Use these links to rapidly review the document
TABLE OF CONTENTS

Table of Contents

As filed with the Securities and Exchange Commission on January 19, 2018

Registration No. 333-

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

FORM S-3
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

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 Number)

620 Memorial Drive, Suite 300
Cambridge, Massachusetts 02139
(617) 744-1340
(Address, Including Zip Code, and Telephone Number, Including Area Code, of Registrant's Principal Executive Offices)

Nancy Simonian, M.D.
President and Chief Executive Officer
Syros Pharmaceuticals, Inc.
620 Memorial Drive, Suite 300
Cambridge, Massachusetts 02139
(617) 744-1340
(Name, Address, Including Zip Code, and Telephone Number, Including Area Code, of Agent for Service)

Copies to:

Gerald E. Quirk
Chief Legal and Administrative Officer and Secretary
Syros Pharmaceuticals, Inc.
620 Memorial Drive, Suite 300
Cambridge, Massachusetts 02139
Telephone: (617) 744-1340

Steven D. Singer
Cynthia T. Mazareas
Wilmer Cutler Pickering Hale and Dorr LLP
60 State Street
Boston, Massachusetts 02109
Telephone: (617) 526-6000
Fax: (617) 526-5000

Approximate date of commencement of proposed sale to the public:
From time to time after this registration statement becomes effective.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box. ☐

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box. ☒

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

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

If this Form is a registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box. ☐

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

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

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act. ☒

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities To Be Registered	Amount to be Registered(1)(2)	Proposed Maximum Offering Price Per Share(3)	Proposed Maximum Aggregate Offering Price(3)	Amount of Registration Fee(3)
Common Stock, $0.001 par value per share	793,021	$10.65	$8,445,674	$1,051.49

(1) The shares will be offered for resale by a selling stockholder pursuant to the prospectus contained herein.

(2) Pursuant to Rule 416 under the Securities Act, this registration statement also covers any additional number of shares of common stock issuable upon stock splits, stock dividends, or other distribution, recapitalization or similar events with respect to the shares of common stock being registered pursuant to this registration statement.

(3) Estimated solely for purposes of calculating the registration fee pursuant to Rule 457(c) under the Securities Act, based on average of high and low price per share of the common stock as reported on the Nasdaq Global Select Market on January 16, 2018.

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

Table of Contents

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

Subject to completion, dated January 19, 2018

PROSPECTUS

793,021 Shares

Common Stock

This prospectus relates to the resale of up to 793,021 shares of our common stock by the selling stockholder listed on page 8, including its transferees, pledgees, donees, assignees or successors-in-interest, which shares were issued to the selling stockholder in a private placement. We are registering these shares on behalf of the selling stockholder, to be offered and sold by it from time to time.

We will not receive any proceeds from the sale of the shares.

The selling stockholder identified in this prospectus, or its pledgees, donees, transferees, assignees or other successors-in-interest, may offer the shares from time to time on terms to be determined at the time of sale through ordinary brokerage transactions or through any other means described in this prospectus under the caption "Plan of Distribution." The shares may be sold at fixed prices, at prevailing market prices, at prices related to prevailing market prices or at negotiated prices.

Our common stock is listed on the Nasdaq Global Select Market ("Nasdaq") under the symbol "SYRS." On January 16, 2018, the last reported closing sale price of our common stock on Nasdaq was $10.52 per share.

We are an "emerging growth company" under applicable Securities and Exchange Commission rules and, as such, have elected to comply with certain reduced public company disclosure requirements for this prospectus and future filings. See "Prospectus Summary—Implications of Being an Emerging Growth Company."

Investing in our common stock involves a high degree of risk. These risks are described in the section titled "Risk Factors" beginning on page 4 of this prospectus.

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

The date of this prospectus is , 2018.

TABLE OF CONTENTS

You should rely only on the information contained or incorporated by reference in this prospectus. We have not authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. This prospectus may only be used where it is legal to offer and sell shares of our common stock. If it is against the law in any jurisdiction to make an offer to sell these shares, or to solicit an offer from someone to buy these shares, then this prospectus does not apply to any person in that jurisdiction, and no offer or solicitation is made by this prospectus to any such person. You should assume that the information appearing in this prospectus is accurate only as of the date on the front cover of this prospectus, regardless of the time of delivery of this prospectus or of any sale of common stock. Our business, financial condition, results of operations and prospects may have changed since such date.

PROSPECTUS SUMMARY

This summary highlights, and is qualified in its entirety by, the more detailed information included elsewhere in this prospectus or incorporated by reference in this prospectus. This summary does not contain all of the information that you should consider before investing. You should read and carefully consider the entire prospectus, especially the "Risk Factors" section of this prospectus, before deciding to invest in our common stock.

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 and drug novel targets linked to genomically defined patient populations. 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 genetic diseases and are building a pipeline of gene control medicines. Our lead drug candidates are SY-1425, a selective retinoic acid receptor alpha, or RARa, agonist that is being evaluated in combination with azacitidine, a hypomethylating agent, and with daratumumab, an anti-CD38 therapeutic antibody, in a Phase 2 clinical trial in genomically defined subsets of patients with acute myeloid leukemia and myelodysplastic syndrome, 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. We also have multiple programs in earlier stages of research and development in oncology, including immuno-oncology, and genetic diseases. Our goal is to build a fully integrated biopharmaceutical company based on our leadership position in gene control.

Corporate Information

We were incorporated under the laws of the State of Delaware on November 9, 2011 under the name LS22, Inc. Our executive offices are located at 620 Memorial Drive, Suite 300, Cambridge, Massachusetts 02139, and our telephone number is (617) 744-1340. Our website address is www.syros.com. The information contained on, or that can be accessed through, our website is not a part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

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

The Syros logo, "Syros" and "Syros Pharmaceuticals" are our trademarks. Solely for convenience, the trademarks and trade names in this prospectus are referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. The trademarks, trade names and service marks appearing in this prospectus are the property of their respective owners.

Implications of Being an Emerging Growth Company

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. As a result, we may take advantage of reduced reporting requirements that are otherwise applicable to public companies, including delaying auditor attestation of internal control over financial reporting and reducing executive compensation disclosures. The JOBS Act also provides that an emerging growth company can take advantage of an extended transition period for complying with

new or revised accounting standards. We have irrevocably elected not to avail ourselves of this exemption and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies. Because we intend to rely on certain disclosure and other requirements of the JOBS Act, the information contained herein may be different than the information you receive from other public companies in which you hold stock. In addition, it is possible that some investors will find our common stock less attractive as a result of our determination to avail ourselves of exemptions under the JOBS Act, which may result in a less active trading market for our common stock and higher volatility in our stock price. We will remain an emerging growth company until the earlier to occur of: (1) the last day of the fiscal year in which we have total annual gross revenues of $1.07 billion or more; (2) the last day of the fiscal year following the fifth anniversary of the date of the closing of our initial public offering; (3) the date on which we have issued more than $1.0 billion in nonconvertible debt during the previous three years; or (4) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission.

THE OFFERING

Common stock offered by selling stockholders	793,021 shares
Terms of the offering	The selling stockholder, including its transferees, donees, pledgees, assignees or successors-in-interest, may sell, transfer or otherwise dispose of any or all of the shares of common stock offered by this prospectus from time to time on the Nasdaq Global Select Market or any other stock exchange, market or trading facility on which the shares are traded or in private transactions. The shares of common stock may be sold at fixed prices, at prevailing market prices, at prices related to prevailing market prices or at negotiated prices.
Use of proceeds	We will not receive any proceeds from the sale of shares in this offering.
Risk factors	You should read the "Risk Factors" section on page 4 of this prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.
Nasdaq Global Select Market symbol	"SYRS"

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before you decide to invest in our common stock, you should carefully consider the risks described in the section captioned "Risk Factors" in our most recent Annual Report on Form 10-K, our most recent Quarterly Report on Form 10-Q and other filings we make with the Securities and Exchange Commission, or SEC, from time to time, which are incorporated by reference herein in their entirety, together with the other information in this prospectus and documents incorporated by reference in this prospectus. The risks described in our most recent Annual Report on Form 10-K, our most recent Quarterly Report on Form 10-Q and the other filings incorporated by reference herein are not the only ones facing our company. Additional risks and uncertainties may also impair our business operations. If any of the risks described in our most recent Annual Report on Form 10-K, our most recent Quarterly Report on Form 10-Q and the other filings incorporated by reference herein occurs, our business, financial condition, results of operations and future growth prospects could be harmed. In these circumstances, the market price of our common stock could decline, and you may lose all or part of your investment.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This prospectus and the documents incorporated by reference herein contain forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this prospectus or incorporated by reference herein, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management and expected market growth, are forward-looking statements. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. The forward-looking statements and opinions contained in this prospectus and incorporated by reference herein are based upon information available to us as of the date such statements are made and, while we believe such information forms a reasonable basis for such statements at the time made, 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 plans to seek to enter into collaborations for the development and commercialization of certain product candidates;
- whether the collaboration with Incyte Corporation, or Incyte, will yield any validated targets, whether Incyte will exercise any of its options to exclusively license any such targets, and whether and when any of the target validation fees, options 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;
- the impact of government laws and regulations; and
- other risks and uncertainties, including those listed under the caption "Risk Factors" in our most recent Annual Report on Form 10-K, our most recent Quarterly Report on Form 10-Q, and other filings we make with the SEC.

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

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

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

USE OF PROCEEDS

We are filing the registration statement of which this prospectus is a part to permit the holder of the shares of our common stock described in the section entitled "Selling Stockholder" to resell such shares. We are not selling any securities under this prospectus and we will not receive any proceeds from the sale of shares by the selling stockholder.

The selling stockholder will pay any underwriting discounts and commissions and expenses incurred by the selling stockholder for brokerage, accounting, tax or legal services or any other expenses incurred by the selling stockholder in disposing of the shares. We will bear all other costs, fees and expenses incurred in effecting the registration of the shares covered by this prospectus, including, without limitation, all registration and filing fees, Nasdaq listing fees and fees and expenses of our counsel and our accountants.

SELLING STOCKHOLDER

This prospectus relates to the possible sale by Incyte Corporation, or Incyte, who we refer to in this prospectus as the "selling stockholder," of up to 793,021 shares of our common stock (plus an indeterminate number of shares of our common stock that may be issued upon stock splits, stock dividends, or similar transactions, in accordance with Rule 416 under the Securities Act) that were issued to the selling stockholder on January 8, 2018, pursuant to a stock purchase agreement. See "Relationship with Selling Stockholder" below for more information regarding the transaction to which these shares of common stock relate.

The table below sets forth, to our knowledge, information concerning the beneficial ownership of shares of our common stock by the selling stockholder as of January 16, 2018. The selling stockholder may sell all, some or none of the shares of common stock subject to this prospectus. See "Plan of Distribution."

The information in the table below with respect to the selling stockholder has been obtained from the selling stockholder, with beneficial ownership and percentage ownership determined in accordance with the rules and regulations of the SEC and including voting or investment power with respect to shares. Unless otherwise indicated below, to our knowledge, the person named in the table has sole voting and investment power with respect to such person's shares of common stock. The inclusion of any shares in this table does not constitute an admission of beneficial ownership for the person named below. The percentage of beneficial ownership is based upon 27,226,781 shares of common stock outstanding on January 16, 2018.

To our knowledge and except as noted under the caption titled "Relationship with Selling Stockholder" below, the selling stockholder does not have, and within the past three years has not had, any position, office or other material relationship with us or any of our predecessors or affiliates.

	Shares of Common Stock Beneficially Owned Prior to Offering		Number of Shares of Common Stock Being Offered	Shares of Common Stock to be Beneficially Owned After Offering(1)	
Name of Selling Stockholder	Number	Percentage		Number	Percentage
Incyte Corporation(2)	793,021	2.91%	793,021	0	—

(1) We do not know when or in what amounts the selling stockholder may offer shares for sale. The selling stockholder might not sell any or all of the shares offered by this prospectus. Because the selling stockholder may offer all or some of the shares pursuant to this offering, and because there are currently no agreements, arrangements or understandings with respect to the sale of any of the shares, we cannot estimate the number of the shares that will be held by the selling stockholder after completion of the offering. However, for purposes of this table, we have assumed that, after completion of the offering, none of the shares covered by this prospectus will be held by the selling stockholder.

(2) The address of Incyte Corporation is 1801 Augustine Cut-Off, Wilmington, DE 19803.

Relationship with Selling Stockholder

Collaboration Agreement

On January 8, 2018, we entered into a Target Discovery, Research Collaboration and Option Agreement, or collaboration agreement, with Incyte. Under the collaboration agreement, we will use our 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 us $10.0 million in up-front consideration, consisting of $2.5 million in cash and $7.5 million in prepaid research funding. Our activities under the collaboration 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.

Should Incyte exercise all of its options under the agreement, we 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, we could receive up to $50 million in development and regulatory milestones, as well as up to $65 million in commercial milestones. We would also be eligible to receive low single-digit royalties on sales of products resulting from the collaboration.

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 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 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.

The foregoing description of the material terms of the collaboration agreement is qualified in its entirety by the terms of the collaboration agreement, which we intend to file as an exhibit to our Annual Report on Form 10-K for the fiscal year ended December 31, 2017.

Stock Purchase Agreement

In addition, on January 8, 2018, we entered into a stock purchase agreement with Incyte, pursuant to which Incyte purchased 793,021 shares of our common stock for an aggregate purchase price of $10.0 million in cash, or $12.61 per share, in a private placement. 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.

Pursuant to the terms of the stock purchase agreement, we agreed to file a registration statement covering the resale by Incyte of the shares within 20 days following the closing. We agreed to use commercially reasonable efforts to cause such registration statement to become effective no later than the last day of the fiscal quarter in which the shares are delivered to Incyte, and to keep such registration statement effective until the date the shares covered by such registration statement have been sold or may be sold without volume restrictions pursuant to Rule 144 under the Securities Act of 1933, as amended. We agreed to be responsible for all fees and expenses incurred in connection with the registration of the shares for resale. We granted to Incyte, and Incyte granted to us, customary indemnification rights in connection with the registration statement.

In addition, from the closing until the earlier of the second anniversary of the 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.

The foregoing description of the terms and conditions of the stock purchase agreement does not purport to be complete and is qualified in its entirety by reference to the full text of such document, which is attached hereto as Exhibit 4.4 and incorporated by reference herein.

PLAN OF DISTRIBUTION

The shares covered by this prospectus may be offered and sold from time to time by the selling stockholder. The term "selling stockholder" includes donees, pledgees, transferees, assignees or other successors-in-interest selling shares received after the date of this prospectus from the selling stockholder as a gift, pledge, partnership distribution or other non-sale related transfer. The selling stockholder will act independently of us in making decisions with respect to the timing, manner and size of each sale. Such sales may be made on one or more exchanges, market or trading facilities, in the over-the-counter market or otherwise, at prices and under terms then prevailing or at prices related to the then current market price, at fixed prices or in negotiated transactions. The selling stockholder may sell its shares by one or more of, or a combination of, the following methods:

- purchases by a broker-dealer as principal and resale by such broker-dealer for its own account pursuant to this prospectus;
- ordinary brokerage transactions and transactions in which the broker solicits purchasers;
- block trades in which the broker-dealer so engaged will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- an exchange distribution in accordance with the rules of the applicable exchange;
- in privately negotiated transactions;
- broker-dealers may agree with the selling stockholder to sell a specified number of such shares at a stipulated price per share;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise; or
- any other method permitted pursuant to applicable law.

In addition, any shares that qualify for sale pursuant to Rule 144 may be sold under Rule 144 rather than pursuant to this prospectus.

To the extent required, this prospectus may be amended or supplemented from time to time to describe a specific plan of distribution. In connection with distributions of the shares or otherwise, the selling stockholder may enter into hedging transactions with broker-dealers or other financial institutions. In connection with such transactions, broker-dealers or other financial institutions may engage in short sales of the common stock in the course of hedging the positions they assume with the selling stockholder. The selling stockholder may also sell the common stock short and redeliver the shares to close out such short positions. The selling stockholder may also enter into option or other transactions with broker-dealers or other financial institutions which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction). The selling stockholder may also pledge shares to a broker-dealer or other financial institution, and, upon a default, such broker-dealer or other financial institution, may effect sales of the pledged shares pursuant to this prospectus (as supplemented or amended to reflect such transaction).

In effecting sales, broker-dealers or agents engaged by the selling stockholder may arrange for other broker-dealers to participate. Broker-dealers or agents may receive commissions, discounts or concessions from the selling stockholder in amounts to be negotiated immediately prior to the sale.

In offering the shares covered by this prospectus, the selling stockholder and any broker-dealers who execute sales for the selling stockholder may be deemed to be "underwriters" within the meaning

of the Securities Act in connection with such sales. Any profits realized by the selling stockholder and the compensation of any broker-dealer may be deemed to be underwriting discounts and commissions.

In order to comply with the securities laws of certain states, if applicable, the shares must be sold in such jurisdictions only through registered or licensed brokers or dealers. In addition, in certain states the shares may not be sold unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and is complied with.

We have advised the selling stockholder that the anti-manipulation rules of Regulation M under the Exchange Act may apply to sales of shares in the market and to the activities of the selling stockholder and their affiliates. In addition, we will make copies of this prospectus available to the selling stockholder for the purpose of satisfying the prospectus delivery requirements of the Securities Act. The selling stockholder may indemnify any broker-dealer that participates in transactions involving the sale of the shares against certain liabilities, including liabilities arising under the Securities Act.

At the time a particular offer of shares is made, if required, a prospectus supplement will be distributed that will set forth the number of shares being offered and the terms of the offering, including the name of any underwriter, dealer or agent, the purchase price paid by any underwriter, any discount, commission and other item constituting compensation, any discount, commission or concession allowed or reallowed or paid to any dealer, and the proposed selling price to the public.

We have agreed to indemnify the selling stockholder against certain liabilities, including certain liabilities under the Securities Act.

We have agreed with the selling stockholder to keep the registration statement of which this prospectus constitutes a part effective until the earlier of (i) such time as all of the shares covered by this prospectus have been disposed of pursuant to and in accordance with the registration statement or (ii) the date on which all of the shares may be sold without volume restrictions pursuant to Rule 144 of the Securities Act.

LEGAL MATTERS

The validity of the shares of our common stock offered hereby is being passed upon for us by Wilmer Cutler Pickering Hale and Dorr LLP.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2016, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file reports, proxy statements and other documents with the SEC. You may read and copy any document we file at the SEC's public reference room at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You should call 1-800-SEC-0330 for more information on the public reference room. Our SEC filings are also available to you on the SEC's Internet site at www.sec.gov.

This prospectus is part of a registration statement that we filed with the SEC. The registration statement contains more information than this prospectus regarding us and our common stock, including certain exhibits and schedules. You can obtain a copy of the registration statement from the SEC at the address listed above or from the SEC's Internet site.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The SEC requires us to "incorporate" into this prospectus information that we file with the SEC in other documents. This means that we can disclose important information to you by referring to other documents that contain that information. The information incorporated by reference is considered to be part of this prospectus. Information contained in this prospectus and information that we file with the SEC in the future and incorporate by reference in this prospectus automatically updates and supersedes previously filed information. We incorporate by reference the documents listed below and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus and prior to the sale of all the shares covered by this prospectus.

(1) Our Annual Report on Form 10-K for the year ended December 31, 2016, filed with the SEC on March 20, 2017 (including information specifically incorporated by reference therein from our Proxy Statement filed with the SEC on April 25, 2017);

(2) Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2017, filed with the SEC on May 15, 2017;

(3) Our Quarterly Report on Form 10-Q for the quarter ended June 30, 2017, filed with the SEC on August 9, 2017;

(4) Our Quarterly Report on Form 10-Q for the quarter ended September 30, 2017, filed with the SEC on November 8, 2017;

(5) Our Current Reports on Form 8-K filed with the SEC on January 9, 2017 (except Item 2.02), January 30, 2017, April 21, 2017, April 26, 2017, June 12, 2017, September 29, 2017, December 11, 2017, January 8, 2018 (except Item 7.01) and January 12, 2018;

(6) The description of our common stock contained in our Registration Statement on Form 8-A/A filed on July 20, 2017, including any amendments or reports filed for the purpose of updating such description; and

(7) Any other filings we make pursuant to the Exchange Act after the date of filing the registration statement of which this prospectus is a part and prior to effectiveness of the registration statement.

A statement contained in a document incorporated by reference into this prospectus shall be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus, any prospectus supplement or in any other subsequently filed document which is also incorporated in this prospectus modifies or replaces such statement. Any statements so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

You may request a copy of these documents, which will be provided to you at no cost, by writing or telephoning us using the following contact information:

Syros Pharmaceuticals, Inc.
620 Memorial Drive, Suite 300
Cambridge, Massachusetts, 02139
Attention: Gerald E. Quirk, Chief Legal and Administrative Officer & Secretary
Telephone: (617) 744-1340

793,021 Shares

Common Stock

PROSPECTUS

, 2018

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution.

Set forth below are estimates (except in the case of the SEC registration fee) of the amount of fees and expenses to be incurred in connection with the issuance and distribution of the offered securities, other than underwriting discounts and commissions.

SEC registration fee	$ 1,052
Accounting fees and expenses	10,000
Legal fees and expenses	40,000
Miscellaneous fees and expenses	3,948
Total	$ 55,000

Item 15. Indemnification of Directors and Officers.

Section 145 of the General Corporation Law of the State of Delaware ("DGCL") provides, generally, that a corporation shall have the power to indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding (except actions by or in the right of the corporation) by reason of the fact that such person is or was a director, officer, employee or agent of the corporation against all expenses, judgments, fines and amounts paid in settlement actually and reasonably incurred by such person in connection with such action, suit or proceeding if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the corporation and, with respect to any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful. A corporation may similarly indemnify such person for expenses actually and reasonably incurred by such person in connection with the defense or settlement of any action or suit by or in the right of the corporation, *provided* that such person acted in good faith and in a manner he or she reasonably believed to be in or not opposed to the best interests of the corporation, and, in the case of claims, issues and matters as to which such person shall have been adjudged liable to the corporation, *provided* that a court shall have determined, upon application, that, despite the adjudication of liability but in view of all of the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which such court shall deem proper.

Section 102(b)(7) of the DGCL provides, generally, that our certificate of incorporation may contain a provision eliminating or limiting the personal liability of a director to the corporation or its shareholders for monetary damages for breach of fiduciary duty as a director, *provided* that such provision may not eliminate or limit the liability of a director (i) for any breach of the director's duty of loyalty to the corporation or its shareholders, (ii) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (iii) under section 174 of the DGCL, or (iv) for any transaction from which the director derived an improper personal benefit. No such provision may eliminate or limit the liability of a director for any act or omission occurring prior to the date when such provision became effective.

Our restated certificate of incorporation provides that we will indemnify each person who was or is a party or threatened to be made a party to or is involved in any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of us) by reason of the fact that he or she is or was, or has agreed to become, our director or officer, or is or was serving, or has agreed to serve, at our request as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (all such persons being referred to as an "Indemnitee"), or by reason

of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding and any appeal therefrom, if such Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, our best interests, and, with respect to any criminal action or proceeding, he or she had no reasonable cause to believe his or her conduct was unlawful. Our restated certificate of incorporation also provides that we will indemnify any Indemnitee who was or is a party to an action or suit by or in the right of us to procure a judgment in our favor by reason of the fact that the Indemnitee is or was, or has agreed to become, our director or officer, or is or was serving, or has agreed to serve, at our request as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise, or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees) and, to the extent permitted by law, amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding, and any appeal therefrom, if the Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, our best interests, except that no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to us, unless a court determines that, despite such adjudication but in view of all of the circumstances, he or she is entitled to indemnification of such expenses. Notwithstanding the foregoing, to the extent that any Indemnitee has been successful, on the merits or otherwise, he or she will be indemnified by us against all expenses (including attorneys' fees) actually and reasonably incurred by him or her or on his or her behalf in connection therewith. If we do not assume the defense, expenses must be advanced to an Indemnitee under certain circumstances.

We have entered into indemnification agreements with our directors and executive officers. In general, these agreements provide that we will indemnify the director or executive officer to the fullest extent permitted by law for claims arising in his or her capacity as a director or officer of our company or in connection with their service at our request for another corporation or entity. The indemnification agreements also provide for procedures that will apply in the event that a director or executive officer makes a claim for indemnification and establish certain presumptions that are favorable to the director or executive officer.

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

Certain of our non-employee directors may, through their relationships with their employers, be insured and/or indemnified against certain liabilities in their capacity as members of our board of directors.

The underwriting agreement we entered into in connection with the initial public offering of our common stock provides that the underwriters will indemnify, under certain conditions, our directors and officers (as well as certain other persons) against certain liabilities arising in connection with such offering.

Insofar as the forgoing provisions permit indemnification of directors, executive officers, or persons controlling us for liability arising under the Securities Act of 1933, as amended, or the Securities Act, we have been informed that, in the opinion of the Securities and Exchange Commission, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

Item 16. Exhibits

Exhibit No.	Description
4.1	Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K filed with the SEC on July 6, 2016 (File No. 001-37813))
4.2	Amended and Restated By-laws of the Registrant (incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K filed with the SEC on July 6, 2016 (File No. 001-37813))
4.3	Second Amended and Restated Investors' Rights Agreement dated October 9, 2014, as amended, among the Registrant and the other parties thereto (incorporated by reference to Exhibit 4.2 to the Registrant's Registration Statement on Form S-1 filed with the SEC on June 3, 2016 (File No. 333-211818))
4.4	Stock Purchase Agreement, dated January 8, 2018, among the Registrant and Incyte Corporation
5.1	Opinion of Wilmer Cutler Pickering Hale and Dorr LLP
23.1	Consent of Ernst & Young LLP, independent registered public accounting firm
23.2	Consent of Wilmer Cutler Pickering Hale and Dorr LLP (included in Exhibit 5.1)
24.1	Powers of Attorney (included in the signature pages to the Registrant's Registration Statement)

Item 17. Undertakings.

The undersigned Registrant hereby undertakes:

(a) (1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) to include any prospectus required by Section 10(a)(3) of the Securities Act of 1933, as amended (the "Securities Act");

(ii) to reflect in the prospectus any facts or events arising after the effective date of this registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in this registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and

(iii) to include any material information with respect to the plan of distribution not previously disclosed in this registration statement or any material change to such information in this registration statement;

provided, *however*, that paragraphs (a)(1)(i), (a)(1)(ii) and (a)(1)(iii) do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the Registrant pursuant to Section 13 or Section 15(d) of the

Securities Exchange Act of 1934, as amended (the "Exchange Act"), that are incorporated by reference in this registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of this registration statement.

(2) That, for the purposes of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at the time shall be deemed to be the initial *bona fide* offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(4) That, for the purpose of determining liability under the Securities Act to any purchaser:

(i) each prospectus filed by the Registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(ii) each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5), or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii) or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof; *provided, however*, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date.

(b) The undersigned Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of the Registrant's annual report pursuant to Section 13(a) or 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Exchange Act) that is incorporated by reference in this registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(c) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to the indemnification provisions described herein, or otherwise, the Registrant has been advised that in the opinion of the Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Cambridge, Commonwealth of Massachusetts, on January 19, 2018.

SYROS PHARMACEUTICALS, INC.

By: /s/ NANCY SIMONIAN

Name: Nancy Simonian, M.D.
Title: *President, Chief Executive Officer and Director*

SIGNATURES AND POWER OF ATTORNEY

We, the undersigned officers and directors of Syros Pharmaceuticals, Inc., hereby severally constitute and appoint Nancy Simonian and Gerald Quirk, and each of them singly, our true and lawful attorneys with full power to any of them, and to each of them singly, to sign for us and in our names in the capacities indicated below the Registration Statement on Form S-3 filed herewith and any and all pre-effective and post-effective amendments to said Registration Statement and generally to do all such things in our name and behalf in our capacities as officers and directors to enable Syros Pharmaceuticals, Inc. to comply with the provisions of the Securities Act of 1933, as amended, and all requirements of the Securities and Exchange Commission, hereby ratifying and confirming our signatures as they may be signed by our said attorneys, or any of them, to said Registration Statement and any and all amendments thereto.

Pursuant to the requirements of the Securities Act of 1933, as amended, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
/s/ NANCY SIMONIAN Nancy Simonian, M.D.	President, Chief Executive Officer and Director (principal executive officer and principal financial officer)	January 19, 2018
/s/ COLLEEN DESIMONE Colleen DeSimone	Vice President, Finance (principal accounting officer)	January 19, 2018
/s/ SRINIVAS AKKARAJU Srinivas Akkaraju, M.D., Ph.D.	Director	January 19, 2018
/s/ MARSHA H. FANUCCI Marsha H. Fanucci	Director	January 19, 2018

Signature	Title	Date
/s/ AMIR NASHAT Amir Nashat, Ph.D.	Director	January 19, 2018
/s/ ROBERT T. NELSEN Robert T. Nelsen	Director	January 19, 2018
/s/ SANJ K. PATEL Sanj K. Patel	Director	January 19, 2018
/s/ VICKI L. SATO Vicki L. Sato, Ph.D.	Director	January 19, 2018
/s/ PHILLIP A. SHARP Phillip A. Sharp, Ph.D.	Director	January 19, 2018
/s/ PETER WIRTH Peter Wirth	Director	January 19, 2018
/s/ RICHARD A. YOUNG Richard A. Young, Ph.D.	Director	January 19, 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.

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

Exhibit 5.1

WILMERHALE

+1 617 526 6000 (t)
+1 617 526 5000 (f)
wilmerhale.com

January 19, 2018

Syros Pharmaceuticals, Inc.
620 Memorial Drive, Suite 300
Cambridge, MA 02139

Registration Statement on Form S-3

Ladies and Gentlemen:

This opinion is furnished to you in connection with a Registration Statement on Form S-3 (the "Registration Statement") filed with the Securities and Exchange Commission (the "Commission") under the Securities Act of 1933, as amended (the "Securities Act"), for the registration of the resale of an aggregate of 793,021 shares (the "Shares") of common stock, $0.001 par value per share (the "Common Stock"), of Syros Pharmaceuticals, Inc., a Delaware corporation (the "Company"). All of the Shares are being registered on behalf of certain stockholders of the Company (the "Selling Stockholder").

We are acting as counsel for the Company in connection with the registration for resale of the Shares. We have examined signed copies of the Registration Statement as filed with the Commission. We have also examined and relied upon minutes of meetings of the stockholders and the Board of Directors of the Company as provided to us by the Company, the Certificate of Incorporation and By-Laws of the Company, each as restated and/or amended to date, and such other documents as we have deemed necessary for purposes of rendering the opinions hereinafter set forth.

In our examination of the foregoing documents, we have assumed the genuineness of all signatures, the authenticity of all documents submitted to us as originals, the conformity to original documents of all documents submitted to us as copies, the authenticity of the originals of such latter documents and the legal competence of all signatories to such documents.

Our opinion below, insofar as it relates to the Shares being fully paid, is based solely on a certificate of the Chief Executive Officer of the Company confirming the Company's receipt of the consideration called for by the applicable resolutions authorizing the issuance of such Shares.

We assume that the appropriate action will be taken, prior to the offer and sale of the Shares by the Selling Stockholder, to register and qualify the Shares for sale under all applicable state securities or "blue sky" laws.

We express no opinion herein as to the laws of any state or jurisdiction other than the state laws of the Commonwealth of Massachusetts, the General Corporation Law of the State of Delaware and the federal laws of the United States of America.

Based upon and subject to the foregoing, we are of the opinion that the Shares have been duly authorized for issuance and are validly issued, fully paid and nonassessable.

It is understood that this opinion is to be used only in connection with the offer and sale of the Shares while the Registration Statement is in effect.

Please note that we are opining only as to the matters expressly set forth herein, and no opinion should be inferred as to any other matters. This opinion is based upon currently existing statutes, rules, regulations and judicial decisions, and we disclaim any obligation to advise you of any change in any of these sources of law or subsequent legal or factual developments which might affect any matters or opinions set forth herein.

We hereby consent to the filing of this opinion with the Commission as an exhibit to the Registration Statement in accordance with the requirements of Item 601(b)(5) of Regulation S-K under the Securities Act and to the use of our name therein and in the related Prospectus under the caption "Legal Matters." In giving such consent, we do not hereby admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations of the Commission.

Very truly yours,

WILMER CUTLER PICKERING

HALE AND DORR LLP

By: /s/ Cynthia Mazareas
Cynthia Mazareas, a Partner

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the reference to our firm under the caption "Experts" in the Registration Statement on Form S-3 and related Prospectus of Syros Pharmaceuticals, Inc. for the registration of 793,021 shares of its common stock and to the incorporation by reference therein of our report dated March 20, 2017, with respect to the consolidated financial statements of Syros Pharmaceuticals, Inc., included in its Annual Report on Form 10-K for the year ended December 31, 2016, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

Boston, Massachusetts
January 17, 2018