

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

**FORM S-4  
REGISTRATION STATEMENT  
UNDER  
THE SECURITIES ACT OF 1933**

**Syros Pharmaceuticals, Inc.**

(Exact Name of Registrant as Specified in Its Charter)

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

**2834**  
(Primary Standard Industrial  
Classification Code Number)

**43-3772460**  
(I. R. S. Employer  
Identification Number)

**35 CambridgePark Drive, 4<sup>th</sup> Floor  
Cambridge, Massachusetts 02140  
(617) 744-1340**

(Address, Including Zip Code, and Telephone Number, Including Area Code, of Registrant's Principal Executive Offices)

**Nancy A. Simonian, M.D.  
President and Chief Executive Officer  
Syros Pharmaceuticals, Inc.  
35 CambridgePark, 4<sup>th</sup> Floor  
Cambridge, Massachusetts 02140  
(617) 744-1340**

(Name, Address, Including Zip Code, and Telephone Number, Including Area Code, of Agent for Service)

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

If the securities being registered on this Form are being offered in connection with the formation of a holding company and there is compliance with General Instruction G, check the following box.

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.  333-266184

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

Indicate by a 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

Accelerated filer

Non-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.

If applicable, place an X in the box to designate the appropriate rule provision relied upon in conducting this transaction:

Exchange Act Rule 13e-4(i) (Cross-Border Issuer Tender Offer)

Exchange Act Rule 14d-1(d) (Cross-Border Third-Party Tender Offer)

**This registration statement will become effective automatically upon filing with the Securities and Exchange Commission pursuant to Rule 462(b) under the Securities Act of 1933, as amended.**

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## EXPLANATORY NOTE AND INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

Pursuant to its Registration Statement on [Form S-4](#) (Registration No. 333-266184) (the “Prior Registration Statement”), which was declared effective on August 8, 2022, Syros Pharmaceuticals, Inc., a Delaware corporation (the “Company”) registered an aggregate of 74,255,612 shares of its common stock, par value \$0.001 per share (the “Common Stock”) and paid an aggregate fee of \$4,629.44. Subsequent to the effectiveness of the Prior Registration Statement, on September 16, 2022, the Company effected a 1-for-10 reverse stock split of the Common Stock (the “Reverse Stock Split”), such that the Prior Registration Statement shall be deemed to cover 7,425,561 shares of Common Stock after giving effect to the Reverse Stock Split. The Company is filing this Registration Statement on Form S-4 pursuant to General Instruction K to Form S-4 and Rule 462(b) under the Securities Act of 1933, as amended, solely to register an additional 120,453 shares of Common Stock (which number of shares gives effect to the Reverse Stock Split) for issuance in connection with the consummation of the merger contemplated by the Agreement and Plan of Merger, dated July 3, 2022, by and among the Company, Tyme Technologies, Inc., and Tack Acquisition Corp.

The contents of the Prior Registration Statement are incorporated in this registration statement by reference. The contents of the Prior Registration Statement, including the consolidated financial statements of the Company contained therein, do not give effect to the Reverse Stock Split. The required opinions and consents are listed on an Exhibit Index attached hereto and filed herewith.

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EXHIBIT INDEX

Exhibit No.	Description
5.1	<a href="#">Opinion of WilmerHale</a>
23.1	<a href="#">Consent of WilmerHale (included in Exhibit 5.1)</a>
23.2	<a href="#">Consent of Ernst &amp; Young LLP</a>
23.3	<a href="#">Consent of Grant Thornton LLP</a>
24*	<a href="#">Powers of Attorney</a>
107	<a href="#">Filing Fee Table</a>

\* Filed as Exhibit 24 to the Registrant's Registration Statement on Form S-4 (File No. 333-266184) filed with the Commission on July 18, 2022.

**SIGNATURES**

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Cambridge, Commonwealth of Massachusetts, on this 19<sup>th</sup> day of September, 2022.

Syros Pharmaceuticals, Inc.

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

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
<u>/s/ Nancy Simonian</u> Nancy Simonian, M.D.	President, Chief Executive Officer and Director (Principal Executive Officer)	September 19, 2022
<u>/s/ Jason Haas</u> Jason Haas	Chief Financial Officer (Principal Financial Officer, Principal Accounting Officer)	September 19, 2022
<u>*</u> Peter Wirth	Chair of the Board of Directors	September 19, 2022
<u>*</u> Srinivas Akkaraju, M.D., Ph.D.	Director	September 19, 2022
<u>*</u> Mark J. Alles	Director	September 19, 2022
<u>*</u> Deborah Dunsire, M.D.	Director	September 19, 2022
<u>*</u> S. Gail Eckhardt, M.D.	Director	September 19, 2022
<u>*</u> Marsha H. Fanucci	Director	September 19, 2022
<u>*</u> Andrew M. Oh	Director	

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Timothy C. Tyson Director

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Richard A. Young, Ph.D. Director

September 19, 2022

\*By: /s/ Jason Haas \_\_\_\_\_  
Name: Jason Haas  
Title: Attorney-in-fact

WILMERHALE

September 19, 2022

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

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

Re: Registration Statement on Form S-4

Ladies and Gentlemen:

This opinion is furnished to you in connection with a Registration Statement on Form S-4 (the "Registration Statement") filed by Syros Pharmaceuticals, Inc., a Delaware corporation (the "Company"), with the Securities and Exchange Commission (the "Commission") pursuant to Rule 462(b) under the Securities Act of 1933, as amended (the "Securities Act"), for the registration of up to 120,453 shares of common stock, \$0.001 par value per share (the "Shares") of the Company, which number gives effect to the 1-for-10 reverse stock split of the Company's common stock that became effective on September 16, 2022.

The Shares are to be issued by the Company pursuant to the Agreement and Plan of Merger (the "Merger Agreement"), dated as of July 3, 2022, by and among the Company, Tack Acquisition Corp. ("Merger Sub"), and Tyme Technologies, Inc. ("Merger Partner"), pursuant to which Merger Sub will merge with and into Merger Partner (the "Merger"), with Merger Partner surviving as a wholly owned subsidiary of the Company, which has been filed as Exhibit 2.1 to the Company's Current Report on Form 8-K filed on July 5, 2022.

We are acting as counsel for the Company in connection with the issuance by the Company of the Shares. We have examined and relied upon signed copies of the Registration Statement to be filed with the Commission, including the exhibits thereto. We have also examined and relied upon the Merger Agreement, the Restated Certificate of Incorporation of the Company (as amended or restated from time to time, the "Certificate of Incorporation"), the Second Amended and Restated By-laws of the Company (as amended or restated from time to time, the "Bylaws"), minutes of meetings of the stockholders and the Board of Directors of the Company as provided to us by the Company, 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 legal capacity of all signatories, 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 such original documents and the completeness and accuracy of the corporate minute books of the Company.

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

Syros Pharmaceuticals, Inc.  
September 19, 2022  
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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. We also express no opinion herein with respect to compliance by the Company with the securities or "blue sky" laws of any state or other jurisdiction of the United States or of any foreign jurisdiction. We express no opinion and make no statement herein with respect to the antifraud laws of any jurisdiction.

Based upon and subject to the foregoing, we are of the opinion that upon the approval by the stockholders of the Company of the issuance of the Shares, the Shares, when issued in accordance with the terms and conditions of the Merger Agreement, will be duly authorized, for issuance, validly issued, fully paid and nonassessable.

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 Joint Proxy Statement/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/ Wilmer Cutler Pickering Hale and Dorr LLP  
WILMER CUTLER PICKERING HALE AND DORR LLP

**Consent of Independent Registered Public Accounting Firm**

We consent to the incorporation by reference in the Registration Statement on Form S-4 filed pursuant to 462(b) of the Securities Act of 1933 of the reference to our firm under the caption "Experts" and to the incorporation by reference of our report dated March 15, 2022, with respect to the consolidated financial statements of Syros Pharmaceuticals, Inc. included in the Registration Statement (Form S-4 No. 333-266184) and the related Prospectus of Syros Pharmaceuticals, Inc. for the registration of its common stock.

/s/ Ernst & Young LLP

Boston, Massachusetts  
September 19, 2022



**CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

We have issued our report dated May 25, 2022, with respect to the consolidated financial statements of Tyme Technologies, Inc. included in the Annual Report on Form 10-K for the year ended March 31, 2022, which are incorporated by reference in this Registration Statement. We consent to the incorporation by reference of the aforementioned report in this Registration Statement, and to the use of our name as it appears under the caption "Experts."

/s/ Grant Thornton LLP

New York, New York  
September 19, 2022

## Calculation of Filing Fee Tables

Form S-4  
(Form Type)SYROS PHARMACEUTICALS, INC.  
(Exact Name of Registrant as Specified in its Charter)

Table 1—Newly Registered and Carry Forward Securities

	Security Type	Security Class Title	Fee Calculation or Carry Forward Rule	Amount Registered	Proposed Maximum Offering Price Per Unit	Maximum Aggregate Offering Price	Fee Rate	Amount of Registration Fee	Carry Forward Form Type	Carry Forward File Number	Carry Forward Initial effective date	Filing Fee Previously Paid In Connection with Unsold Securities to be Carried Forward
Newly Registered Securities												
Fees to Be Paid	Equity	Common Stock, \$0.001 par value per share	Other	120,453(1)	—	\$769,668(2)	\$0.0000927	\$71.35				
Fees Previously Paid	—	—	—	—	—	—	—	—				
Carry Forward Securities												
Carry Forward Securities	—	—	—	—	—	—	—	—	—	—	—	—
	Total Offering Amounts					\$769,668(2)	—	\$71.35				
	Total Fees Previously Paid							—				
	Total Fee Offsets							—				
	Net Fee Due							\$71.35				

- (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.

Represents the estimated maximum number of additional shares of common stock, par value \$0.001 (“Syros common stock”), of the registrant Syros Pharmaceuticals, Inc., a Delaware corporation (“Syros”) to be issued upon completion of the merger transaction as described herein. Syros has previously registered 74,255,612 shares of Syros common stock pursuant to the Registration Statement on Form S-4 (Registration No. 333-266184), which was declared effective on August 8, 2022 (the “Prior Registration Statement”). Subsequent to the effectiveness of the Prior Registration Statement, on September 16, 2022, Syros effected a 1-for-10 reverse stock split of the Syros common stock (the “Reverse Stock Split”), such that the Prior Registration Statement shall be deemed to cover 7,425,561 shares of Syros common stock after giving effect to the Reverse Stock Split.

The number of shares registered on the Prior Registration Statement was based on the product of (a) 172,206,894 shares of common stock, \$0.0001 par value per share (“Tyme common stock”) of Tyme Technologies, Inc., a Delaware corporation (“Tyme”) outstanding as of July 5, 2022, multiplied by (b) an assumed exchange ratio of 0.4312 shares of Syros common stock for each outstanding share of Tyme common stock. Such exchange ratio was an estimate of the actual exchange ratio to be determined in connection with the closing of the merger. The merger transaction closed on September 16, 2022, and on such date, the exchange ratio was determined to be 0.4382 shares of Syros common stock for each outstanding share of Tyme common stock. Accordingly, Syros now anticipates that up to 120,453 additional shares of Syros common stock (which number of shares gives effect to the Reverse Stock Split) may be issued in the merger transaction.

- (2) Estimated solely for purposes of calculating the registration fee required by Section 6(b) of the Securities Act of 1933, as amended (the “Securities Act”), and computed in accordance with Rules 457(c) and 457(f)(1) of the Securities Act. The proposed maximum aggregate offering price is solely for the purposes of calculating the registration fee and was calculated based upon the market value of shares of Tyme common stock (the securities to be cancelled in the merger) in accordance with Rule 457(c) under the Securities Act as follows: the product of (a) \$0.28, the average of the high and low prices per share of Tyme common stock on September 15, 2022, as quoted on The Nasdaq Stock Market and (b) 2,748,814, the estimated maximum number of shares of Tyme common stock that may be cancelled in exchange for the additional shares of Syros common stock being registered in connection with the merger transaction on this registration statement.