1)-(3)), in the MPN Field.

3.3.2 Grant to Syros. Subject to the terms and conditions of this Agreement, Incyte hereby grants to Syros and its Affiliates a non-exclusive, worldwide license under any Know-How, Patents or other intellectual property rights Controlled by Incyte as of the Effective Date or during the Research Program, in each case, as necessary and for the sole purpose of conducting the

Research Program. The license granted under this Section 3.3.2 shall terminate automatically upon the completion or termination of the Research Program.

3.3.3 Sublicensing.

(a) The research licenses granted in Section 3.3.1(a) and Section 3.3.2 shall not include the right to grant sublicenses; *provided* that either Party shall be free to utilize Affiliates or retain Third Party (sub)contractors and service providers as may be necessary or useful to have conducted the activities assigned to it under the Research Plan.

(b) Upon a Program Target becoming a Validated Target, Incyte may grant sublicenses to Affiliates and Third Parties under the applicable license granted with respect to such Validated Target pursuant to Section 3.3.1(b); *provided* that (i) any such sublicense shall be granted only pursuant to a written sublicense agreement; (ii) Incyte shall remain obligated to pay all amounts due to Syros under this Agreement in accordance with the terms hereof; (iii) the terms of any such sublicense agreement shall be subject to the terms and conditions of this Agreement and Incyte shall cause each Sublicensee to perform, and comply with, the terms and conditions of this Agreement to the same extent as such terms and conditions apply to Incyte (to the extent pertaining or relevant to the Sublicensee and, in each case, regardless of whether a particular term or condition of this Agreement makes express reference to Sublicensees); and (iv) Incyte shall be responsible for the performance by, and compliance of, any Sublicensee with the applicable terms and conditions of this Agreement. Within [**] after the execution of any sublicense agreement with respect to any rights granted in Section 3.3.1(b), Incyte shall notify Syros of the identity of the applicable Sublicensee and provide Syros with a copy of such sublicense agreement; *provided* that Incyte may redact from such copy any economic terms and other terms that are not relevant to the terms of this Agreement, so long as the terms that are relevant to the terms of this Agreement remain comprehensible.

3.3.4 Retained Rights. Neither Party grants to the other Party any intellectual property licenses or other rights, express or implied, by estoppel or otherwise, other than those licenses or rights expressly set forth in this Agreement. Without limitation to the foregoing, any rights granted by Syros to Incyte pursuant to Section 3.3.1 expressly exclude any rights to or under: (a) any Syros Platform Improvements; (b) any Know-How, Patents or other intellectual property rights Covering or otherwise relating to (i) the Syros Platform, (ii) any Syros Therapeutic or (iii) any Syros Excluded Target; (c) any (i) Drug Discovery and Development Know-How Controlled by Syros or any of its Affiliates or (ii) Patent Covering such Drug Discovery and Development Know-How; and (d) without limitation to clauses (a) - (c), any rights granted to Syros or any of its Affiliates by [**] under that certain License Agreement dated as of [**] between Syros and [**], including rights granted with respect to any PATENT RIGHTS (as defined in the [**]) or [**] (as defined in the [**]); which rights shall, in each case ((a) - (d)) and subject to Section 3.5, be retained by Syros in their entirety for any and all uses, worldwide.

3.4 Substitution of Program Targets.

3.4.1 Substitution Rights. Syros hereby grants to Incyte:

(a) subject to Section 2.8.9, for the period commencing on the date that [**] Program Targets have become Initial Research Targets and ending [**], an option to substitute any Initial Research Target that is not also a Validated Target with any Original Target in accordance with Section 3.4.2;

(b) subject to Section 2.8.9, for the period commencing on the date that [**] Program Targets have become Definitive Research Targets and ending [**], an option to substitute any Definitive Research Target that is not also a Validated Target with any Original Target in accordance with Section 3.4.2; and

(c) subject to Section 2.8.9, for the period commencing on the date that [**] Program Targets have become Extended Research Targets and ending [**], an option to substitute any Extended Research Target that is not also a Validated Target with any Original Target in accordance with Section 3.4.2.

3.4.2 Substitution Requirements.

(a) Limitations.

(i) Number of Substitutions. Incyte shall only have the right to substitute [**] Initial Research Targets, Definitive Research Targets and Extended Research Targets, in the aggregate, pursuant to this Section 3.4.

(ii) No Substitution of Validated Targets. For clarity, Incyte shall not have any right to substitute any Initial Research Target, Definitive Research Target or Extended Research Target that has become a Validated Target.

(b) Notices. If Incyte wishes to substitute any Initial Research Target, Definitive Research Target or Extended Research Target with an Original Target, then Incyte shall propose such substitution by written notice to (i) the Gatekeeper, designating each of the applicable Program Targets by their ENSEMBL ID and name and (ii) Syros, informing Syros that the notice in clause (i) has been submitted to the Gatekeeper. If Incyte submits such notice to Syros [**], then Incyte shall include in such notice to Syros (A) the ENSEMBL ID and name of the applicable Original Target and (B) a biological rationale sufficient to demonstrate that such Original Target is directly relevant to an Indication in the MPN Field (the "Nexus"), which Nexus must be demonstrated by [**].

(c) Gatekeeping. If applicable, Syros shall notify the Gatekeeper in writing whether it accepts the Nexus (such acceptance not to be unreasonably withheld). Within [**] after the later of (i) delivery of Incyte's written notice to the Gatekeeper under Section 3.4.2(b) and (ii) Syros' written acceptance to the Gatekeeper under the preceding sentence, if applicable, the Gatekeeper shall be required to notify (A) Incyte in writing if any Original Target selected by Incyte for substitution is an Incyte Excluded Target, and the identity of such Incyte Excluded Target; (2) Syros in writing if any Original Target selected by Incyte for substitution is an Incyte Excluded Target, but not the identity of such Incyte Excluded Target; and (3) the Parties in writing if any Original Target selected by Incyte for substitution is (I) a Syros Excluded Target or (II) neither an

Incyte Excluded Target nor a Syros Excluded Target. If such Original Target is a Syros Excluded Target or Incyte Excluded Target, then such Original Target shall not be substituted for the applicable Initial Research Target, Definitive Research Target or Extended Research Target. If such Original Target is not a Syros Excluded Target or Incyte Excluded Target, then (x) such Original Target shall be deemed to be substituted for the applicable Initial Research Target, Definitive Research Target or Extended Research Target and (y) the Initial Research Target, Definitive Research Target or Extended Research Target for which such Original Target is substituted shall no longer constitute an Initial Research Target, Definitive Research Target or Extended Research Target, as applicable, and shall become an Unreserved Target, in each case ((x) and (y)), as of the date of the Gatekeeper's written notice.

3.5 Syros Restrictive Covenants. Except pursuant to this Agreement, Syros covenants to Incyte that, during the MPN Exclusivity Period, it shall not, and shall cause its Affiliates not to, [**]. Subject to the foregoing sentence, Syros reserves the right, during and after the MPN Exclusivity Period, on behalf of itself and its Affiliates, to Exploit the Syros Platform and any Syros Platform Improvements for any and all purposes, including on behalf of any Third Party. Notwithstanding the foregoing, in the event of a Change of Control of Syros, from and after the date of such Change of Control, the foregoing covenant shall no longer have any force or effect and in lieu thereof Syros covenants to Incyte, that during the MPN Exclusivity Period, it shall not, and shall cause its Affiliates not to, use the Syros Platform with the specific intent of [**].

3.6 Incyte Restrictive Covenants. Without limiting Section 2.14.1, Incyte covenants to Syros that it shall not, and shall not permit any of its Affiliates to (a) file an IND for any Associated Compound or Associated Product with respect to any Program Target or (b) use any Drug Discovery and Development Know-How conceived, discovered, generated or otherwise made in connection with this Agreement to [**], unless and until such Program Target has been selected by Incyte as a Validated Target in accordance with Section 3.1.

3.7 Successors in Interest. Incyte covenants to Syros that Incyte shall not, and shall cause its Affiliates not to (and Incyte and its Affiliates shall cause their successors not to), sell, assign, or otherwise transfer to any Third Party any ownership, license or other rights in or to any Associated Compound or Associated Product with respect to any Validated Target, or any patent or other intellectual property right owned or Controlled by Incyte or any of its Affiliates (or its or their successors, as applicable) necessary for the Exploitation of such Associated Compound or Associated Product, without Syros' prior written consent, unless, as a condition to the consummation of such sale, assignment or transfer, such Third Party expressly undertakes in writing to comply with all applicable obligations of Incyte under this Agreement with respect to such Associated Compound and Associated Product, including the payment obligations set forth in Article 5. Any purported sale, assignment or transfer of such rights shall be void if such Third Party does not expressly undertake such obligations.

ARTICLE 4 - DEVELOPMENT AND COMMERCIALIZATION

4.1 Diligence. Following the selection of each Validated Target in accordance with Section 3.1, as between the Parties, Incyte shall have the sole right to conduct discovery and Development of Associated Compounds Controlled by Incyte or any of its Affiliates or (sub)licensees that Modulate such Validated Target, and the Development and Commercialization of Associated Products containing such Associated Compound(s), in the Associated Licensed Field for such Validated Target, at Incyte's sole cost and expense. Incyte shall use Commercially Reasonable Efforts to (a) Develop, including to obtain and maintain Regulatory Approvals in the Associated Licensed Field for, at least one (1) Associated Product with respect to each Validated Target and (b) if any Associated Product receives Regulatory Approval, Commercialize such Associated Product in such Associated Licensed Field.

4.2 Progress Reports; Other Notification. Without limiting any reporting obligations under Article 5, Incyte shall provide to Syros periodic written reports detailing the status of Development and Commercialization activities with respect to all Validated Targets and their Associated Products, including the status of in-progress and completed: (a) drug discovery activities with respect to all Validated Targets; and (b) clinical trials and Regulatory Approvals with respect to such Associated Products ("Progress Reports"); *provided* that until the first IND filing with respect to any Associated Product with respect to a Validated Target, Incyte shall have the right to redact [**]. The first Progress Report shall be due no later than the first day of the first Calendar Year following the date that Incyte selects the first Validated Target, and subsequent Progress Reports shall be provided to Syros by the first day of each subsequent Calendar Year. In addition to the Progress Reports, Incyte shall promptly notify Syros in writing upon if a decision has been made to suspend or permanently discontinue research, Development or Commercialization of any Associated Product with respect to a Validated Target.

ARTICLE 5 - PAYMENTS

5.1 Initial Payment. In partial consideration for the rights granted hereunder, within [**] after the Effective Date and receipt of an invoice from Syros, Incyte shall pay to Syros an initial amount equal to Ten Million Dollars ($10,000,000), which amount shall be non-refundable (except as otherwise provided in Section 10.5.3(b)) and non-creditable against any other amounts owed Syros under this Agreement. The Parties acknowledge and agree that (a) Seven Million Five-Hundred Thousand Dollars of such initial amount ($7,500,000) shall constitute a prepaid reimbursement of research and development costs anticipated to be incurred by Syros during the Research Term (the "Prepaid Research Amount") and (b) Two Million Five-Hundred Thousand Dollars of such initial amount ($2,500,000) shall constitute an upfront payment.

5.2 Purchase of Equity. Incyte will purchase such number of shares of Syros' common stock, $0.001 par value per share, as set forth in, and subject to the terms and conditions of, that certain Stock Purchase Agreement.

5.3 Target Selection Payments.

5.3.1 Definitive Research Target Payments. Incyte shall pay to Syros a target selection payment of [**] Dollars ($[**]) (the "Definitive Research Target Payment") for each Definitive Research Target designated by Incyte under this Agreement (including each Original Target that becomes a Definitive Research Target through substitution pursuant to Section 3.4). Each Definitive Research Target Payment shall be due within [**] after Incyte's receipt of an invoice from Syros subsequent to (a) Incyte notifying Syros that Incyte is selecting the applicable Initial Research Target as a Definitive Research Target, for any Definitive Research Target selected pursuant to Section 2.8.6(a); (b) the date of the Gatekeeper's written notice informing the Parties that the applicable Original Target is not a Syros Excluded Target or Incyte Excluded Target, for any Definitive Research Target selected pursuant to Section 2.8.6(b); and (c) the date any Original Target is deemed to be substituted as a Definitive Research Target for any Definitive Research Target selected through substitution pursuant to Section 3.4.

5.3.2 Validated Target Payments. Incyte shall pay to Syros one of the following target selection payments (each, a "Validated Target Payment") for each Initial Research Target, Definitive Research Target or Extended Research Target selected by Incyte as a Validated Target, with the amount of each Validated Target Payment in accordance with the table listed below and determined based on (a) the period during which the Initial Research Target, Definitive Research Target or Extended Research Target becomes a Validated Target in accordance with Section 3.1; (b) whether such notice relates to an Initial Validated Target or a Supplemental Validated Target; and (c) whether such Validated Target is a Premium Target. Each Validated Target Payment shall be due within [**] after Incyte's receipt of an invoice from Syros subsequent to Incyte notifying Syros that Incyte is selecting the applicable Program Target as a Validated Target pursuant to Section 3.1.1, 3.1.2 or 3.1.3, as applicable.

Milestone Number	**Period**	**For Each Initial Validated Target**		**For Each Supplemental Validated Target**	
		Not a Premium Target	**Premium Target**	**Not a Premium Target**	**Premium Target**
(1)	[**]	[**]	[**]	[**]	[**]
(2)	[**]	[**]	[**]	[**]	[**]
(3)	[**]	[**]	[**]	[**]	[**]
(4)	[**]	[**]	[**]	[**]	[**]
(5)	[**]	[**]	[**]	[**]	[**]
(6)	[**]	[**]	[**]	[**]	[**]

By way of example, [**].

5.4 Development Milestone Payments. On a Validated Target-by-Validated Target and Indication-by-Indication basis, upon first achievement of each of the following development milestone events (each, a "Development Milestone Event") with respect to such Validated Target and applicable Indication by Incyte, any of its Affiliates, or its or their (sub)licensees, Incyte shall provide written notice of such achievement to Syros, which notice shall be provided no later than [**] after the achievement of the applicable Development Milestone Event. Syros shall invoice Incyte following the achievement of each applicable Development Milestone Event and Incyte shall pay to Syros the corresponding milestone payment within [**] after receipt of such invoice from Syros (each, a "Development Milestone Payment"), which shall be non-refundable, non-creditable and fully earned upon the achievement of the applicable Development Milestone Event:

Milestone Number	Development Milestone Event	Development Milestone Payment with respect to the first Indication with respect to each Validated Target	Development Milestone Payment with respect to the second Indication with respect to each Validated Target	Development Milestone Payment with respect to the third Indication with respect to each Validated Target
(1)	[**]	[**]	[**]	[**]
(2)	[**]	[**]	[**]	[**]
(3)	[**]	[**]	[**]	[**]
(4)	[**]	[**]	[**]	[**]
(5)	[**]	[**]	[**]	[**]
(6)	[**]	[**]	[**]	[**]

For purposes of determining whether the first Indication is distinct from the second Indication and whether the third Indication is distinct from the first Indication and second indication for purposes of payment of milestone payments under this Section 5.4, the following shall apply:

With respect to cancer, Indications of the same cancer type shall be deemed the same Indication unless they [**].

With respect to all Indications other than those in cancer, a first Indication shall not be distinct from a second Indication if [**].

For the avoidance of doubt, (a) each of the Development Milestone Payments shall be payable only once for each of the first, second and third Indications with respect to a given Validated Target based, in each case, on an Associated Product with respect to the applicable Validated Target achieving such Development Milestone with respect to the applicable Indication; (b) the Development Milestone Payments for the first, second and third Indications for any Associated Product(s) with respect to the applicable Validated Target may be triggered by the achievement of a Development Milestone Event with respect to the same or different Associated Product(s) with respect to such Validated Target; and (c) the maximum amount payable to Syros under this Section 5.4 with respect to each Validated Target shall be Fifty Million Dollars ($50,000,000). In the event that Development Milestone Event number (4), (5) or (6) is achieved with respect to any Indication prior to Development Milestone Event number (2) having been achieved or paid with respect to such Indication, without limitation to or modification of Incyte's obligations hereunder, Incyte shall pay to Syros the corresponding milestone payment due with respect to Development Milestone Event number (2) no later than the date on which the Development Milestone Payment for Development Milestone Events (4), (5) or (6), as applicable, is due.

5.5 Sales Milestone Payments. On a Validated Target-by-Validated Target basis, in the event of the achievement of each of the following sales milestone events based on annual aggregate Net Sales of any and all Royalty Products with respect to a given Validated Target (each, a "Sales Milestone Event"), Incyte shall pay to Syros the corresponding milestone payment (each, a " Sales Milestone Payment"), which in each case shall be non-refundable, non-creditable and fully earned upon the achievement of the applicable Sales Milestone Event:

Milestone Number	Sales Milestone Event	Sales Milestone Payment
(1)	Annual aggregate Net Sales of any and all Royalty Products with respect to a given Validated Target, worldwide, exceed [**] Dollars ($[**])	[**]
(2)	Annual aggregate Net Sales of any and all Royalty Products with respect to a given Validated Target, worldwide, exceed [**] Dollars ($[**])	[**]
(3)	Annual aggregate Net Sales of any and all Royalty Products with respect to a given Validated Target, worldwide, exceed [**]Dollars ($[**])	[**]
(4)	Annual aggregate Net Sales of any and all Royalty Products with respect to a given Validated Target, worldwide, exceed [**] Dollars ($[**])	[**]

For the avoidance of doubt, (a) each of the Sales Milestone Payments shall be payable only once with respect to each Validated Target and the maximum amount payable to Syros under this Section 5.5 with respect to each Validated Target shall be Sixty-Five Million Dollars ($65,000,000), (b) in the event that in a given Calendar Year more than one Sales Milestone Event is achieved, a separate Sales Milestone Payment shall become due with respect to each Sales Milestone Event that is achieved in such Calendar Year, and (c) Sales Milestone Events with respect to a given Validated Target may be achieved in separate Calendar Years (for example, in the event that for Calendar Year 2020, annual aggregate Net Sales of any and all Royalty Products with respect to a given Validated Target, worldwide, are $[**] and in Calendar Year 2021 annual aggregate Net Sales of any and all Royalty Products with respect to such Validated Target, worldwide, are $[**], Sales Milestone Event number (1) would be achieved with respect to such Validated Target in Calendar Year 2020 and Sales Milestone Event number (2) would be achieved with respect to such Validated Target in Calendar Year 2021).

5.6 Royalties.

5.6.1 Royalties; Royalty Rates. Subject to Section 5.6.2, Incyte shall pay to Syros royalties on worldwide annual Net Sales of each Royalty Product. The royalty rate shall be determined on a Validated Target-by-Validated Target basis based on annual aggregate Net Sales of any and all Royalty Products with respect to a given Validated Target, as follows:

That portion of annual aggregate Net Sales of any and all Royalty Products with respect to a given Validated Target, worldwide, during any Calendar Year that is:	**Royalty Rate**
Less than or equal to [**] Dollars ($[**])	[**]%
Greater than [**] Dollars ($[**]) and less than or equal to [**] Dollars ($[**])	[**]%
Greater than [**] Dollars ($[**])	[**]%

For the avoidance of doubt, if Royalty Product #1 with respect to a given Validated Target achieves annual Net Sales of $[**], and Royalty Product #2 with respect to the same Validated Target achieves annual Net Sales of $[**], then the royalty rate for both Royalty Product #1 and Royalty Product #2 shall be [**]%.

5.6.2 Royalty Term; Royalty Reductions and Floor.

(a) Royalty Term. Incyte shall have no obligation to pay any royalty with respect to Net Sales of a Royalty Product in any country with respect to any period after the Royalty Term in such country has expired with respect to such Royalty Product, and Net Sales of such Royalty Product with respect to any period after the Royalty Term for such Royalty Product in such country has expired shall be excluded for purposes of calculating the applicable royalty rate in Section 5.6.1.

(b) Royalty Reductions and Floor. If, during any portion of the Royalty Term for any Royalty Product in any country (i) there is no Valid Claim of a [**]; or (ii) a Generic Product with respect to such Royalty Product is commercially sold and continues to be sold in such country, then, in each cases ((i) or (ii)), the royalty rates specified in Section 5.6.1 shall be reduced by [**] percent ([**]%) with respect to Net Sales of such Royalty Product in such country during such portion of the Royalty Term. Notwithstanding the foregoing, in no event shall the royalty rates specified in Section 5.6.1 be reduced by more than [**] percent ([**]%), in the aggregate, in any Calendar Quarter, as a result of the reductions set forth in this Section 5.6.2(b).

5.6.3 Royalty Payment, Sales Milestone Payments and Reports . Incyte shall calculate all amounts payable to Syros pursuant to Section 5.5 and this Section 5.6 at the end of each Calendar Quarter, which amounts shall be converted to Dollars in accordance with Section 5.7. No later than [**] after the end of each Calendar Quarter in which Net Sales occur, Incyte shall provide to Syros a good faith estimate of (a) Net Sales for such Calendar Quarter, any expected adjustments that will be made pursuant to Section 5.6.2 and the estimated royalty amounts and (b) any estimated Sales Milestones Payments, in each case ((a) and (b)) that will be due to Syros with respect to such Calendar Quarter. No later than [**] after the end of each Calendar Quarter in which Net Sales occur, Incyte shall provide to Syros a statement specifying, on a Royalty Product-by-Royalty Product, Validated Target-by-Validated Target and country-by-country basis, the Net Sales for such Calendar Quarter, the amount of Invoiced Sales and Net Sales of each Royalty Product in each country during the applicable Calendar Quarter (including such amounts expressed in local currency and as converted to Dollars), in the case of any Combination Product, the volume-weighted average sales with respect to each Combination Product in each country and the calculation of any adjustment to Net Sales to account for such Combination Product (calculated in accordance with the definition of "Net Sales") in such country, and a calculation of the amount of royalty payments due on such Net Sales for such Calendar Quarter and the Sales Milestone Payments due for such Calendar Quarter. Syros shall invoice Incyte for amounts due as royalty payments pursuant to Section 5.6 and Sales Milestone Payments pursuant to Section 5.5 with respect to a given Calendar Quarter and Incyte shall pay to Syros the amounts due with respect to a given Calendar Quarter within [**] after the receipt by Incyte of an invoice therefor.

5.7 Payment Method. All payments to Syros under this Agreement shall be made by deposit of Dollars in the requisite amount to such bank account as Syros may from time to time designate by notice to Incyte. For the purpose of calculating any sums due under, or otherwise reimbursable pursuant to, this Agreement (including the calculation of Net Sales expressed in currencies other than Dollars), Incyte shall convert any amount expressed in a foreign currency into Dollar equivalents using the arithmetic average of the exchange rates for the purchase of Dollars as published in *The Wall Street Journal*, Eastern Edition, for the Calendar Quarter to which such payments relate.

5.8 Taxes. All payments owed by Incyte to Syros pursuant to this Agreement (each, a "Payment") shall be paid free and clear of any and all taxes, except for any withholding taxes required by Applicable Law. Syros shall be solely responsible for paying any and all taxes (other than withholding taxes required by Applicable Law to be deducted from Payments and remitted by Incyte) levied on account of, or measured in whole or in part by reference to, any Payments it receives. Incyte shall deduct or withhold from the Payments

any taxes that it is required by Applicable Law to deduct or withhold. If Incyte takes any actions that would increase any required withholding taxes that otherwise would not be required absent such action, including a change in tax residence, (sub)license or assignment of this Agreement or any rights or obligations hereunder by law or otherwise, or any merger, acquisition, asset purchase or sale of all or substantially all of its business or assets, Incyte shall increase the amount so payable as necessary so that after such deduction or withholding of withholding taxes has been made, Syros receives the amount it would have received had no such deduction or withholding been made. Notwithstanding the foregoing, if Syros is entitled under any applicable tax treaty to a reduction in the rate of, or the elimination of, applicable withholding tax, it may deliver to Incyte or the appropriate governmental authority (with the assistance of Incyte to the extent that this is reasonably required and is expressly requested in writing) the prescribed forms necessary to reduce the applicable rate of withholding or to relieve Incyte of its obligation to withhold such tax and Incyte shall apply the reduced rate of withholding or dispense with withholding, as the case may be; *provided* that Incyte has received evidence of Syros' delivery of all applicable forms (and, if necessary, its receipt of appropriate governmental authorization) at least [**] prior to the date that an applicable Payment is due. If, in accordance with the foregoing, Incyte withholds any amount, it shall pay to Syros the balance when due, make timely payment to the proper taxing authority of the withheld amount and send to Syros proof of such payment within [**] following such payment.

5.9 Interest on Overdue Payments. Incyte shall be liable for interest on the aggregate amount of any payments that are not paid on or before the date such payments are due under this Agreement at a rate per annum equal to [**]; *provided* that with respect to any disputed payments, no interest payment shall be due until such dispute is resolved and the interest which shall be payable thereon shall be based on the finally-resolved amount of such payment, calculated from the original date on which the disputed payment was due through the date on which payment is actually made.

5.10 Financial Records.

5.10.1 Incyte Financial Records. Incyte shall and shall cause its Affiliates and its and their direct or indirect successors (whether as a successor-in-interest with respect to any of the foregoing Persons or an Associated Product by way of product acquisition or otherwise), or any licensee or sublicensee of any of the foregoing, to, keep complete and accurate financial books and records pertaining to the Commercialization of Royalty Products hereunder, including books and records of Invoiced Sales and Net Sales of Royalty Products, in sufficient detail to calculate and verify all amounts payable hereunder. Incyte shall and shall cause its Affiliates and its and their (sub)licensees to, retain such books and records until the later of (a) [**] after the end of the period to which such books and records pertain; (b) the expiration of the applicable tax statute of limitations (or any extensions thereof); or (c) such longer period as may be required by Applicable Law.

5.10.2 Syros Financial Records. Syros shall and shall cause its Affiliates and its and their direct or indirect successors (whether as a successor-in-interest with respect to any of the foregoing Persons or an Associated Product by way of product acquisition or otherwise), to keep complete and accurate financial books and records pertaining to the costs incurred by Syros that Syros is allocating to the Prepaid Research Amount, including books and records with respect to FTEs, in sufficient detail to calculate and verify all such allocated costs. Syros shall and shall cause

its Affiliates to retain such books and records until the later of (a) [**] after the end of the period to which such books and records pertain; (b) the expiration of the applicable tax statute of limitations (or any extensions thereof); or (c) such longer period as may be required by Applicable Law.

5.11 Audits.

5.11.1 Syros Audit Right. At the request of Syros, Incyte shall, and shall cause its Affiliates and its and their (sub)licensees to, permit an independent auditor designated by Syros, at reasonable times and upon reasonable notice, to audit the books and records maintained pursuant to Section 5.10.1 to ensure the accuracy of all reports and payments made hereunder. The cost of such audit shall be borne by [**]. If such audit concludes that additional amounts were owed by Incyte, then Incyte shall pay such additional amounts, with interest from the date originally due as provided in Section 5.9, within [**] after the date on which such audit is completed.

5.11.2 Incyte Audit Right. At the request of Incyte, in the event that (a) Syros seeks payment or reimbursement from Incyte for any Permitted Overrun Costs pursuant to Section 2.6.3(d), or for amounts in addition to the Prepaid Research Amount pursuant to Section 2.6.3(c), or (b) Syros becomes obligated to refund to Incyte any portion of the Prepaid Research Amount pursuant to Section 10.5.3(b), Syros shall, and shall cause its Affiliates to, permit an independent auditor designated by Incyte, at reasonable times and upon reasonable notice, to audit the books and records maintained pursuant to Section 5.10.2 to ensure the accuracy of all costs allocated to the performance of the applicable activities under the Research Plan. The cost of such audit shall be borne by [**].

ARTICLE 6 - INTELLECTUAL PROPERTY

6.1 Ownership and Use.

6.1.1 Syros Existing Background Target IP and Syros Platform Improvements. As between the Parties, Syros shall (a) retain all right, title and interest in and to the Syros Existing Background Target IP and (b) own all right, title and interest in and to the Syros Platform Improvements.

6.1.2 Ownership and Use of Program IP. The Parties shall [**], the "Joint Program IP"). As between the Parties, Syros [**]. As between the Parties, Incyte [**]. Unless otherwise agreed in writing, each Party covenants to the other Party that it shall not use any Program IP for any purpose other than [**].

6.1.3 Use of Program Data.

(a) Super-Enhancer Data.

(i) By Incyte for Selection of Program Targets. Except as expressly permitted in Section 6.1.3(a)(ii) with respect to any Program Target that becomes a Validated Target in accordance with Section 3.1, Incyte shall have the right to use the Super-Enhancer Data with respect to such Program Target solely for purposes of exercising its rights under Section 3.3.1(a), including (A) selecting Preliminary Targets in accordance with Section 2.8.2; (B)

selecting Initial Research Targets in accordance with Section 2.8.4; (C) selecting Definitive Research Targets in accordance with Section 2.8.6; (D) selecting Extended Research Targets in accordance with Section 2.8.8; (E) selecting Validated Targets in accordance with Section 3.1; or (F) substituting an Initial Research Target, Definitive Research Target or Extended Research Target with an Original Target in accordance with Section 3.4, in each case ((A)-(F)), in accordance with this Agreement.

(ii) By Incyte for Validated Targets. Upon a Program Target becoming a Validated Target, Incyte shall have the right to use the Super-Enhancer Data with respect to such Validated Target for purposes of exercising the applicable rights granted to Incyte with respect to such Validated Target pursuant to Section 3.3.1(b).

(b) Circuitry Map Data.

(i) By Incyte for Selection of Program Targets. Except as expressly permitted in Section 6.1.3(b)(ii) with respect to any Program Target that becomes a Validated Target in accordance with Section 3.1, Incyte shall have the right to use the Circuitry Map Data with respect to such Program Target solely for purposes of exercising its rights under Section 3.3.1(a), including (A) selecting Preliminary Targets in accordance with Section 2.8.2; (B) selecting Initial Research Targets in accordance with Section 2.8.4; (C) selecting Definitive Research Targets in accordance with Section 2.8.6; (D) selecting Extended Research Targets in accordance with Section 2.8.8; (E) selecting Validated Targets in accordance with Section 3.1; or (F) substituting an Initial Research Target, Definitive Research Target or Extended Research Target with an Original Target in accordance with Section 3.4, in each case ((A)-(F)), in accordance with this Agreement.

(ii) By Incyte for Validated Targets. Upon a Program Target becoming a Validated Target, Incyte shall have the right to use the Circuitry Map Data with respect to such Validated Target for purposes of exercising the rights granted to Incyte with respect to such Validated Target pursuant to Section 3.3.1(b).

(c) Initial Research Target Validation Data.

(i) By Incyte for Selection of Program Targets. Except as expressly permitted in Section 6.1.3(c)(ii) with respect to any Program Target that becomes a Validated Target in accordance with Section 3.1, Incyte shall have the right to use the Initial Research Target Validation Data with respect to such Program Target solely for purposes of exercising its rights under Section 3.3.1(a), including (A) selecting Initial Research Targets in accordance with Section 2.8.4; (B) selecting Definitive Research Targets in accordance with Section 2.8.6; (C) selecting Extended Research Targets in accordance with Section 2.8.8; (D) selecting Validated Targets in accordance with Section 3.1; or (E) substituting an Initial Research Target, Definitive Research Target or Extended Research Target with an Original Target in accordance with Section 3.4, in each case ((A)-(E)), in accordance with this Agreement.

(ii) By Incyte for Validated Targets. Upon a Program Target becoming a Validated Target, Incyte shall have the right to use the Initial Research Target Validation

Data with respect to such Validated Target for purposes of exercising the applicable rights granted to Incyte with respect to such Validated Target pursuant to Section 3.3.1(b).

(d) Definitive Research Target Validation Data.

(i) By Incyte for Selection of Program Targets. Except as expressly permitted in Section 6.1.3(d)(ii) with respect to any Program Target that becomes a Validated Target in accordance with Section 3.1, Incyte shall have the right to use the Definitive Research Target Validation Data with respect to such Program Target solely for purposes of exercising its rights under Section 3.3.1(a), including (A) selecting Initial Research Targets in accordance with Section 2.8.4; (B) selecting Definitive Research Targets in accordance with Section 2.8.6; (C) selecting Extended Research Targets in accordance with Section 2.8.8; (iv) selecting Validated Targets in accordance with Section 3.1; or (D) substituting an Initial Research Target, Definitive Research Target or Extended Research Target with an Original Target in accordance with Section 3.4, in each case ((A)-(D)), in accordance with this Agreement.

(ii) By Incyte for Validated Targets. Upon a Program Target becoming a Validated Target, Incyte shall have the right to use the Definitive Research Target Validation Data with respect to such Validated Target for purposes of exercising the applicable rights granted to Incyte with respect to such Validated Target pursuant to Section 3.3.1(b).

(e) Other Program Data.

(i) By Incyte for Selection of Program Targets. Except as expressly permitted in Section 6.1.3(e)(ii) with respect to any Program Target that becomes a Validated Target in accordance with Section 3.1, Incyte shall have the right to use the Program Data described in clause (b) of the definition of "Program Know-How" with respect to such Program Target solely for purposes of exercising its rights under Section 3.3.1(a), including (A) selecting Initial Research Targets in accordance with Section 2.8.4; (B) selecting Definitive Research Targets in accordance with Section 2.8.6; (C) selecting Extended Research Targets in accordance with Section 2.8.8; (iv) selecting Validated Targets in accordance with Section 3.1; or (D) substituting an Initial Research Target, Definitive Research Target or Extended Research Target with an Original Target in accordance with Section 3.4, in each case ((A)-(D)), in accordance with this Agreement.

(ii) By Incyte for Validated Targets. Upon a Program Target becoming a Validated Target, Incyte shall have the right to use the Program Data described in clause (b) of the definition of "Program Know-How" with respect to such Validated Target for purposes of exercising the applicable rights granted to Incyte with respect to such Validated Target pursuant to Section 3.3.1(b).

(f) Excluded Programs. Without limitation to Section 2.14, (i) Syros shall not have the right to use any Program Know-How, including any Program Data, in performing any Internal Syros Program or any program under a Third Party Collaboration Agreement, including with respect to any Unreserved Target or Syros Excluded Target; *provided, however,* that, notwithstanding this Section 6.1 or Section 2.14.2, Syros may use lists of Program Targets, Reserved Targets and Unreserved Targets for purposes of ensuring its compliance with the terms of this

Agreement and (ii) Incyte shall not have the right to use any Program Know-How, including any Program Data, in performing any Internal Incyte Program with respect to any Incyte Excluded Target.

6.1.4 Disclosure of Inventions. Each Party shall promptly disclose to the other Party in writing the conception, discovery, development or other making of any invention included in the Program Know-How by or on behalf of such Party or any of its Affiliates or its or their (sub)licensees. Incyte shall promptly disclose to Syros in writing the conception, discovery, development or other making of any invention included in the Syros Platform Improvements by or on behalf of Incyte or any of its Affiliates or its or their (sub)licensees.

6.1.5 Assignment.

(a) To Syros. Incyte shall, and does hereby, assign, and shall cause its Affiliates to assign, to Syros, without additional compensation, its and their entire right, title and interest in, to and under the Super-Enhancer Data and Syros Platform Improvements.

(b) To Incyte. Syros shall, and does hereby, assign, and shall cause its Affiliates to assign, to Incyte, without additional compensation, its and their entire right, title and interest in, to and under the Definitive Research Target Validation Data.

(c) Joint Interests. Each Party shall, and does hereby, assign, and shall cause its Affiliates and its and their (sub)licensees to so assign, to the other Party, without additional compensation, such right, title and interest in, to and under the Joint Program IP [**].

6.1.6 Assignment Obligation. Each Party shall (a) cause all of its employees and agents and (b) use commercially reasonable efforts to cause all other Persons, in each case ((a) and (b)), who perform activities on behalf of such Party in connection with this Agreement, to be under a written obligation to assign their rights in any intellectual property resulting therefrom to such Party, except where Applicable Law requires otherwise.

6.2 Patent Prosecution and Maintenance.

6.2.1 Syros Existing Background Target Patents and Patents within the Syros Platform Improvements. As between the Parties, Syros shall have the sole right, but not the obligation, to be the Prosecuting Party for (a) the Syros Existing Background Target Patents and (b) any Patents within the Syros Platform Improvements, in each case ((a) and (b)), worldwide, at its sole cost and expense and using counsel of its own choice.

6.2.2 Non-Validated Target Patents. The provisions of this Section 6.2.2 shall apply with respect to any Program Patent that solely Covers Program Know-How relating to a given Program Target that has not yet been selected as a Validated Target in accordance with Section 3.1 and not any other Program Know-How (each, a "Non-Validated Target Patent").

(a) Generally. Except as otherwise agreed by the Parties in writing, unless and until a Program Target is selected as a Definitive Research Target, [**]. Following selection of

a Program Target as a Definitive Research Target and payment of the applicable Definitive Research Target Payment, [**] with respect to such Definitive Research Target, in accordance with this Section 6.2.2; *provided* that [**].

(b) Notice from Incyte and Evaluation by the JPC. For each Non-Validated Target Patent that Incyte desires to file with respect to a Definitive Research Target, Incyte shall notify Syros in writing via the JPC, and in such notice shall identify such Definitive Research Target (by ENSEMBL ID and name) and the Associated Optioned Field(s) with respect to such Definitive Research Target. Promptly following receipt of such notice, [**], and Incyte shall provide to the JPC Program Data generated by Incyte with respect to such Definitive Research Target, to the extent reasonably necessary to demonstrate that the applicable patentability criteria have been fulfilled. If (i) [**], as determined by the JPC and (ii) the [**] in accordance with Section 6.2.2(c).

(c) Prosecution and Maintenance.

(i) Disclosure and Claim Scope. The disclosure and claim scope of any Non-Validated Target Patent shall be limited, as of the filing date of such Patent, to the broadest Associated Optioned Field for the applicable Definitive Research Target. For example, if, as of the filing date of a Non-Validated Target Patent, Incyte retains an unexercised Option in only the MPN Field to select the applicable Definitive Research Target as Validated Target, then the disclosure and claim scope of such Non-Validated Target Patent shall be limited to the MPN Field.

(ii) Prosecution Activities. As between the Parties, Syros shall have the sole right to be the Prosecuting Party for the Non-Validated Target Patents, worldwide, at Incyte's sole cost and expense and using counsel mutually agreed upon by the Parties. Unless otherwise agreed by the Parties in writing, and subject to Incyte fulfilling its obligations with respect to such costs and expenses, Syros shall not abandon any Non-Validated Target Patent that Covers any Know-How relating to any Definitive Research Target during the period that Incyte retains an unexercised Option to select such Definitive Research Target as a Validated Target.

(iii) [**]. With respect to a particular Definitive Research Target, upon expiration or termination of Incyte's Option to select such Definitive Research Target as a Validated Target (for clarity, without exercise of such option):

(A) any Non-Validated Target Patent that Covers any Program Know-How relating to such Definitive Research Target and does not Cover any Program Know-How relating to a Validated Target shall be deemed to (1) be a "Reverted Target Patent" and (2) [**];

(B) (1) any Program Data disclosed in a published Reverted Target Patent shall be deemed to (I) be "Reverted Target Data" and (II) [**];

(C) Incyte shall, and does hereby, and shall cause its Affiliates and its and their (sub)licensees to, assign to Syros all right,

title and interest in and to any Program Know-How (including any inventions) to the extent related to such Definitive Research Target, which Program Know-How [**] shall be deemed the Confidential Information of Syros as of the date of expiration or termination of such Option; and

(D) [**].

6.2.3 Validated Target Patents. The provisions of this Section 6.2.3 shall apply with respect to any Program Patent that (x) Covers Program Know-How relating to a given Program Target that has been selected as a Validated Target in accordance with Section 3.1 and (y) does not Cover any Program Know-How relating to a Definitive Research Target that has not been selected as a Validated Target in accordance with Section 3.1 (each, a "Validated Target Patent"). Upon selection of any Validated Target in accordance with Section 3.1, any Non-Validated Target Patent that Covers any Program Know-How relating to such Validated Target shall become a "Validated Target Patent".

(a) Prosecution and Maintenance.

(i) Disclosure and Claim Scope.

(A) Patents Filed Before Selection of the Relevant Program Target as a Validated Target. If Incyte selects a Program Target as a Validated Target and such Program Target was the subject of a Non-Validated Target Patent that becomes a Validated Target Patent pursuant to Section 6.2.3, then the claims of such Validated Target Patent shall, if applicable, be amended to limit their scope to the Associated Licensed Field for such Validated Target. For example, if Incyte exercises its Option with respect to a Validated Target in only the MPN Field, and such Validated Target was the subject of a Non-Validated Target Patent that claimed such Validated Target in the All Uses Field, then the claims of such Non-Validated Target Patent that becomes a Validated Target Patent shall be amended to limit their scope to the MPN Field.

(B) Patents Filed Following Selection of the Relevant Program Target as a Validated Target. If Incyte selects a Program Target as a Validated Target and such Program Target was not the subject of a Non-Validated Target Patent, then the disclosure and claim scope of any Validated Target Patent filed after such selection shall be limited, as of the filing date of such Patent, to the Associated Licensed Field for such Validated Target. For example, if, as of the filing date of a Validated Target Patent, Incyte holds an exclusive license in only the MPN Field, then the disclosure and claim scope of such Validated Target Patent shall be limited to the MPN Field.

(b) Prosecution Activities. As between the Parties, and in accordance with Section 6.2.5, Syros shall have the first right, but not the obligation, to be the Prosecuting Party for the Validated Target Patents, worldwide, at Incyte's sole cost and expense and using counsel mutually agreed upon by the Parties. If Syros decides that it will not conduct, or will cease to conduct, the Prosecution Activities with respect to any Validated Target Patent, in any country, then, subject to Incyte fulfilling its obligations with respect to such costs and expenses, Syros shall provide written notice to Incyte of such intention at least [**] in advance of any deadline for avoiding abandonment of (or other loss of rights with respect to) such Validated Target Patent, and Incyte shall thereupon have the option, in its sole discretion and in accordance with Section 6.2.5, to become the Prosecuting Party for such Validated Target Patent in such country, at Incyte's sole cost and expense and using counsel mutually agreed upon by the Parties.

6.2.4 Separation of Disclosures and Claims .

(a) Program Targets. Unless otherwise agreed by the Parties in writing, each Non-Validated Target Patent and each Validated Target Patent will only Cover Program Know-How relating to one Definitive Research Target or Validated Target, as applicable.

(b) Program Patents and Patents within Syros Platform Improvements . If an invention necessary for the Exploitation of a Validated Target in its Associated Licensed Field can be claimed in a Program Patent and Syros reasonably desires to also claim such invention in a Patent within the Syros Platform Improvements, then the Parties shall cooperate to implement reasonable patent prosecution strategies via the JPC, such as filing two separate Patent applications on the same day, or filing continuation or divisional applications, as necessary to grant Incyte rights under such invention necessary for the Exploitation of an Associated Product in its Associated Licensed Field pursuant to the applicable license grant in Section 3.3.1(b)(i) or Section 3.3.1(b)(ii).

6.2.5 Rights of the Non-Prosecuting Party . The Prosecuting Party with respect to any Non-Validated Target Patent or Validated Target Patent shall periodically inform the non-Prosecuting Party of all material steps with regard to the Prosecution Activities for such Non-Validated Target Patent or Validated Target Patent, including by providing the non-Prosecuting Party with a copy of all material communications to and from any patent authority regarding such Non-Validated Target Patent or Validated Target Patent, any and all communications to and from any patent authority regarding such Non-Validated Target Patent or Validated Target Patent that are requested by the non-Prosecuting Party via the JPC, and by providing the non-Prosecuting Party drafts of any material filings or responses to be made to such patent authorities sufficiently in advance of submitting such filings or responses so as to allow a reasonable opportunity for the non-Prosecuting Party to review and comment thereon. The Prosecuting Party shall consider in good faith the timely requests and suggestions of the non-Prosecuting Party with respect to such drafts; *provided, however,* that if the non-Prosecuting Party is paying all costs for such Prosecution Activities, the Prosecuting Party shall not unreasonably withhold its agreement to the adoption of such comments to the extent consistent with a patent strategy established by the JPC.

6.2.6 Cooperation. The non-Prosecuting Party with respect to any Non-Validated Target Patent, Validated Target Patent or Patent within the Syros Platform Improvements shall, and shall cause its Affiliates to, assist and cooperate with the Prosecuting Party, as the Prosecuting Party

may reasonably request from time to time, in connection with Prosecution Activities conducted in accordance with this Section 6.2, including by: (a) offering comments, if any, promptly; (b) providing access to relevant documents and other evidence and making its employees available at reasonable business hours; and (c) executing necessary legal documents; *provided* that (i) Incyte, if it is the Prosecuting Party for any Non-Validated Target Patent or Validated Target Patent, shall reimburse Syros and its Affiliates for its or their reasonable and verifiable legal fees and expenses incurred in connection therewith and (ii) Syros, as the Prosecuting Party for any Patent within the Syros Platform Improvements, shall reimburse Incyte and its Affiliates for its or their reasonable and verifiable legal fees and expenses incurred in connection therewith.

6.2.7 Common Ownership Under Joint Research Agreements. Notwithstanding anything to the contrary in this Article 6, neither Party shall have the right to make an election under 35 U.S.C. §102(c) when exercising its rights under this Article 6 without the prior written consent of the other Party. With respect to any such permitted election, the Parties shall coordinate their activities with respect to any submissions, filings or other activities in support thereof. The Parties acknowledge and agree that this Agreement is a "joint research agreement" as defined in 35 U.S.C. §100(h).

6.2.8 [**]. Unless otherwise agreed by the Parties in writing, [**], other than (a) Non-Validated Target Patents filed in accordance with Section 6.2.2; (b) Validated Target Patents filed in accordance with Section 6.2.3 or (c) Patents within the Syros Platform Improvements filed in accordance with Section 6.2.4(b). In the event that [**], the Parties shall discuss in good faith and agree upon responsibilities for Prosecution Activities, enforcement and defense of such Program Patent.

6.3 Enforcement of Intellectual Property Rights.

6.3.1 Syros Existing Background Target IP and Syros Platform Improvements. As between the Parties, Syros shall have the sole right, but not the obligation, to be the Enforcing Party with respect to any alleged or threatened infringement or misappropriation (collectively, "Infringement") of any (a) Syros Existing Background Target IP or (b) Syros Platform Improvements, in each case ((a) and (b)), at its sole cost and expense and using counsel of its own choice.

6.3.2 Notice. Each Party shall promptly notify the other Party in writing of any Infringement of any: (a) (i) Non-Validated Target Patent or (ii) Program Know-How that specifically relates to a Definitive Research Target that is the subject of a Non-Validated Target Patent and the Associated Licensed Field for such Definitive Research Target (such Non-Validated Target Patents and Program Know-How, collectively, the "Non-Validated Target Program IP"); and (b) (i) Validated Target Patent or (ii) Program Know-How that specifically relates to a Validated Target and its Associated Licensed Field (such Validated Target Patents and Program Know-How, collectively, the "Validated Target Program IP"), in each case ((a) and (b)), of which such Party becomes aware.

6.3.3 Non-Validated Target Program IP. As between the Parties, Syros shall have the sole right, but not the obligation, to be the Enforcing Party with respect to the Infringement of any Non-Validated Target Program IP, at its sole cost and expense and using counsel of its own choice.

6.3.4 Validated Target Program IP. As between the Parties, Incyte shall have the first right, but not the obligation, to be the Enforcing Party with respect to the Infringement of any Validated Target Program IP, at its sole cost and expense and using counsel of its own choice. If Incyte notifies Syros that Incyte does not wish to be the Enforcing Party with respect to any Infringement, or fails to prosecute or resolve any Infringement of any Validated Target Program IP by the earlier of (a) [**] after notice of such Infringement is provided under Section 6.3.2 or (b) [**] prior to any final deadline under Applicable Law to prosecute or resolve such Infringement, then Syros shall have the right, but not the obligation, to become the Enforcing Party with respect to such Infringement, at its sole cost and expense and using counsel of its own choice.

6.3.5 Rights of the Non-Enforcing Party . The non-Enforcing Party with respect to any Non-Validated Target Program IP or Validated Target Program IP shall be entitled, at its own expense, to be represented in any action to prosecute the Infringement of such Non-Validated Target Program IP or Validated Target Program IP by counsel of its own choice, and to participate in decisions regarding the appropriate course of conduct for such action, and the additional right to join and participate in such action; *provided* that the Enforcing Party shall retain control of the applicable claim, suit or proceeding, including, notwithstanding anything to the contrary in Section 6.4, the response to any defense or defense of any counterclaim raised in connection therewith; and *provided*, *further*, that in connection with any action with respect to any Non-Validated Target Program IP or Validated Target Program IP, the Enforcing Party shall (a) keep the non-Enforcing Party reasonably informed of any material steps taken and provide copies of all material documents filed in connection with such action, and (b) consider in good faith any reasonable comments from the non-Enforcing Party.

6.3.6 Cooperation. The Parties shall, and shall cause their respective Affiliates to, cooperate fully in any enforcement action pursuant to this Section 6.3, including, as applicable, by making the inventors, developers, applicable records and documents (including laboratory notebooks) with respect to the relevant Non-Validated Target Program IP, Validated Target Program IP or Syros Platform Improvements available upon the Enforcing Party's reasonable request. Each Party shall, and shall cause its Affiliates to, assist and cooperate with the Enforcing Party, as such Enforcing Party may reasonably request from time to time, in connection with its activities set forth in this Section 6.3, including, where necessary, joining in or being named as a necessary party to such action (or furnishing a power of attorney for such purpose), providing access to relevant documents and other evidence and making its employees available at reasonable business hours; *provided* that the Enforcing Party shall reimburse the non-Enforcing Party (or its Affiliate(s)) for its reasonable and verifiable out-of-pocket costs and expenses incurred in connection therewith.

6.3.7 Settlements. The Enforcing Party with respect to any Infringement under this Section 6.3 shall have the right to settle any claim with respect to such Infringement; *provided* that neither Party shall have the right to settle any such claim with respect to any (a) Validated Target Program IP or (b) Non-Validated Target Program IP, in the case of this clause (b), solely (i) during

the period that Incyte retains an unexercised Option to obtain an exclusive license under such Non-Validated Target Program IP and (ii) in the applicable Associated Optioned Field, in each case ((a) and (b)), in a manner that has a material adverse effect on the rights or interests of the other Party or its Affiliates, or in a manner that imposes any costs or liability on, or involves any admission by, the other Party or its Affiliates, without the express written consent of such other Party (which consent shall not be unreasonably withheld, conditioned or delayed).

6.3.8 Recoveries.

(a) Generally. Except as otherwise agreed by the Parties in connection with a cost sharing arrangement, any recovery realized as a result of any enforcement action under this Section 6.3 (whether by way of settlement or otherwise) shall be first allocated to reimburse the Parties for their costs and expenses in making such recovery (which amounts shall be allocated *pro rata* if insufficient to cover the totality of such expenses). Any remainder after such reimbursement is made shall be allocated as set forth in Section 6.3.8(b).

(b) Remainders. If Incyte is the Enforcing Party, then (i) to the extent not representing treble or punitive damages, any remainder after reimbursement pursuant to Section 6.3.8(a) shall be retained by Incyte and treated as "Net Sales" in the Calendar Year in which it is actually received for purposes of Incyte's payment obligations to Syros pursuant to Article 5 and (ii) to the extent representing treble or punitive damages, any remainder after reimbursement pursuant to Section 6.3.8(a) shall be allocated [**] percent ([**]%) to [**] and [**] percent ([**]%) to [**]. If Syros is the Enforcing Party with respect to any Syros Existing Background Target IP, Syros Platform Improvements or Non-Validated Target IP, then any remainder after reimbursement pursuant to Section 6.3.8(a) shall be retained by Syros. If Syros is the Enforcing Party with respect to any Validated Target IP, then any remainder after reimbursement pursuant to Section 6.3.8(a) shall be allocated [**] percent ([**]%) to [**] and [**] percent ([**]%) to [**].

6.3.9 Biosimilar Applications. Without limitation to the foregoing, and notwithstanding Section 6.4.4, in the case of a Biosimilar Application, each Party shall promptly notify the other Party in writing if it becomes aware of the submission to a Regulatory Authority of such Biosimilar Application, including if such Party receives a notice of commercial marketing provided by the applicant for such Biosimilar Application pursuant to Section 351(l)(8)(A) of the PHSA. If requested by Syros and permitted by Applicable Law, Incyte shall (a) seek to obtain access to the Biosimilar Application and related confidential information (including in accordance with Section 351(l)(1)(B)(iii) of the PHSA) and (b) provide copies of such Biosimilar Application and related confidential information to Syros. As requested by Syros and permitted by Applicable Law, Incyte shall list any Program Patent(s) pursuant to Section 351(l)(1)(3)(A) or Section 351(l)(7) of the PHSA. Incyte shall, as permitted by Applicable Law, (i) provide Syros copies of the lists, statements, and other communications exchanged with the applicant for a Biosimilar Application pursuant to Section 351(l)(3)-(5) and (7) of the PHSA, (ii) keep Syros informed of any material steps taken in the process described in Section 351(l)(3)-(5) and (7) of the PHSA, and (iii) consult with and consider in good faith any comments from Syros with respect to Incyte's performance of the obligations of the reference product sponsor pursuant to Section 351(l)(3)-(5) and (7) of the PHSA, including the preparation of the lists, statements, and other communications described therein.

6.4 Invalidity or Unenforceability Actions .

6.4.1 Syros Existing Background Target Patents and Patents Within the Syros Platform Improvements. As between the Parties, Syros shall have the sole right, but not the obligation, to be the Defending Party with respect to any (a) Syros Existing Background Target Patent or (b) Patent within the Syros Platform Improvements, in each case ((a) and (b)), at its sole cost and expense and using counsel of its own choice.

6.4.2 Notice. Each Party shall promptly notify the other Party in writing of any Invalidity or Unenforceability Action with respect to any Non-Validated Target Patent or Validated Target Patent of which such Party becomes aware.

6.4.3 Non-Validated Target Program Patents. If any Invalidity or Unenforceability Action is initiated with respect to any Non-Validated Target Patent, then the Parties shall confer in good faith and agree upon a strategy for defending such Invalidity or Unenforceability Action at Incyte's cost and expense, including which Party will be the Defending Party and the selection of counsel for such defense. If the Parties are unable to agree upon such matters, then Syros shall have the sole right, but not the obligation, to be the Defending Party for such Invalidity or Unenforceability Action at its sole cost and expense and using counsel of its own choice.

6.4.4 Validated Target Program Patents. Subject to Section 6.3.4, as between the Parties, Incyte shall have the first right, but not the obligation, to be the Defending Party for any Invalidity or Unenforceability Action with respect to any Validated Target Patent, at its sole cost and expense and using counsel of its own choice. If the Defending Party with respect to any Validated Target Patent notifies the other Party that it does not wish to be the Defending Party for such Invalidity or Unenforceability Action, or fails to defend such Invalidity or Unenforceability Action by the earlier of (a) [**] after notice of such Invalidity or Unenforceability Action is provided under Section 6.4.2 or (b) [**] prior to any final deadline under Applicable Law to defend such Invalidity or Unenforceability Action, then such other Party shall have the right, but not the obligation, to become the Defending Party for such Invalidity or Unenforceability Action, at its sole cost and expense and using counsel of its own choice.

6.4.5 Rights of the Non-Defending Party . The non-Defending Party with respect to any Non-Validated Target Patent or Validated Target Patent shall be entitled, at its own expense, to be represented in any Invalidity or Unenforceability Action with respect to such Non-Validated Target Patent or Validated Target Patent by counsel of its own choice, and to participate in decisions regarding the appropriate course of conduct for such action, and the additional right to join and participate in such action; *provided* that the Defending Party shall retain control of the applicable Invalidity or Unenforceability Action; and *provided*, *further*, that in connection with any Invalidity or Unenforceability Action with respect to any Non-Validated Target Patent or Validated Target Patent, the Defending Party shall (a) keep the non-Defending Party reasonably informed of any material steps taken and provide copies of all material documents filed in connection with such action, and (b) consider in good faith any reasonable comments from the non-Defending Party.

6.4.6 Cooperation. The Parties shall, and shall cause their respective Affiliates to, cooperate fully in any action pursuant to this Section 6.4, including, as applicable, by making the inventors, developers, applicable records and documents (including laboratory notebooks) with respect to the relevant Non-Validated Target Patent, Validated Target Patent or Patent within the Syros Platform Improvements available upon the Defending Party's reasonable request. Each Party shall, and shall cause its Affiliates to, assist and cooperate with the Defending Party, as such Defending Party may reasonably request from time to time, in connection with its activities set forth in this Section 6.4, including, where necessary, joining in or being named as a necessary party to such action (or furnishing a power of attorney for such purpose), providing access to relevant documents and other evidence and making its employees available at reasonable business hours; *provided* that the Defending Party shall reimburse the non-Defending Party (or its Affiliate(s)) for its reasonable and verifiable out-of-pocket costs and expenses incurred in connection therewith.

6.4.7 Settlements. The Defending Party for any Invalidity or Unenforceability Action under this Section 6.4 shall have the right to settle such action; *provided* that neither Party shall have the right to settle any such action with respect to any Non-Validated Target Patent or Validated Target Patent in a manner that has a material adverse effect on the rights or interests of the other Party or its Affiliates, or in a manner that imposes any costs or liability on, or involves any admission by, the other Party or its Affiliates, without the express written consent of such other Party (which consent shall not be unreasonably withheld, conditioned or delayed).

6.5 Defense of Infringement Claims by Third Parties .

6.5.1 Notice. Incyte shall promptly notify Syros in writing if it becomes aware that the Exploitation of any Associated Product with respect to a Validated Target pursuant to this Agreement has resulted in, or is expected to result in, any claim, suit, or proceeding by a Third Party alleging infringement of a Patent or misappropriation of another intellectual property right by either Party or its Affiliates (a "Third Party Infringement Claim").

6.5.2 Defense of Associated Products . Subject to Article 9, as between the Parties, each Party against which a Third Party Infringement Claim is brought shall have the right, but not the obligation, to defend and control the defense of such Third Party Infringement Claim to the extent applicable to such Party, at its sole cost and expense, and using counsel of its own choice. The other Party may participate in the defense of any such Third Party Infringement Claim, at its sole cost and expense, and using counsel of its own choice; *provided* that the Party against which such Third Party Infringement Claim is brought shall continue to have the right to control the defense of such Third Party Infringement Claim, to the extent applicable to it. Notwithstanding the foregoing, in the event that a Third Party Infringement Claim is brought against both Parties, each Party shall have the right, but not the obligation, to jointly defend and control the defense of such Third Party Infringement Claim, and the Parties shall discuss in good faith the defense of such Third Party Claim and may enter into a cost sharing arrangement with respect thereto.

6.5.3 Cooperation. Each Party shall, and shall cause its Affiliates to, assist and cooperate with the other Party, as such other Party may reasonably request from time to time, in

connection with the defense of any Third Party Infringement Claim, including, where necessary, joining in, or being named as a necessary party to, such action (or furnishing a power of attorney for such purpose), providing access to relevant documents and other evidence and making its employees available at reasonable business hours; *provided* that the Party defending such Third Party Infringement Claim shall reimburse the other Party (or its Affiliate(s)) for its reasonable and verifiable out-of-pocket costs and expenses incurred in connection therewith. The Party defending any Third Party Infringement Claim shall (a) keep the other Party reasonably informed of all material developments in connection with such Third Party Infringement Claim; (b) provide such other Party with copies of all material pleadings filed in such action; and (c) allow such other Party reasonable opportunity to participate in the defense of such Third Party Infringement Claim.

6.6 Third Party Rights.

6.6.1 Related to the Syros Platform.

(a) Existing License Agreements. As between the Parties, [**] pursuant to any agreement existing as of the Effective Date to which Syros or any of its Affiliates is a party, as a result of Syros' and its Affiliates' use of the Syros Platform in conducting the Research Program.

(b) Third Party Platform Rights. As between the Parties, Syros shall have the sole right, but not the obligation, to negotiate and obtain a license or other rights from any Third Party as necessary or desirable for Syros or its Affiliates to Exploit the Syros Platform ("Third Party Platform Rights") and shall be solely responsible for any payments owed to any such Third Party under such license with respect to such Third Party Platform Rights as a result of Syros' and its Affiliates' activities under the Research Program. For clarity, this Section 6.6.1(b) is not intended, and shall not be construed, to impose on Syros any payment or other obligations with respect to securing Patent or other intellectual property rights necessary or useful for the Exploitation of any Associated Compound, Associated Product or Program Target.

6.6.2 Other Rights. Except as otherwise set forth in Section 6.6.1, as between the Parties, Incyte shall be solely responsible for any payments owed to any Third Party with respect to the Exploitation of any (a) Validated Target, (b) Associated Compound with respect to such Validated Target or (c) Associated Product containing such Associated Compound.

ARTICLE 7 - CONFIDENTIALITY

7.1 Confidentiality Obligations. At all times during the Term and for a period of [**] years following termination or expiration of this Agreement in its entirety, each Party shall and shall cause its Affiliates, and its and their officers, directors, employees and agents to, keep confidential and not publish or otherwise disclose to any Third Party and not use, directly or indirectly, for any purpose, any Confidential Information furnished or otherwise made known to it, directly or indirectly, by the other Party, except to the extent such disclosure or use is expressly permitted by the terms of this Agreement. "Confidential Information" means any technical, business or other information provided by or on behalf of one Party to the other Party in connection with this

Agreement, whether prior to, on or after the Effective Date, including information relating to any Target or the scientific, regulatory or business affairs or other activities of either Party. Any Confidential Information relating to the subject matter of this Agreement and disclosed prior to the Effective Date under the Confidentiality Agreement shall be deemed to have been disclosed under this Agreement. Notwithstanding the foregoing, (a) subject to Sections 6.2.2(c)(iii) and 10.5.1(d), all Program Know-How and the terms of this Agreement shall be deemed to be the Confidential Information of both Parties, and each Party shall be deemed to be a disclosing Party and a receiving Party with respect thereto, and (b) Syros Platform Improvements shall be deemed to be the Confidential Information of Syros, and Syros shall be deemed to be the disclosing Party and Incyte shall be deemed to be the receiving Party with respect thereto. Notwithstanding the foregoing, the confidentiality and non-use obligations under this Section 7.1 shall not apply to any information that:

7.1.1 is or hereafter becomes publicly known by public use, publication, general knowledge or the like through no breach of this Agreement by the receiving Party;

7.1.2 is demonstrated by documentation to have been in the receiving Party's possession prior to disclosure by the disclosing Party; *provided* that the foregoing exception shall not apply with respect to any Confidential Information that is deemed to be the Confidential Information of a Party under the fourth sentence of Section 7.1, regardless of whether such Confidential Information was in the receiving Party's possession prior to such disclosure;

7.1.3 is demonstrated by documentation to have been received by the receiving Party from a Third Party that is not bound by any obligation of confidentiality with respect to such information; or

7.1.4 is demonstrated by documentation to have been independently developed by or on behalf of the receiving Party without use of or reference to the disclosing Party's Confidential Information; *provided* that the foregoing exception shall not apply with respect to any Confidential Information that is deemed to be the Confidential Information of a Party under the fourth sentence of Section 7.1, regardless of whether such Confidential Information was in the receiving Party's possession prior to such disclosure.

Specific aspects or details of Confidential Information shall not be deemed to be publicly known or in the possession of the receiving Party merely because the Confidential Information is embraced by more general information that is publicly known or in the possession of the receiving Party. Further, any combination of Confidential Information shall not be considered publicly known or in the possession of the receiving Party merely because individual elements of such Confidential Information are publicly known or in the possession of the receiving Party unless such combination and its principles are publicly known or in the possession of the receiving Party.

7.2 Permitted Disclosures. Notwithstanding Section 7.1, each Party may disclose Confidential Information of the other Party to the extent that such disclosure is:

7.2.1 made in response to a valid order of a court or other governmental authority of competent jurisdiction; *provided, however*, that (a) the receiving Party shall provide the disclosing

Party with (i) prior written notice of such proposed disclosure, (ii) a reasonable opportunity to review and comment on such proposed disclosure, (iii) a reasonable opportunity to quash such order and (iv) a reasonable opportunity to request a protective order or confidential treatment requiring that any Confidential Information that is the subject of such valid order be held in confidence; and (b) any Confidential Information so disclosed shall be limited to the information that is required to be disclosed by such valid order and shall be used only for the purposes required by such valid order. The disclosing Party shall promptly provide any comments in a reasonable manner in order to allow the receiving Party to make, file or otherwise submit such disclosure within the periods required by such valid order, which comments shall be considered in good faith by the receiving Party;

7.2.2 in the reasonable opinion of the receiving Party's legal counsel, required by Applicable Law, including by reason of filing with securities regulators; *provided, however,* that (a) the receiving Party shall provide the disclosing Party with (i) prior written notice of such proposed disclosure, (ii) a reasonable opportunity to review and comment on such proposed disclosure, (iii) a reasonable opportunity to propose redactions to any Confidential Information contained in such proposed disclosure and (iv) a reasonable opportunity to request a protective order or confidential treatment requiring that any Confidential Information that is the subject of such disclosure be held in confidence; and (b) any Confidential Information so disclosed shall be limited to the information that is required to be disclosed by Applicable Law and shall be used only for the purposes required by Applicable Law. The disclosing Party shall promptly provide any comments in a reasonable manner in order to allow the receiving Party to make, file or otherwise submit such disclosure within the periods required by Applicable Law, which comments shall be considered in good faith by the receiving Party;

7.2.3 following the prior written consent of the disclosing Party (such consent not to be unreasonably withheld), made by or on behalf of (a) the receiving Party to a patent authority as may be reasonably necessary or useful for purposes of obtaining or enforcing a Non-Validated Target Patent or Validated Target Patent or (b) Syros to a patent authority as may be reasonably necessary or useful for purposes of obtaining or enforcing a Patent with respect to the Syros Platform Improvements, in each case in accordance with Article 6; *provided, however*, that reasonable measures shall be taken to assure confidential treatment of such information, to the extent such protection is available;

7.2.4 in connection with a filing, or other communication with, a Regulatory Authority related to obtaining or maintaining Regulatory Approval for an Associated Product with respect to a Validated Target; *provided* that such Associated Product is, at the time of such disclosure, being Developed or Commercialized under and in accordance with the terms of this Agreement; and *provided, further*, that reasonable measures shall be taken to assure confidential treatment of such information, to the extent such protection is available;

7.2.5 made by or on behalf of the receiving Party to subcontractors or service providers engaged in connection with this Agreement; *provided*, *however*, that any Person to which the terms of this Agreement are disclosed shall be subject to commercially reasonable written obligations of confidentiality and non-use with respect to such information;

7.2.6 made by or on behalf of the receiving Party to actual or bona fide potential investors, acquirers or Sublicensees; *provided*, *however*, that any Person to which the terms of this Agreement are disclosed shall be subject to commercially reasonable written obligations of confidentiality and non-use with respect to such information; or

7.2.7 made by or on behalf of Syros as the receiving Party to [**], as reasonably necessary to comply with the terms and conditions of the [**]; *provided*, *however*, that [**] shall be subject to commercially reasonable written obligations of confidentiality and non-use with respect to such information as set forth in the [**] with respect to confidential information of Syros.

7.3 Disclosure of Terms of this Agreement .

7.3.1 In General. Notwithstanding the foregoing, without the consent of the other Party, the terms of this Agreement may be disclosed by (a) either Party to actual or bona fide potential investors, acquirers, partners or other Third Party transactional parties, including licensees and sublicensees (and to their bankers, lawyers and accountants) as may be necessary in connection with the evaluation of such potential or actual investment, acquisition or partnership; and (b) by Syros to any Third Party licensor with respect to any Know-How, Patents or other intellectual property rights that (i) may be used or practiced by Syros in carrying out the activities under the Research Plan (including any Third Party licensor with respect to aspects of the Syros Platform or any Syros Platform Improvements) or (ii) are optioned or licensed by Syros to Incyte under this Agreement, in the case of this clause (b), to the extent reasonably necessary to comply with the terms and conditions of an agreement between Syros and such Third Party licensor (and otherwise redacted); *provided*, *however*, that, in each case ((a) and (b)), any Person to which the terms of this Agreement are disclosed shall be subject to commercially reasonable written obligations of confidentiality and non-use with respect to such terms.

7.3.2 Required by Applicable Law. Without limitation to the foregoing, each Party acknowledges and agrees that the other Party may submit this Agreement (including for clarity, the Exhibits and Schedules hereto) to the United States Securities and Exchange Commission (the "SEC") or any other securities exchange if and as required by Applicable Law or the rules of any such securities exchange. If a Party intends to submit this Agreement to the SEC or any other securities exchange, such Party agrees to consult with the other Party with respect to the preparation and submission of a confidential treatment request for this Agreement, and to comply with the terms of this Section 7.3.2. The Party seeking to make such disclosure in a filing with or other submission to the SEC, any other securities exchange or other regulatory or Governmental Authority shall (i) provide copies of the proposed disclosure to the other Party reasonably in advance of such filing or submission (as practicable under the circumstances), and (ii) provide the notified Party an opportunity to comment upon or request confidential treatment for such disclosure. If such other Party provides comments within the reasonably in advance of the filing or submission date, the Party seeking to make such disclosure or its counsel, as the case may be, shall in good faith consider such comments, *provided* that in all events the Party seeking to make such disclosure shall have the right to make such disclosure at the time and in the manner reasonably determined by its counsel to be required by Applicable Law.

7.4 Press Release. Promptly after the Effective Date, the Parties shall coordinate the issuance of the mutually agreed press release(s) attached hereto as Schedule 7.4. Except as expressly provided herein, or as otherwise required by Applicable Law, neither Party shall issue any other public announcement, press release, or other public disclosure regarding the terms of this Agreement or its subject matter relating to the Research Program without the other Party's prior written consent. Notwithstanding the foregoing, Syros shall be permitted to disclose the receipt of milestone payments under this Agreement and the corresponding milestone events.

7.5 Return or Destruction of Confidential Information . Upon the effective date of termination of this Agreement for any reason, following the written request of the disclosing Party, the receiving Party shall, at the receiving Party's election, either: (a) promptly destroy all copies of the disclosing Party's Confidential Information in the possession or control of the receiving Party and confirm such destruction in writing to the disclosing Party or (b) promptly deliver to the disclosing Party, at the receiving Party's sole cost and expense, all copies of the disclosing Party's Confidential Information in the possession or control of the receiving Party. Notwithstanding the foregoing, the receiving Party shall be permitted to retain (i) such Confidential Information to the extent (A) necessary or useful for purposes of performing any continuing obligations or exercising any ongoing licenses or rights hereunder and, in any event, a single copy of such Confidential Information for archival purposes or (B) such Confidential Information is also the Confidential Information of the receiving Party; and (ii) any computer records or files containing such Confidential Information that have been created by the receiving Party's automatic archiving and back-up procedures, to the extent created and retained in a manner consistent with the receiving Party's standard archiving and back-up procedures, but not for any other uses or purposes. All retained Confidential Information shall continue to be subject to the terms of this Agreement for the period set forth in Section 7.1.

ARTICLE 8 - REPRESENTATIONS, WARRANTIES AND COVENANTS

8.1 Representations, Warranties and Covenants of Both Parties . Each Party hereby represents and warrants to the other Party as of the Effective Date, and covenants to the other Party, that:

8.1.1 it is a corporation duly organized, validly existing and in good standing under the laws of the jurisdiction of its organization and has all requisite power and authority, corporate or otherwise, to execute, deliver and perform this Agreement;

8.1.2 the execution and delivery of this Agreement and the performance by it of the transactions contemplated hereby have been duly authorized by all necessary corporate action and do not violate: (a) such Party's charter documents, bylaws or other organizational documents; (b) in any material respect, any agreement, instrument or contractual obligation to which such Party is bound; (c) any requirement of any Applicable Law; or (d) any order, writ, judgment, injunction, decree, determination or award of any court or governmental agency presently in effect and applicable to such Party;

8.1.3 this Agreement is a legal, valid and binding obligation of such Party enforceable against it in accordance with its terms and conditions, subject to the effects of bankruptcy, insolvency or other laws of general application affecting the enforcement of creditor rights, judicial principles affecting the availability of specific performance and general principles of equity (whether enforceability is considered a proceeding at law or equity); and

8.1.4 neither it nor any of its Affiliates has been debarred or is subject to debarment and neither it nor any of its Affiliates will use in any capacity, in connection with the activities to be performed under this Agreement, any Person who has been debarred pursuant to Section 306 of the FFDCA or who is the subject of a conviction described in such section; and each Party covenants to inform the other Party in writing promptly if such Party or any such Person who is performing activities hereunder is debarred or is the subject of a conviction described in Section 306 or if any action, suit, claim, investigation or legal or administrative proceeding is pending or, to the best of its or its Affiliates' knowledge, is threatened, relating to the debarment or conviction of it or any such Person performing activities hereunder.

8.2 Additional Representations and Warranties of Syros. Syros hereby represents and warrants to Incyte that:

8.2.1 as of the Effective Date, to Syros' knowledge, Syros has not entered into any agreements with any Third Party or any Affiliate of Syros to use the Syros Platform to screen samples obtained from subjects diagnosed with a disease or condition in the MPN Field;

8.2.2 it has the right to grant the applicable rights and licenses provided for under this Agreement and to perform the Syros activities described in the Research Plan;

8.2.3 as of the Effective Date, there are no claims or litigation pending or, to its current knowledge, threatened, against it or any of its Affiliates that would prevent Syros from using the Syros Platform to perform its activities under the Initial Research Plan; and

8.2.4 as of the Effective Date, [**] is in effect. To its knowledge, Syros has not materially breached [**]. During the Research Term, Syros shall not (a) terminate the [**]; (b) commit any material breach of [**] that results in termination of such agreement; or (c) amend [**], in the case of this clause (c), in a manner that would materially adversely affect Syros' performance of its activities under the Research Plan.

8.3 DISCLAIMERS.

8.3.1 NEITHER PARTY MAKES ANY REPRESENTATIONS OR GRANTS ANY WARRANTIES, EXPRESS OR IMPLIED, (A) IN THE CASE OF BOTH PARTIES, THAT THE OBJECTIVES OF THE RESEARCH PROGRAM CAN OR WILL BE ACHIEVED OR AS TO THE TIMING OR COST AND EXPENSE ASSOCIATED WITH THE ACHIEVEMENT OF ANY SUCH OBJECTIVES; (B) IN THE CASE OF INCYTE, WITH RESPECT TO WHETHER ANY ASSOCIATED PRODUCT WITH RESPECT TO A VALIDATED TARGET WILL BE APPROVED FOR COMMERCIAL SALE BY ANY APPLICABLE REGULATORY

AUTHORITIES OR AS TO THE COMMERCIAL POTENTIAL OR SUCCESS OF ANY SUCH ASSOCIATED PRODUCT; AND (C) IN THE CASE OF SYROS, THAT ANY SPECIFIED OR MINIMUM NUMBER OF PROGRAM TARGETS (INCLUDING ORIGINAL TARGETS) CAN OR WILL BE IDENTIFIED IN CONNECTION WITH THE RESEARCH PROGRAM OR WITH RESPECT TO WHETHER ANY PROGRAM TARGET WILL BE THERAPEUTICALLY RELEVANT OR USEFUL FOR THE DEVELOPMENT OR COMMERCIALIZATION OF ANY ASSOCIATED COMPOUND OR ASSOCIATED PRODUCT WITH RESPECT TO SUCH PROGRAM TARGET.

8.3.2 EXCEPT FOR THE EXPRESS REPRESENTATIONS, WARRANTIES AND COVENANTS SET FORTH HEREIN, NEITHER PARTY MAKES ANY REPRESENTATIONS OR GRANTS ANY WARRANTIES OR COVENANTS, EXPRESS OR IMPLIED, EITHER IN FACT OR BY OPERATION OF LAW, BY STATUTE OR OTHERWISE, AND EACH PARTY SPECIFICALLY DISCLAIMS ANY OTHER REPRESENTATION, WARRANTY OR COVENANT, WHETHER WRITTEN OR ORAL OR EXPRESS OR IMPLIED, INCLUDING ANY WARRANTY OF QUALITY, MERCHANTABILITY OR FITNESS FOR A PARTICULAR USE OR PURPOSE OR ANY WARRANTY AS TO THE VALIDITY OF ANY PATENTS OR THE NON-INFRINGEMENT OF ANY INTELLECTUAL PROPERTY RIGHTS OF THIRD PARTIES.

ARTICLE 9 - INDEMNITY; LIMITATIONS OF LIABILITY; INSURANCE

9.1 Indemnification by Incyte. Incyte shall indemnify Syros, its Affiliates and its and their respective directors, officers, employees and agents and defend and save each of them harmless, from and against any and all losses, damages, liabilities, costs and expenses (including reasonable attorneys' fees and expenses) (collectively, "Losses") in connection with any and all suits, investigations, claims or demands of Third Parties (collectively, "Third Party Claims") to the extent arising from or occurring as a result of (a) the breach by Incyte of this Agreement; (b) the gross negligence or willful misconduct on the part of Incyte or its Affiliates, or its or their (sub)licensees, or its or their respective directors, officers, employees or agents in connection with this Agreement; or (c) the Exploitation by or on behalf of Incyte or any of its Affiliates, or its or their (sub)licensees, of any (i) compound or product (including any Associated Compound or Associated Product) with respect to any Program Target or (ii) Program Target; except, in each case ((a) - (c)), for those Losses for which Syros has an obligation to indemnify Incyte pursuant to Section 9.2 hereof, as to which Losses each Party shall indemnify the other to the extent of their respective liability.

9.2 Indemnification by Syros. Syros shall indemnify Incyte, its Affiliates and its and their respective directors, officers, employees and agents and defend and save each of them harmless, from and against any and all Losses in connection with any and all Third Party Claims to the extent arising from or occurring as a result of (a) the breach by Syros of this Agreement; (b) the gross negligence or willful misconduct on the part of Syros or its Affiliates or its or their respective directors, officers, employees or agents in connection with this Agreement; or (c) such Third Party Claims alleging the infringement or misappropriation of any intellectual property rights of such Third Party arising from or occurring as

a result of Syros' use of the Syros Platform to perform its activities under the Research Plan, except, in each case ((a) - (c)), for those Losses for which Incyte has an obligation to indemnify Syros pursuant to Section 9.1 hereof, as to which Losses each Party shall indemnify the other to the extent of their respective liability.

9.3 Notice of Claims. All indemnification claims in respect of a Party, its Affiliates, or their respective directors, officers, employees and agents shall be made solely by such Party (the "Indemnified Party"). The Indemnified Party shall give the other Party (the " Indemnifying Party") written notice (an "Indemnification Claim Notice") of any Losses or discovery of fact upon which such Indemnified Party intends to base a request for indemnification under this Article 9 within [**] after receipt by such Indemnified Party of actual notice of the Third Party Claim; *provided* that failure to give such notification shall not affect the indemnification provided under Section 9.1 or Section 9.2, as applicable, except to the extent that the Indemnifying Party has been actually prejudiced as a result of such failure. Each Indemnification Claim Notice shall include (a) a description in reasonable detail of the Third Party Claim and the nature and amount of the Loss (to the extent that the nature and amount of such Loss is known at the time) and (b) copies of all papers and official documents received in respect of such Third Party Claim and Loss.

9.4 Control of Defense.

9.4.1 In General. At its option, the Indemnifying Party may assume the defense of any Third Party Claim by giving written notice to the Indemnified Party within [**] after the Indemnifying Party's receipt of an Indemnification Claim Notice. Upon assuming the defense of a Third Party Claim, the Indemnifying Party may appoint as lead counsel in the defense of the Third Party Claim any legal counsel selected by the Indemnifying Party. In the event that the Indemnifying Party assumes the defense of a Third Party Claim, the Indemnified Party shall promptly deliver to the Indemnifying Party all original notices and documents (including court papers) received by the Indemnified Party in connection with the Third Party Claim. Should the Indemnifying Party assume the defense of a Third Party Claim, except as provided in Section 9.4.2, the Indemnifying Party shall not be liable to the Indemnified Party for any legal expenses subsequently incurred by the Indemnified Party in connection with the analysis, defense or settlement of such Third Party Claim unless specifically requested in writing by the Indemnifying Party. So long as the Indemnifying Party maintains control of the defense of such Third Party Claim, the Indemnifying Party shall keep the Indemnified Party timely apprised of the status of the Third Party Claim. If it is ultimately determined that the Indemnifying Party is not obligated to indemnify, defend or hold harmless the Indemnified Party from and against any Third Party Claim (in part or in its entirety), then the Indemnified Party shall reimburse the Indemnifying Party for any and all costs and expenses (including attorneys' fees and costs of suit) and any Losses incurred by the Indemnifying Party in its defense of the Third Party Claim, to the extent that the Indemnifying Party did not have such obligation.

9.4.2 Right to Participate in Defense. Without limiting Section 9.4.1, the Indemnified Party shall be entitled to participate in, but not control, the defense of any Third Party Claim and to retain counsel of its choice for such purpose; *provided, however*, that such retention

shall be at the Indemnified Party's own cost and expense unless (a) the retention thereof, and the Indemnifying Party's responsibility for the costs and expenses associated therewith, have been specifically authorized by the Indemnifying Party in writing; (b) the Indemnifying Party has failed to assume the defense and retain counsel in accordance with Section 9.4.1 or, after assuming the defense of such Third Party Claim, fails to diligently prosecute the defense thereof (in which case the Indemnified Party shall control the defense); or (c) the interests of the indemnitee and the Indemnifying Party with respect to such Third Party Claim are sufficiently adverse to prohibit the representation by the same counsel of both the indemnitee and the Indemnifying Party under Applicable Law, ethical rules or equitable principles.

9.4.3 Settlement. With respect to any monetary Losses relating to a Third Party Claim, the Indemnifying Party shall have the sole right to consent to the entry of any judgment, enter into any settlement or otherwise dispose of such Loss, at its own cost and expense, on such terms as the Indemnifying Party, in its sole discretion, shall deem appropriate; *provided* that such settlement shall not result in the Indemnified Party's becoming subject to injunctive or other non-monetary relief materially adversely affecting the business of the Indemnified Party. For any other settlement, the Indemnifying Party shall have the right to consent to the entry of any judgment, enter into any settlement or otherwise dispose of such Loss only if it obtains the prior written consent of the Indemnified Party (which consent shall not be unreasonably withheld or delayed). If the Indemnifying Party does not assume and conduct the defense of a Third Party Claim as provided above, then the Indemnified Party may defend against such Third Party Claim at the Indemnifying Party's cost and expense; *provided* that the Indemnified Party shall have the right to consent to the entry of any judgment, enter into any settlement or otherwise dispose of such Loss only if it obtains the prior written consent of the Indemnifying Party (which consent shall not be unreasonably withheld or delayed).

9.4.4 Cooperation. Regardless of whether the Indemnifying Party chooses to defend any Third Party Claim, the Indemnified Party shall, and shall cause each indemnitee to, cooperate in the defense or prosecution thereof and shall furnish such records, information and testimony, provide such witnesses and attend such conferences, discovery proceedings, hearings, trials and appeals as may be reasonably requested in connection therewith, including in order to permit the Indemnifying Party to decide whether to assume the defense of a Third Party Claim. Such cooperation shall include access during normal business hours afforded to the Indemnifying Party to, and reasonable retention by the Indemnified Party of, records and information that are relevant to such Third Party Claim, and making the Indemnified Party and other employees and agents available on a mutually convenient basis to provide additional information and explanation of any material provided hereunder; *provided* that where the Indemnifying Party has assumed the defense of the applicable Third Party Claim the Indemnifying Party shall reimburse the Indemnified Party for all of its reasonable out-of-pocket expenses in connection therewith.

9.4.5 Expenses. Except as provided above, the costs and expenses, including fees and disbursements of counsel, incurred by the Indemnified Party in connection with any claim shall be reimbursed on a Calendar Quarter basis by the Indemnifying Party, without prejudice to the Indemnifying Party's right to contest the Indemnified Party's right to indemnification and subject to refund in the event that the Indemnifying Party is ultimately held not to be obligated to indemnify the Indemnified Party.

9.5 LIMITATIONS OF LIABILITY.

9.5.1 SPECIAL, INDIRECT, AND OTHER LOSSES. EXCEPT (A) IN THE EVENT OF THE WILLFUL MISCONDUCT OR FRAUD OF A PARTY; (B) A PARTY'S BREACH OF ITS CONFIDENTIALITY OBLIGATIONS UNDER ARTICLE 7; (C) A PARTY'S BREACH OF ITS OBLIGATIONS UNDER SECTION 6.1.2, SECTION 6.1.3 OR SECTION 2.14; (D) SYROS' BREACH OF ITS OBLIGATIONS UNDER SECTION 3.5; (E) INCYTE'S BREACH OF ITS OBLIGATIONS UNDER SECTION 3.6 OR SECTION 10.5.1(G); AND (F) WITH RESPECT TO LOSSES IN CONNECTION WITH THIRD PARTY CLAIMS THAT ARE SUBJECT TO EACH PARTY'S RESPECTIVE INDEMNITY OBLIGATIONS UNDER SECTION 9.1 OR SECTION 9.2, NEITHER PARTY, NOR ANY OF ITS AFFILIATES, SHALL BE LIABLE UNDER THIS AGREEMENT IN CONTRACT, TORT, NEGLIGENCE, BREACH OF STATUTORY DUTY OR OTHERWISE FOR ANY SPECIAL, CONSEQUENTIAL, INCIDENTAL, INDIRECT OR PUNITIVE DAMAGES, OR FOR LOSS OF PROFITS (EVEN IF DEEMED DIRECT DAMAGES) SUFFERED BY THE OTHER PARTY.

9.5.2 GENERAL LIMITATION. EXCEPT FOR (A) LOSSES (AS DEFINED IN THIS AGREEMENT) ARISING OUT OF (I) A BREACH OF SYROS' CONFIDENTIALITY OBLIGATIONS UNDER ARTICLE 7 OR SYROS' OBLIGATIONS UNDER SECTION 3.5, SECTION 6.1.2, SECTION 6.1.3 OR SECTION 2.14.2 OR (II) THE WILLFUL MISCONDUCT OR FRAUD OF SYROS; AND (B) SYROS' INDEMNITY OBLIGATIONS UNDER SECTION 9.2, IN NO EVENT SHALL SYROS OR ITS AFFILIATES' TOTAL AGGREGATE LIABILITY TO INCYTE AND ITS AFFILIATES FOR ANY LOSSES (AS DEFINED IN THIS AGREEMENT) UNDER OR IN CONNECTION WITH THIS AGREEMENT EXCEED TEN MILLION DOLLARS ($10,000,000).

9.6 Insurance. Each Party shall have and maintain such types and amounts of insurance covering its activities under this Agreement as is (a) normal and customary in the pharmaceutical industry generally for parties similarly situated and (b) otherwise required by Applicable Law. Upon request by the other Party, each Party shall provide to the other Party evidence of its insurance coverage. If such insurance is on a claims-made (rather than occurrence basis), then such Party shall continue to maintain such insurance (i) in the case of Syros, for a period of five (5) years after the expiration of termination of the Research Term and (ii) in the case of Incyte, for a period of five (5) years after the expiration or termination of this Agreement in its entirety or, in the event that Incyte has caused any Associated Compound or Associated Product to be used in humans (including human clinical trials or following Regulatory Approval of such Associated Product), any longer period that corresponds to the statute of limitations for product liability claims in applicable countries. Notwithstanding the foregoing, either Party may self-insure in whole or in part the insurance requirements described above as follows: (A) in the case of Syros, at any time after either (1) a Change of Control of Syros in which the ultimate parent of Syros or the surviving entity following such Change of Control has a market capitalization that exceeds [**] Dollars ($[**]) or (2) the date on which Syros' market capitalization first exceeds [**] Dollars ($[**]); and (B) in the case of Incyte, at any time during the Term.

ARTICLE 10 - TERM AND TERMINATION

10.1 Term. The term of this Agreement (the " Term") commences on the Effective Date and, unless terminated earlier in accordance with its terms, shall continue until the date of expiration of the last Royalty Term for the last Royalty Product. Following the expiration of this Agreement in its entirety, the license grants in Section 3.3.1(b) shall become fully-paid, royalty-free and irrevocable.

10.2 Termination of this Agreement in its Entirety .

10.2.1 Material Breach. If either Party (the " Breaching Party") has materially breached any of its obligations under this Agreement, then, in addition to any other right or remedy the other Party (the "Non-Breaching Party") may have, the Non-Breaching Party may terminate this Agreement in its entirety by providing thirty (30) days' ("Notice Period"), prior written notice (the " Termination Notice") to the Breaching Party and specifying the breach and its claim of right to terminate this Agreement; *provided* that any proposed termination shall not become effective at the end of the Notice Period if the Breaching Party cures the breach specified in the Termination Notice during the Notice Period (or, if such breach is curable but cannot be cured within the Notice Period, such longer period not to exceed [**] if the Breaching Party commences actions to cure such breach within the Notice Period and thereafter diligently continues such actions during such [**] period). If a Party delivers a Termination Notice under this Section 10.2.1, and the other Party disputes whether such Termination Notice was proper, or whether the relevant breach has been cured within the applicable period set forth in this Section 10.2.1, then such dispute shall be resolved in accordance with Section 11.4, and this Agreement shall remain in full force and effect until such dispute is resolved. If, as a result of such dispute resolution process, it is determined that such Termination Notice was proper, or that such breach was not cured within the applicable period, then this Agreement shall be deemed to have been terminated as of the date on which such Termination Notice was first delivered. On the other hand, if as a result of such dispute resolution process it is determined that such Termination Notice was improper, or that such breach was cured within the applicable period, then no termination shall have occurred and this Agreement shall remain in full force and effect.

10.2.2 Insolvency. If either Party (a) files for protection under bankruptcy or insolvency laws; (b) makes an assignment for the benefit of creditors; (c) appoints or suffers appointment of a receiver or trustee over substantially all of its property that is not discharged within ninety (90) days after such filing; (d) proposes or is a party to any dissolution or liquidation; or (e) files a petition under any bankruptcy or insolvency act or has any such petition filed against it that is not discharged within ninety (90) days of the filing thereof, then the other Party may terminate this Agreement in its entirety effective immediately upon written notice to such Party.

10.2.3 By Incyte for Convenience. Incyte may terminate this Agreement in its entirety, for any or no reason, at any time, upon sixty (60) days' written notice to Syros.

10.2.4 By Mutual Agreement. The Parties may terminate this Agreement in its entirety at any time by mutual written agreement.

10.2.5 Patent Challenge.

(a) If during the Term, Incyte or any of its Affiliates challenges the validity or enforceability or actively assists any Person in challenging the validity or enforceability of: (i) (A) [**], (B) [**], (C) [**], or (D) any foreign equivalents of any of the foregoing Patents of clauses (A) - (C); (ii) any Program Patent or (iii) any Syros Background Target Patent, in each case ((i)-(iii)), before any court, administrative agency, or regulatory body including any patent opposition, re-examination or invalidation proceeding (a "Patent Challenge"), then, to the extent permitted by Applicable Law and except as otherwise set forth in this Section 10.2.5, Syros shall have the right, in its sole discretion, to terminate this Agreement upon thirty (30) days' prior written notice to Incyte; *provided* that Syros shall not have the right to terminate this Agreement if Incyte withdraws or causes to be withdrawn all such Patent Challenges within thirty (30) days after Incyte's receipt of notice from Syros under this Section 10.2.5.

(b) If during the Term, any (sub)licensee of Incyte brings a Patent Challenge, then, to the extent permitted by Applicable Law and except as otherwise set forth in this Section 10.2.5, Syros shall have the right, in its sole discretion, to terminate this Agreement upon thirty (30) days' prior written notice to Incyte; *provided* that Syros shall not have the right to terminate this Agreement if (i) the (sub)licensee withdraws or causes to be withdrawn all such Patent Challenges within thirty (30) days after Incyte's receipt of notice from Syros under this Section 10.2.5 or (ii) Incyte terminates its agreement with the (sub)licensee within thirty (30) days after Incyte's receipt of notice from Syros under this Section 10.2.5.

(c) Notwithstanding the foregoing, nothing in this Section 10.2.5 shall: (i) prevent Incyte or any of its Affiliates or (sub)licensees from asserting any defense or counterclaim in, or responding in any other manner to, an action for infringement of intellectual property brought by Syros or any of its Affiliates against Incyte or any of its Affiliates or its or their (sub)licensees; (ii) prevent Incyte or any of its Affiliates or (sub)licensees from responding to a validly issued subpoena or discovery request; or (iii) allow Syros to terminate this Agreement if Incyte or such Affiliate or (sub)licensee asserts its rights as provided in clause (i) or (ii).

10.3 Termination of this Agreement in Relation to a Validated Target .

10.3.1 Material Breach. Without limiting Section 10.2.1, if the Breaching Party has materially breached any of its obligations with respect to a Validated Target or any Associated Compound or Associated Product with respect thereto, then, in addition to any other right and remedy the Non-Breaching Party may have, the Non-Breaching Party may terminate this Agreement with respect to such Validated Target and all Associated Compounds and Associated Products with respect thereto by providing a Termination Notice to the Breaching Party and specifying the breach and its claim of right to terminate; *provided* that any proposed termination shall not become effective at the end of the Notice Period if the Breaching Party cures the breach specified in the Termination Notice during the Notice Period (or, if such breach is curable but cannot be cured within the Notice

Period, such longer period not to exceed [**] if the Breaching Party commences actions to cure such breach within the Notice Period and thereafter diligently continues such actions during such [**] period). If a Party delivers a Termination Notice under this Section 10.3.1, and the other Party disputes whether such Termination Notice was proper, or whether the relevant breach has been cured within the applicable period set forth in this Section 10.3.1, then such dispute shall be resolved in accordance with Section 11.4, and this Agreement shall remain in full force and effect until such dispute is resolved. If, as a result of such dispute resolution process, it is determined that such Termination Notice was proper, or that such breach was not cured within the applicable period, then this Agreement shall be deemed to have been terminated, with respect to the applicable Validated Target and all Associated Compounds and Associated Products with respect thereto, as of the date on which such Termination Notice was first delivered. On the other hand, if as a result of such dispute resolution process it is determined that such Termination Notice was improper, or that such breach was cured within the applicable period, then no termination shall have occurred and this Agreement shall remain in full force and effect.

10.3.2 By Incyte for Convenience. Incyte may terminate this Agreement with respect to one or more Validated Targets and the Associated Compounds and Associated Products with respect thereto, for any or no reason, at any time, upon sixty (60) days' written notice to Syros.

10.3.3 By Mutual Agreement. The Parties may terminate this Agreement with respect to one or more Validated Targets and the Associated Compounds and Associated Products with respect thereto at any time by mutual written agreement.

10.4 Rights in Bankruptcy. All rights and licenses granted under or pursuant to this Agreement by Syros or Incyte are and shall otherwise be deemed to be, for purposes of Section 365(n) of the U.S. Bankruptcy Code or any analogous provisions in any other country or jurisdiction, licenses of rights to "intellectual property" as defined under Section 101 of the U.S. Bankruptcy Code. The Parties agree that the Parties, as licensees of such rights under this Agreement, shall retain and may fully exercise all of their rights and elections under the U.S. Bankruptcy Code or any analogous provisions in any other country or jurisdiction. The Parties further agree that, in the event of the commencement of a bankruptcy proceeding by or against either Party under the U.S. Bankruptcy Code or any analogous provisions in any other country or jurisdiction, the Party hereto that is not a party to such proceeding shall be entitled to a complete duplicate of (or complete access to, as appropriate) any such intellectual property and all embodiments of such intellectual property, which, if not already in the non-subject Party's possession, shall be promptly delivered to it (a) upon any such commencement of a bankruptcy proceeding upon the non-subject Party's written request therefor, unless the Party subject to such proceeding elects to continue to perform all of its obligations under this Agreement or (b) if not delivered under clause (a), following the rejection of this Agreement by or on behalf of the Party subject to such proceeding upon written request therefor by the non-subject Party.

10.5 Consequences of Termination.

10.5.1 Termination of this Agreement in its Entirety. In the event of a termination of this Agreement in its entirety for any reason, then, without limiting Section 10.7, the following terms and conditions shall apply as of the effective date of termination of this Agreement:

(a) the Research Term, if then in effect, shall terminate;

(b) any and all (i) rights and licenses granted by Syros hereunder other than the license described in Section 10.1, including any licenses granted pursuant to Section 3.3.1, and any sublicenses granted (directly or indirectly) thereunder, and (ii) unexercised Option rights, in each case ((i) and (ii)) shall automatically terminate;

(c) Incyte shall, and does hereby, and shall cause its Affiliates and its and their (sub)licensees to, effective as of the effective date of termination, assign to Syros all right, title and interest in and to all Program Know-How, and:

(i) as of such effective date of termination, all rights of Incyte relating to such assigned Program Know-How as provided in Sections 6.2 and 6.3 shall terminate,

(ii) as of such effective date of termination, all Program Patents shall be deemed to (A) be Reverted Target Patents and (B) [**],

(iii) as of such effective date of termination, all Program Data disclosed in published Reverted Target Patents shall be deemed to (A) be Reverted Target Data and (B) [**],

(iv) [**], and

(v) [**];

(d) all Program IP, [**], shall be deemed the Confidential Information of Syros and not the Confidential Information of Incyte;

(e) Syros' obligations under Section 3.5 shall terminate;

(f) each Party shall, upon the written request of the other Party, return or destroy the Confidential Information of the other Party in accordance with Section 7.5; and

(g) Incyte covenants to Syros that Incyte shall not, and shall cause each of its Affiliates not to, directly or indirectly, (i) use any Program Data for purposes of researching, developing or commercializing any compound or product or (ii) license, authorize, appoint or otherwise enable any Third Party to conduct any of the activities set forth in clause (i), including by assigning or otherwise granting or transferring any rights to any Third Party to or under any Program Data.

10.5.2 Termination of this Agreement other than in its Entirety. In the event of a termination of this Agreement pursuant to Section 10.3 with respect to a particular Validated Target and any and all Associated Compounds and Associated Products with respect thereto (but not in any

such case in the event of any termination of this Agreement in its entirety), (a) the provisions set forth above in Section 10.5.1 shall apply solely with respect to such Validated Target and any and all Associated Compounds and Associated Products with respect to such Validated Target and (b) without limitation to the foregoing, from and after the date of the applicable termination notice, any unexercised Option rights shall automatically terminate and Incyte shall have no further right to exercise any Options with respect to any Program Target.

10.5.3 Post-Termination Payment Obligations.

(a) Payment of Amounts Owed. If, prior to Incyte paying Syros any amounts incurred by Syros for (i) research or development costs (in the form of FTEs or out-of-pocket costs or expenses) or (ii) noncancelable commitments, this Agreement is terminated in its entirety or with respect to any Validated Target, for any reason, then Incyte shall pay to Syros any unpaid amounts then owed within [**] of the effective date of such termination.

(b) Refund of Certain Prepaid Research Amount. If this Agreement is terminated in its entirety by Incyte pursuant to Section 10.2.1 (for Syros' material breach), then provided that Incyte provides a written notice no later than [**] after the effective date of termination requesting a refund of any unexpended portion of the Prepaid Research Amount, Syros shall refund to Incyte within [**] after the later of the date of such notice or the effective date of such termination any portion of the Prepaid Research Amount for which Syros has not yet incurred research or development costs (in the form of FTEs or out-of-pocket costs or expenses) as of the effective date of such termination or made documented noncancelable commitments as of the effective date of such termination.

10.6 Other Remedies. Except as otherwise expressly provided herein, termination of this Agreement in accordance with the provisions hereof shall not limit any remedies that may otherwise be available in law or equity.

10.7 Accrued Rights; Surviving Obligations. Termination of this Agreement for any reason shall be without prejudice to any rights that shall have accrued to the benefit of a Party prior to such termination, including, for clarity, any royalties or other payments owed to Syros in relation to the period prior to such termination. Such termination shall not relieve a Party from obligations that are expressly indicated to survive the termination or expiration of this Agreement. Without limiting the foregoing, Sections 2.6.3(a) (with respect to any costs or expenses incurred prior to the effective date of termination), 2.6.3(c)(ii) (solely with respect to those amounts agreed to and incurred prior to the effective date of termination), 2.6.3(d) (with respect to any overspend incurred prior to the effective date of termination), 2.6.3(e) (with respect to any Permitted Overrun Costs incurred prior to the effective date of termination), 2.7.7 (with respect to any costs or expenses incurred or non-cancelable commitments made prior to the effective date of termination), 2.8.5(b)(iii) (second, third and fourth sentences; with respect to any costs or expenses incurred prior to the effective date of termination), 2.9(b) (with respect to any costs or expenses incurred prior to the effective date of termination), 2.11 (for the period set forth therein), 2.12.2 (penultimate sentence), 3.3.4, 5.1 (with respect to any amounts that remain unpaid as of the effective date of termination), 5.2 (with respect to any shares that remain unpurchased as of the effective date of termination), 5.3.1 (with respect to each

Definitive Research Target designated prior to the effective date of termination), 5.3.2 (with respect to each Program Target that becomes a Validated Target prior to the effective date of termination), 5.4 (with respect to any Development Milestone Events achieved thereunder prior to the effective date of termination), 5.5 (with respect to any Sales Milestone Events achieved thereunder prior to the effective date of termination), 5.6.1 (with respect to Net Sales for the period prior to the effective date of termination), 5.6.2 (for purposes of calculating surviving royalties under Section 5.6.1), 5.6.3 (with respect to Net Sales for the period prior to the effective date of termination), 5.7 through 5.9, 5.10 (for the periods set forth therein), 5.11 (for the periods set forth in Section 5.10), 6.1.1, 6.1.2, 6.1.4, 6.1.5, 6.1.6, 6.2.1, 6.2.2(c)(iii), 6.2.6 (with respect to Syros Platform Improvements), 6.2.8, 6.3.1, 6.3.6 (with respect to Syros Platform Improvements), 6.3.7 (to the extent relating to Syros Platform Improvements), 6.3.8 (to the extent relating to Syros Platform Improvements), 6.4.1, 6.4.6 (with respect to Syros Platform Improvements), 6.4.7 (with respect to Syros Platform Improvements), 6.6.1(a), 6.6.2 (with respect to any amounts owed to any Third Party in connection with the applicable Exploitation prior to the effective date of termination), 7.1 (except for clause (a) of the fourth sentence, and for the period set forth therein), 7.2.1 (for the period set forth in Section 7.1), 7.2.2 (for the period set forth in Section 7.1), 7.2.3(b) (for the period set forth in Section 7.1), 7.2.6 (for the period set forth in Section 7.1), 7.2.7 (for the period set forth in Section 7.1), 7.3 (for the period set forth in Section 7.1), 7.4 (last two sentences), 7.5, 9.1 through 9.5, 9.6 (for the periods set forth therein), 10.1 (solely in the case of expiration of this Agreement, with respect to the license described therein), 10.4, 10.5, 10.6, 11.1 through 11.14, and this Section 10.7 and Article 1 (to the extent necessary to construe the other surviving provisions) of this Agreement in its entirety shall survive the termination or expiration of this Agreement for any reason. If this Agreement is terminated pursuant to Section 10.3 with respect to a particular Validated Target and Associated Compounds and Associated Products with respect thereto (but not in any such case in the event of any termination of this Agreement in its entirety), then, following such termination, the foregoing provisions of this Agreement shall survive with respect to such Validated Target and its Associated Compounds and Associated Products, and all provisions not surviving in accordance with the foregoing shall terminate with respect to such Validated Target and its Associated Compounds and Associated Products (but, for the avoidance of doubt, all provisions of this Agreement shall remain in effect for purposes other than with respect to the terminated Validated Target(s) and Associated Compounds and Associated Products with respect thereto).

ARTICLE 11 - MISCELLANEOUS

11.1 Force Majeure. Neither Party shall be held liable or responsible to the other Party or be deemed to have defaulted under or breached this Agreement for failure or delay in fulfilling or performing any obligation under this Agreement (other than an obligation to make payments) when such failure or delay is caused by or results from events beyond the reasonable control of the non-performing Party, including fires, floods, earthquakes, hurricanes, embargoes, shortages, epidemics, quarantines, war, acts of war (whether war be declared or not), terrorist acts, insurrections, riots, civil commotion, strikes, lockouts or other labor disturbances (whether involving the workforce of the non-performing Party or of any other Person), acts of God or acts, omissions or delays in acting by any governmental authority (except to the extent such delay results from the breach by the non-performing Party or any of its Affiliates of any term or condition of this Agreement). The non-performing Party shall notify the other Party of such force majeure within thirty (30) days after such occurrence by giving written notice to the other

Party stating the nature of the event, its anticipated duration and any action being taken to avoid or minimize its effect. The suspension of performance shall be of no greater scope and no longer duration than is necessary and the non-performing Party shall use commercially reasonable efforts to remedy its inability to perform.

11.2 Assignment.

11.2.1 Neither Party may assign its rights or, except as provided in Section 3.3.3(a), delegate its obligations under this Agreement, whether by operation of law or otherwise, in whole or in part without the prior written consent of the other Party, which consent shall not be unreasonably withheld, conditioned or delayed, except that either Party shall have the right, without such consent (a) to perform any or all of its obligations and exercise any or all of its rights under this Agreement through any of its Affiliates and (b) assign its rights and delegate its obligations hereunder to any of its Affiliates or to any successor in interest (whether by merger, acquisition, asset purchase or otherwise) to all or substantially all of the business to which this Agreement relates, including, in the case of Syros, to any successor in interest (whether by merger, acquisition, asset purchase or otherwise) of the Syros Platform used in connection with the Research Plan; *provided* that (i) such Party shall provide written notice to the other Party within [**] after such assignment or delegation, (ii) such successor in interest shall assume in writing all of such Party's obligations under this Agreement and shall deliver a copy of such written assumption to the other Party, and (iii) with respect to Syros, such successor in interest to which this Agreement is assigned or one or more Affiliates of such successor in interest (which Affiliate may be Syros in the event that Syros survives as an Affiliate of such successor in interest) [**] by such successor in interest or its Affiliate until the expiration of the last to expire Option, and (B) in Section 3.3.1(b), [**]. For the avoidance of doubt, such successor in interest or its Affiliate shall have right [**] described in the foregoing clause (iii); *provided* that such successor in interest or its Affiliate [**] Incyte hereunder. Any permitted successor of a Party or any permitted assignee of all of a Party's rights under this Agreement that has also assumed all of such Party's obligations hereunder in writing shall, upon any such succession or assignment and assumption, be deemed to be a party to this Agreement as though named herein in substitution for the assigning Party, whereupon the assigning Party shall cease to be a party to this Agreement and shall cease to have any rights or obligations under this Agreement. All validly assigned rights of a Party shall inure to the benefit of and be enforceable by, and all validly delegated obligations of such Party shall be binding on and be enforceable against, the permitted successors and assigns of such Party. Any attempted assignment or delegation in violation of this Section 11.2.1 shall be void and of no effect.

11.2.2 Whether or not this Agreement is assigned pursuant to Section 11.2.1, the Parties agree as follows: (a) the rights to information, materials, Patents, Know-How or other intellectual property rights: (i) controlled by a Third Party permitted assignee of a Party or any of its Affiliates that were controlled by such assignee or any of its Affiliates (and not such Party) immediately prior to such assignment (other than as a result of a license or other grant of rights, covenant or assignment by such Party or its Affiliates to, or for the benefit of, such Third Party); or (ii) controlled by any successor-in-interest of a Party as a result of a Change of Control or any Person that becomes an Affiliate of a Party through any Change of Control of such Party, that were controlled by such successor or Person (and not such Party) immediately prior to such Change of Control (other than as a result of a license or other grant of rights, covenant or assignment by such

Party or its other Affiliates to, or for the benefit of, such Person), in each case ((i) and (ii)), shall be automatically excluded from the rights licensed or granted to the other Party under this Agreement; and (b) in the event of any assignment of this Agreement by Syros or any Change of Control of Syros, for purposes of this Agreement the "Syros Platform" shall be limited to the Syros Platform as existing immediately prior to such assignment or Change of Control and, for clarity, shall exclude any other platform or any platform improvements, including instruments, analytical methods, algorithms, procedures, reagents, techniques and software controlled by (1) a Third Party permitted assignee of Syros or any of its Affiliates or (2) any successor-in-interest of Syros as a result of a Change of Control or any Person that becomes an Affiliate of Syros through any Change of Control of Syros.

11.3 Severability. If any provision of this Agreement is held to be illegal, invalid, or unenforceable under any present or future law, and if the rights or obligations of either Party under this Agreement shall not be materially and adversely affected thereby, then (a) such provision shall be fully severable; (b) this Agreement shall be construed and enforced as if such illegal, invalid, or unenforceable provision had never comprised a part hereof; (c) the remaining provisions of this Agreement shall remain in full force and effect and shall not be affected by the illegal, invalid, or unenforceable provision or by its severance therefrom; and (d) in lieu of such illegal, invalid, or unenforceable provision, there shall be added automatically as a part of this Agreement a legal, valid, and enforceable provision as similar in terms to such illegal, invalid, or unenforceable provision as may be possible and reasonably acceptable to the Parties. To the fullest extent permitted by Applicable Law, each Party hereby waives any provision of Applicable Law that would render any provision hereof illegal, invalid, or unenforceable in any respect.

11.4 Dispute Resolution.

11.4.1 Referral to Senior Executives. Except as provided in Section 2.4.3 or 11.8, if a dispute arises between the Parties in connection with or relating to this Agreement, or any document or instrument delivered in connection herewith (collectively, a "Dispute"), then either Party shall have the right to refer such Dispute to the Senior Executives for attempted resolution by good faith negotiations during a period of [**] (the "Executive Resolution Period").

11.4.2 Resolution. Any final decision mutually agreed to by the Senior Executives shall be conclusive and binding on the Parties. If the Senior Executives are unable to resolve any such Dispute within the Officer Resolution Period, then, either Party shall be free commence litigation in accordance with Section 11.5.

11.5 Governing Law, Jurisdiction, Venue and Service.

11.5.1 Governing Law. This Agreement shall be governed by and construed in accordance with the laws of the State of Delaware, excluding any conflicts or choice of law rule or principle that might otherwise refer construction or interpretation of this Agreement to the

substantive law of another jurisdiction. The Parties agree to exclude the application to this Agreement of the United Nations Convention on Contracts for the International Sale of Goods.

11.5.2 Jurisdiction. The Parties hereby irrevocably and unconditionally consent to the jurisdiction of the State and Federal courts in the State of Delaware for any action, suit or proceeding (other than appeals therefrom) arising out of or relating to this Agreement and agree not to commence any action, suit or proceeding (other than appeals therefrom) related thereto except in such courts. The Parties irrevocably and unconditionally waive their right to a jury trial.

11.5.3 Venue. The Parties further hereby irrevocably and unconditionally waive any objection to the laying of venue of any action, suit or proceeding (other than appeals therefrom) arising out of or relating to this Agreement in the courts of the State of Delaware and hereby further irrevocably and unconditionally waive and agree not to plead or claim in any such court that any such action, suit or proceeding brought in any such court has been brought in an inconvenient forum.

11.5.4 Service. Each Party further agrees that service of any process, summons, notice or document by registered mail to its address set forth in Section 11.6 shall be effective service of process for any action, suit or proceeding brought against it under this Agreement in any such court.

11.6 Notices.

11.6.1 Notice Requirements.

(a) Subject to Section 11.6.1(b), any notice, request, demand, waiver, consent, approval or other communication permitted or required under this Agreement shall be in writing, shall refer specifically to this Agreement and shall be deemed given only if delivered by hand or by internationally recognized overnight delivery service that maintains records of delivery, addressed to a Party at its address specified in Section 11.6.2, or to such other address as such Party may have provided to the other Party in accordance with this Section 11.6. Such notice shall be deemed to have been given as of the date delivered by hand or on the second Business Day (at the place of delivery) after deposit with an internationally recognized overnight delivery service. This Section 11.6 is not intended to govern the day-to-day business communications necessary between the Parties in performing their obligations under the terms of this Agreement.

(b) Notwithstanding Section 11.6.1(a), any notice by Incyte designating Preliminary Target(s), Initial Research Target(s), Definitive Research Target(s), Extended Research Target(s) or Validated Target(s) shall be electronically mailed to Syros' Alliance Manager, with a printed copy of such electronic mail delivered to Syros' Chief Business Officer, in accordance with Section 11.6.1(a), at the address provided in Section 11.6.2. Such notice shall be deemed to have been given as of the date that the applicable electronic mail is received by Syros' Alliance Manager.

11.6.2 Addresses for Notice.

If to Syros, to:
Syros Pharmaceuticals, Inc.
620 Memorial Drive
Suite 300
Cambridge, MA 02139
Attention: Chief Business Officer

With copy to:
Syros Pharmaceuticals, Inc.
620 Memorial Drive
Suite 300
Cambridge, MA 02139
Attention: Chief Legal Officer

If to Incyte, to:
Incyte Corporation
1801 Augustine Cut-Off
Wilmington, DE 19803
Attention: CEO

With copy to:
Incyte Corporation
1801 Augustine Cut-Off
Wilmington, DE 19803
Attention: General Counsel

11.7 Entire Agreement; Amendments. This Agreement, together with the Stock Purchase Agreement, sets forth and constitute the entire agreement and understanding between the Parties with respect to the subject matter hereof, and all prior agreements, understandings, promises and representations, whether written or oral, with respect thereto, are superseded hereby; *provided* that the Confidentiality Agreement is superseded only with respect to the subject matter of this Agreement and information exchanged by the Parties prior to the Effective Date in connection with discussions or negotiations pertaining to this Agreement (which information shall constitute Confidential Information under this Agreement pursuant to Section 7.1 to the same extent as if disclosed or generated hereunder), and in other respects the Confidentiality Agreement shall remain in effect in accordance with the terms thereof. Each Party confirms that it is not relying on any representations or warranties of the other Party except as specifically set forth in this Agreement. No amendment, modification, release or discharge with respect to this Agreement (or the Research Plan hereunder) shall be binding upon the Parties unless in writing and duly executed by authorized representatives of both Parties.

11.8 Equitable Relief. Each Party acknowledges and agrees that the restrictions set forth in Section 2.14, Sections 3.5 through 3.7, Section 10.5.1(g), Article 6 and Article 7 are reasonable and necessary to protect the legitimate

interests of the other Party and that such other Party would not have entered into this Agreement in the absence of such restrictions and that any breach or threatened breach of any provision of such Articles may result in irreparable injury to such other Party for which there may be no adequate remedy at law. In the event of a breach or threatened breach of any provision of such Articles the non-breaching Party shall be authorized and entitled to seek injunctive relief from any court of competent jurisdiction, whether preliminary or permanent, specific performance and an equitable accounting of all earnings, profits and other benefits arising from such breach, which rights shall be cumulative and in addition to any other rights or remedies to which such non-breaching Party may be entitled in law or equity. Nothing in this Section 11.8 is intended or shall be construed, to limit either Party's right to equitable relief or any other remedy for a breach of any other provision of this Agreement.

11.9 Waiver and Non-Exclusion of Remedies. Any term or condition of this Agreement may be waived at any time by the Party that is entitled to the benefit thereof, but no such waiver shall be effective unless set forth in a written instrument duly executed by or on behalf of the Party waiving such term or condition. The waiver by either Party hereto of any right under this Agreement, or of the failure to perform or of a breach by the other Party, shall not be deemed a waiver of any other right under this Agreement or of any other breach or failure by such other Party whether of a similar nature or otherwise. The rights and remedies provided herein are cumulative and do not exclude any other right or remedy provided by Applicable Law or otherwise available except as expressly set forth herein.

11.10 No Benefit to Third Parties. Except as provided in Article 9, the covenants and agreements set forth in this Agreement are for the sole benefit of the Parties hereto and their successors and permitted assigns and they shall not be construed as conferring any rights on any other Persons.

11.11 Further Assurance. Each Party shall duly execute and deliver or cause to be duly executed and delivered, such further instruments and do and cause to be done such further acts and things, including the filing of such assignments, agreements, documents and instruments, as may be necessary or as the other Party may reasonably request in connection with this Agreement or to carry out more effectively the provisions and purposes hereof or to better assure and confirm unto such other Party its rights and remedies under this Agreement.

11.12 Relationship of the Parties. It is expressly agreed that Syros, on the one hand, and Incyte, on the other hand, shall be independent contractors and that the relationship between the Parties shall not constitute a partnership, joint venture or agency. Neither Syros, on the one hand, nor Incyte, on the other hand, shall have the authority to make any statements, representations or commitments of any kind, or to take any action that will be binding on the other, without the prior written consent of the other Party to do so. All persons employed by a Party shall be employees of such Party and not of the other Party and all costs and obligations incurred by reason of any such employment shall be for the account and expense of such first Party.

11.13 References. Unless otherwise specified, (a) references in this Agreement to any Article, Section or Schedule shall mean references to such Article, Section or Schedule of this Agreement; (b) references in any Section to any clause are references to such clause of such Section; and (c) references in this Agreement to any agreement, instrument or other document refer to such agreement, instrument or other document as originally executed or, if subsequently amended, replaced or supplemented from time to time, as so amended, replaced or supplemented and in effect at the relevant time of reference thereto.

11.14 Construction. Except where the context otherwise requires, wherever used, the singular shall include the plural, the plural the singular, the use of any gender shall be applicable to all genders and the word "or" is used in the inclusive sense ("and/or"). As used herein, the term "compound" is intended to include both small molecules and biologics, as applicable. Whenever this Agreement refers to a number of days, unless otherwise specified, such number refers to calendar days. The captions of this Agreement are for convenience of reference only and in no way define, describe, extend or limit the scope or intent of this Agreement or the intent of any provision contained in this Agreement. The terms "including," "include," or "includes" as used herein shall mean including, without limiting the generality of any description preceding such term. The language of this Agreement shall be deemed to be the language mutually chosen by the Parties and no rule of strict construction shall be applied against either Party hereto. When used to describe activities in Section 2.14.1 and Section 3.6 hereunder, the phrase "in connection with this Agreement" means in connection with the conduct of any activities (a) relying on or using any Syros Confidential Information or Program Know-How, (b) under the Research Plan (c) supporting a program initiated under the Research Plan or (d) enabled under the license granted to Incyte in Section 3.3.1(a).

11.15 Counterparts. This Agreement may be executed in counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. This Agreement may be executed by facsimile, PDF format via electronic mail or other electronically transmitted signatures and such signatures shall be deemed to bind each Party hereto as if they were original signatures.

[SIGNATURE PAGE FOLLOWS]

THIS AGREEMENT IS EXECUTED by the authorized representatives of the Parties and shall be effective as of the Effective Date.

Syros Pharmaceuticals, Inc.

By: /s/ Nancy Simonian

Name: Nancy Simonian, M.D.

Title: Chief Executive Officer

Date: January 8, 2018

Incyte Corporation

By: /s/ Hervé Hoppenot

Name: Hervé Hoppenot

Title: President & CEO

Date: January 8, 2018

Schedule 1.85

Initial Research Plan

Capitalized terms used without definition in this Initial Research Plan have the meanings provided in the Agreement.

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. A total of 5 pages were omitted. [**]

Schedule 3.1.5

Validated Targets

This Schedule 3.1.5 will be amended by the Parties on or after the date on which any Initial Research Target, Definitive Research Target or Extended Research Target becomes a Validated Target pursuant to Section 3.1.

Schedule 7.4

Press Release

For Immediate Release

Incyte and Syros Announce Global Target Discovery and Validation Collaboration Focused on Myeloproliferative Neoplasms

WILMINGTON, Del. AND CAMBRIDGE, Mass. January 8, 2018 – Incyte Corporation (NASDAQ:INCY) and Syros Pharmaceuticals, Inc. (NASDAQ:SYRS) announced today that the companies have entered into a target discovery, research collaboration and option agreement. Under the agreement, Syros will use its proprietary gene control platform to identify novel therapeutic targets with a focus in myeloproliferative neoplasms (MPNs), and Incyte will receive options to obtain exclusive worldwide rights to intellectual property resulting from the collaboration for up to seven validated targets. Incyte will have exclusive worldwide rights to develop and commercialize any therapies under the collaboration that modulate those validated targets.

"The discovery and development of novel therapeutic approaches to treat MPNs is an important area of focus at Incyte," said Reid Huber, Ph.D., Chief Scientific Officer of Incyte. "Through this collaboration, we believe that Syros' gene control platform will allow us to advance our understanding of the underlying biology of MPNs and potentially uncover new molecular targets for drug discovery."

"Our gene control platform has broad applicability across diseases," said Nancy Simonian, M.D., Chief Executive Officer of Syros. "By working with Incyte, a leader in the discovery, development and commercialization of therapies for MPNs, we aim to leverage the promise of our platform to benefit patients with diseases beyond our current areas of focus. Meanwhile, we can continue advancing our own pipeline to achieve our long-term goal of building a fully integrated company with therapies that make a profound difference for patients."

Terms of the Agreement

Under the terms of the agreement, Incyte will pay Syros $10 million upfront, including $2.5 million in cash and $7.5 million in prepaid R&D, and purchase a total of $10 million in Syros common stock at $12.61 per share.

Should Incyte exercise all of its options under the agreement, Syros could receive up to $54 million from Incyte in target selection and option exercise fees. For products resulting from the

collaboration against each of the up to seven selected and validated targets, Syros could receive up to $50 million in development and regulatory milestones, as well as up to $65 million in commercial milestones. Syros would also be eligible to receive low single-digit royalties on sales of products resulting from the collaboration.

The transaction is effective immediately.

About Incyte Corporation

Incyte Corporation is a Wilmington, Delaware-based biopharmaceutical company focused on the discovery, development and commercialization of proprietary therapeutics. For additional information on Incyte, please visit the Company's website at www.incyte.com.

Follow @Incyte on Twitter at https://twitter.com/Incyte.

About Syros Pharmaceuticals

Syros is pioneering the understanding of the non-coding region of the genome to advance a new wave of medicines that control expression of genes. Syros has built a proprietary platform that is designed to systematically and efficiently analyze this unexploited region of DNA in human disease tissue to identify and drug novel targets linked to genomically defined patient populations. Because gene expression is fundamental to the function of all cells, Syros' gene control platform has broad potential to create medicines that achieve profound and durable benefit across a range of diseases. Syros is currently focused on cancer and monogenic diseases and is advancing a growing pipeline of gene control medicines. Syros' lead drug candidates are SY-1425, a selective RARα agonist in a Phase 2 clinical trial for genomically defined subsets of patients with acute myeloid leukemia and myelodysplastic syndrome, and SY-1365, a selective CDK7 inhibitor in a Phase 1 clinical trial for patients with advanced solid tumors. Led by a team with deep experience in drug discovery, development and commercialization, Syros is located in Cambridge, Mass.

Forward-looking Statements

Except for the historical information set forth herein, the matters set forth in this press release contain predictions, estimates and other forward-looking statements, including without limitation statements regarding: whether the collaboration will yield any validated targets, advance the understanding of MPNs or benefit patients; whether Incyte will exercise any of its options to exclusively license any such targets; and whether and when any of the target validation fee, options exercise fees, milestone payments or royalties under this collaboration will ever be paid by Incyte. These forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially, including unanticipated developments in and risks related to: research and development efforts related to the collaboration programs; the possibility that results of clinical trials may be unsuccessful or insufficient to meet applicable regulatory standards or warrant continued development; other market or economic factors; unanticipated delays; each company's ability to compete against parties with greater financial or other resources; greater than expected expenses; and such other risks detailed from time to time in each company's reports filed with the Securities and Exchange Commission, including the Form 10-Q for the quarter ended September 30, 2017 filed by each company. Each party disclaims any intent or obligation to update these forward-looking statements.

# # #

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Investors
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Investors
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+1 212 362 1200
hannahd@sternir.com

Exhibit 21.1

Subsidiaries of the Registrant

Syros Securities Corporation, a Massachusetts corporation and wholly-owned subsidiary of the Registrant.

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

1. Registration Statement (Form S-8 No. 333-212363) pertaining to the 2012 Equity Incentive Plan, 2016 Stock Incentive Plan, and 2016 Employee Stock Purchase Plan of Syros Pharmaceuticals, Inc.,

2. Registration Statement (Form S-8 No. 333-216821) pertaining to the 2016 Stock Incentive Plan and 2016 Employee Stock Purchase Plan of Syros Pharmaceuticals, Inc.,

3. Registration Statement (Form S-3 No. 333-222634) of Syros Pharmaceuticals, Inc.,

4. Registration Statement (Form S-3 No. 333-219369) of Syros Pharmaceuticals, Inc., and

5. Registration Statement (Form S-1 No. 333-218012) of Syros Pharmaceuticals, Inc.;

of our report dated March 12, 2018, with respect to the consolidated financial statements of Syros Pharmaceuticals, Inc., included in this Annual Report (Form 10-K) for the year ended December 31, 2017.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 12, 2018

Exhibit 31.1

CERTIFICATIONS

I, Nancy Simonian, certify that:

1. I have reviewed this Annual Report on Form 10-K of Syros Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 12, 2018

By:/s/ Nancy Simonian, M.D.
Nancy Simonian, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, Nancy Simonian, certify that:

1. I have reviewed this Annual Report on Form 10-K of Syros Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 12, 2018

By:/s/ Nancy Simonian, M.D.
Nancy Simonian, M.D.
President and Chief Executive Officer
(Principal Financial Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Syros Pharmaceuticals, Inc. (the "Company") for the fiscal year ended December 31, 2017 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Nancy Simonian, President and Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of her knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 12, 2018

By: /s/ Nancy Simonian, M.D.
Nancy Simonian, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Syros Pharmaceuticals, Inc. (the "Company") for the fiscal year ended December 31, 2017 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Nancy Simonian, President and Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to the best of his knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 12, 2018

By: /s/ Nancy Simonian, M.D.
Nancy Simonian, M.D.
President and Chief Executive Officer
(Principal Financial Officer)