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

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**FORM S-8  
REGISTRATION STATEMENT**  
*UNDER  
THE SECURITIES ACT OF 1933*

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**SYROS PHARMACEUTICALS, INC.**  
(Exact Name of Registrant as Specified in Its Charter)

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**Delaware**  
(State or Other Jurisdiction of  
Incorporation or Organization)

**45-3772460**  
(I.R.S. Employer  
Identification No.)

**35 CambridgePark Drive, 4th Floor**  
**Cambridge, Massachusetts**  
(Address of Principal Executive Offices)

**02140**  
(Zip Code)

**2016 Stock Incentive Plan**  
**2016 Employee Stock Purchase Plan**  
(Full Title of the Plan)

**Nancy Simonian, M.D.**  
**President and Chief Executive Officer**  
**Syros Pharmaceuticals, Inc.**  
**35 CambridgePark Drive, 4th Floor**  
**Cambridge, Massachusetts**  
(Name and Address of Agent for Service)

**(617) 744-1340**  
(Telephone Number, Including Area Code, of Agent for Service)

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Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, anon-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   
Non-accelerated filer

Accelerated filer   
Smaller reporting company   
Emerging growth company

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

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**CALCULATION OF REGISTRATION FEE**

<b>Title of Securities to be Registered</b>	<b>Amount to be Registered (1)</b>	<b>Proposed Maximum Offering Price Per Share</b>	<b>Proposed Maximum Aggregate Offering Price</b>	<b>Amount of Registration Fee</b>
Common Stock, \$0.001 par value per share	2,162,227 shares (2)	\$8.78 (3)	\$18,984,353.06 (3)	\$2,071.20

- (1) In accordance with Rule 416 under the Securities Act of 1933, as amended (the "Securities Act"), this registration statement shall be deemed to cover any additional securities that may from time to time be offered or issued to prevent dilution resulting from stock splits, stock dividends or similar transactions.
- (2) Consists of (i) 1,600,000 additional shares issuable under the 2016 Stock Incentive Plan and (ii) 562,227 additional shares issuable under the 2016 Employee Stock Purchase Plan.
- (3) Estimated solely for the purpose of calculating the registration fee pursuant to Rules 457(c) and 457(h) of the Securities Act and based upon the average of the high and low prices of the Registrant's Common Stock as reported on the Nasdaq Global Select Market on February 26, 2021.
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## EXPLANATORY NOTE

This Registration Statement on Form S-8, relating to the 2016 Stock Incentive Plan (the “**2016 Plan**”) of Syros Pharmaceuticals, Inc. (the “**Registrant**”) and the 2016 Employee Stock Purchase Plan (the “**ESPP**”) of the Registrant, is being filed for the purpose of registering additional securities of the same class as other securities for which a Registration Statement on Form S-8 has previously been filed and is effective. Accordingly, this Registration Statement incorporates by reference the contents of the following Registration Statements on Form S-8 filed by the Registrant with the Securities and Exchange Commission (“**SEC**”) relating to the 2016 Plan and the ESPP, except in each case the contents of Item 8, Exhibits thereof, with respect to which the Exhibit Index immediately preceding the exhibits attached hereto is incorporated by reference.

<u>SEC File No.</u>	<u>Date Filed with SEC</u>
333-212363	<a href="#">June 30, 2016</a>
333-216821	<a href="#">March 20, 2017</a>
333-223574	<a href="#">March 12, 2018</a>
333-230116	<a href="#">March 7, 2019</a>
333-236895	<a href="#">March 5, 2020</a>

### Item 8. Exhibits.

The following exhibits are incorporated herein by reference:

<u>Number</u>	<u>Description</u>
4.1	<a href="#">Restated Certificate of Incorporation of the Registrant, including the Certificate of Designation of Preferences, Rights and Limitations of Series A Convertible Preferred Stock of the Registrant (previously filed with the Securities and Exchange Commission on May 1, 2019 as Exhibit 3.1 to the Registrant’s Quarterly Report on Form 10-Q (File No. 001-37813) and incorporated herein by reference).</a>
4.2	<a href="#">Amended and Restated Bylaws of the Registrant (previously filed with the Securities and Exchange Commission on July 6, 2016 as Exhibit 3.2 to the Registrant’s Current Report on Form 8-K (File No. 001-37813) and incorporated herein by reference).</a>
5.1	<a href="#">Opinion of Wilmer Cutler Pickering Hale and Dorr LLP, counsel to the Registrant.</a>
23.1	<a href="#">Consent of Wilmer Cutler Pickering Hale and Dorr LLP (included in Exhibit 5.1).</a>
23.2	<a href="#">Consent of Ernst &amp; Young LLP, independent registered public accounting firm.</a>
24.1	<a href="#">Power of attorney (included on the signature pages of this registration statement).</a>
99.1	<a href="#">2016 Stock Incentive Plan (previously filed with the Securities and Exchange Commission on June 3, 2016 as Exhibit 10.5 to the Registrant’s Registration Statement on Form S-1 (File No. 333-211818) and incorporated herein by reference).</a>
99.2	<a href="#">2016 Employee Stock Purchase Plan (previously filed with the Securities and Exchange Commission on June 3, 2016 as Exhibit 10.8 to the Registrant’s Registration Statement on Form S-1 (File No. 333-211818) and incorporated herein by reference).</a>

## SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-8 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 this 4<sup>th</sup> day of March, 2021.

### SYROS PHARMACEUTICALS, INC.

By: /s/ Nancy Simonian, M.D.

Nancy Simonian, M.D.

President and Chief Executive Officer

## POWER OF ATTORNEY AND SIGNATURES

We, the undersigned officers and directors of Syros Pharmaceuticals, Inc., hereby severally constitute and appoint Nancy Simonian, M.D. and Gerald E. Quirk, and each of them singly, our true and lawful attorneys with full power to them, and each of them singly, to sign for us and in our names in the capacities indicated below, the registration statement on Form S-8 filed herewith and any and all subsequent amendments to said registration statement, and generally to do all such things in our names and on our 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, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Nancy Simonian, M.D.</u> Nancy Simonian, M.D.	President, Chief Executive Officer and Director (principal executive officer)	March 4, 2021
<u>/s/ Joseph J. Ferra, Jr.</u> Joseph J. Ferra, Jr.	Chief Financial Officer (principal financial officer and principal accounting officer)	March 4, 2021
<u>/s/ Peter Wirth</u> Peter Wirth	Chair of the Board of Directors	March 4, 2021
<u>/s/ Srinivas Akkaraju, M.D., Ph.D.</u> Srinivas Akkaraju, M.D., Ph.D.	Director	March 4, 2021
<u>/s/ Mark J. Alles</u> Mark J. Alles	Director	March 4, 2021
<u>/s/ S. Gail Eckhardt, M.D.</u> S. Gail Eckhardt, M.D.	Director	March 4, 2021
<u>/s/ Marsha H. Fanucci</u> Marsha H. Fanucci	Director	March 4, 2021
<u>/s/ Amir Nashat, Ph.D.</u> Amir Nashat, Ph.D.	Director	March 4, 2021
<u>/s/ Phillip A. Sharp, Ph.D.</u> Phillip A. Sharp, Ph.D.	Director	March 4, 2021
<u>/s/ Richard A. Young, Ph.D.</u> Richard A. Young, Ph.D.	Director	March 4, 2021

WILMERHALE

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wilmerhale.com

March 4, 2021

Syros Pharmaceuticals, Inc.  
35 CambridgePark Drive, 4<sup>th</sup> Floor  
Cambridge, MA 02140

Re: 2016 Stock Incentive Plan  
2016 Employee Stock Purchase Plan

Ladies and Gentlemen:

We have assisted in the preparation of a Registration Statement on Form S-8 (the "Registration Statement") to be filed with the Securities and Exchange Commission (the "Commission") under the Securities Act of 1933, as amended (the "Securities Act"), relating to an aggregate of 2,162,227 shares of common stock, \$0.001 par value per share (the "Shares"), of Syros Pharmaceuticals, Inc., a Delaware corporation (the "Company"), issuable under the Company's 2016 Stock Incentive Plan and the Company's 2016 Employee Stock Purchase Plan (collectively, the "Plans").

We have examined the Certificate of Incorporation and By-Laws of the Company, each as amended and restated to date, and originals, or copies certified to our satisfaction, of all pertinent records of the meetings of the directors and stockholders of the Company, the Registration Statement and such other documents relating to the Company as we have deemed material for the purposes of this opinion.

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 certified, photostatic or other copies, the authenticity of the originals of any such documents and the legal competence of all signatories to such documents.

We assume that the appropriate action will be taken, prior to the offer and sale of the Shares in accordance with the Plans, 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 General Corporation Law of the State of Delaware.

Wilmer Cutler Pickering Hale and Dorr LLP, 60 State Street, Boston, Massachusetts 02109

Beijing Berlin Boston Brussels Denver Frankfurt London Los Angeles New York Palo Alto San Francisco Washington

March 4, 2021  
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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.

Based on the foregoing, we are of the opinion that the Shares have been duly authorized for issuance and, when the Shares are issued and paid for in accordance with the terms and conditions of the Plans, the Shares will be validly issued, fully paid and nonassessable.

We hereby consent to the filing of this opinion with the Commission in connection with the Registration Statement in accordance with the requirements of Item 601(b)(5) of Regulation S-K under the Securities Act. 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

**Consent of Independent Registered Public Accounting Firm**

We consent to the incorporation by reference in the Registration Statement (FormS-8) pertaining to the 2016 Stock Incentive Plan and the 2016 Employee Stock Purchase Plan of Syros Pharmaceuticals, Inc. of our report dated March 4, 2021, with respect to the consolidated financial statements of Syros Pharmaceuticals, Inc., included in its Annual Report (Form 10-K) for the year ended December 31, 2020, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

Boston, Massachusetts  
March 4, 2021