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

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of The Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): August 12, 2024

Syros Pharmaceuticals, Inc.
(Exact Name of Registrant as Specified in its Charter)

Delaware	**001-37813**	**45-3772460**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

35 CambridgePark Drive **Cambridge, Massachusetts**	**02140**
(Address of Principal Executive Offices)	**(Zip Code)**

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

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (*see* General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered or to be registered pursuant to Section 12(b) of the Act.

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, $0.001 par value	SYRS	Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

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

Item 8.01 Other Events.

On August 12, 2024, Syros Pharmaceuticals, Inc. (the "**Company**") issued a press release announcing its decision to discontinue enrollment in the SELECT-AML-1 Phase 2 clinical trial evaluating the triplet regimen of tamibarotene in combination with venetoclax and azacitidine compared to the doublet regimen of venetoclax and azacitidine in newly diagnosed, unfit patients with acute myeloid leukemia and *RARA* gene overexpression, based on the results of a prespecified interim analysis of the trial. A copy of this press release is filed as Exhibit 99.1 to this Current Report on Form 8-K and incorporated herein by reference. The information contained on websites referenced in this press release is not incorporated herein.

Cautionary Note Regarding Forward-Looking Statements

This Current Report on Form 8-K contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995, including without limitation statements regarding the Company's clinical development plans, the progression of its clinical trials, the timing to report clinical data, and the ability to commercialize tamibarotene and deliver benefit to patients. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "hope," "intend," "may," "plan," "potential," "predict," "project," "target," "should," "would," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward-looking statements as a result of various important factors, including the Company's ability to: advance the development of its programs under the timelines it projects in current and future clinical trials; demonstrate in any current and future clinical trials the requisite safety, efficacy and combinability of its drug candidates; sustain the response rates and durability of response seen to date with its drug candidates; successfully develop a diagnostic test to identify patients with the *RARA* biomarker; obtain and maintain patent protection for its drug candidates and the freedom to operate under third party intellectual property; obtain and maintain necessary regulatory approvals; identify, enter into and maintain collaboration agreements with third parties; manage competition; manage expenses; raise the substantial additional capital needed to achieve its business objectives; attract and retain qualified personnel; and successfully execute on its business strategies; risks described under the caption "Risk Factors" in the Company's Annual Report on Form 10-K for the year ended December 31, 2023 and Quarterly Report on Form10-Q for the quarters ended March 31, 2024 and June 30, 2024, each of which is on file with the Securities and Exchange Commission; and risks described in other filings that the Company makes with the Securities and Exchange Commission in the future.

Item 9.01 Financial Statements and Exhibits.

Exhibit No.	Description
99.1	Press Release dated August 12, 2024.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

SYROS PHARMACEUTICALS, INC.

Date: August 12, 2024

By: /s/ Gerald Quirk
Gerald Quirk
Chief Legal & Compliance Officer;
Chief Business Officer

Exhibit 99.1

Syros Provides Update on SELECT-AML-1 Phase 2 Clinical Trial

CAMBRIDGE, Mass., August 12, 2024 – Syros Pharmaceuticals (NASDAQ:SYRS), a biopharmaceutical company committed to advancing new standards of care for the frontline treatment of hematologic malignancies, today announced that it will discontinue enrollment in the SELECT-AML-1 Phase 2 clinical trial evaluating the triplet regimen of tamibarotene in combination with venetoclax and azacitidine compared to the doublet regimen of venetoclax and azacitidine in newly diagnosed, unfit patients with acute myeloid leukemia (AML) and *RARA* gene overexpression. This decision is based on the results of a prespecified interim analysis of the trial.

Data from 51 patients enrolled in SELECT-AML-1 were reviewed on August 9, 2024. This review included a prespecified non-binding futility analysis conducted on the first 40 randomized patients after the fortieth randomized patient received approximately three months of study drug or discontinued treatment. A similar complete response (CR)/complete response with incomplete hematologic recovery (CRi) rate was observed in the triplet arm (n=20; 65%, CI: 40.8-84.6) and the doublet arm (n=20; 70%, CI: 45.7-88.1). As a result, the probability for success of the SELECT-AML-1 study to demonstrate superiority at the final analysis in 80 randomized patients was considered low, and Syros made the decision to discontinue further enrollment. There were no new safety signals associated with the use of tamibarotene in combination with venetoclax and azacitidine. Patients currently enrolled in SELECT-AML-1 will have the opportunity to remain on study at the discretion of study investigators. Syros plans to present data from SELECT-AML-1 at the 12th Annual Meeting of the Society of Hematologic Oncology (SOHO) in September 2024.

“We are disappointed by this unexpected outcome, especially for people living with AML,” said David A. Roth, M.D., Chief Medical Officer of Syros. “In our prior Phase 2 clinical trial, the doublet combination of tamibarotene and azacitidine delivered a 61% CR/CRi rate in newly diagnosed AML patients with *RARA* overexpression. This supports our conviction in pursuing a doublet strategy in higher-risk MDS, where we are comparing tamibarotene and azacitidine to azacitidine alone. We remain steadfast in our commitment to delivering tamibarotene for the treatment of HR-MDS and look forward to sharing pivotal data from SELECT-MDS-1 by mid-fourth quarter.”

Syros continues to evaluate tamibarotene, an oral, selective, retinoic acid receptor alpha (RARα) agonist, in combination with azacitidine in the SELECT-MDS-1 Phase 3 clinical trial in newly diagnosed higher-risk myelodysplastic syndrome (MDS) patients with *RARA* gene overexpression. The SELECT-MDS-1 trial passed a prespecified futility analysis in the first quarter of 2024 and is continuing as planned, with pivotal CR data expected by the middle of the fourth quarter of 2024.

About Syros Pharmaceuticals

Syros is committed to developing new standards of care for the frontline treatment of patients with hematologic malignancies. Driven by the motivation to help patients with blood disorders that have largely eluded other targeted approaches, Syros is developing tamibarotene, an oral selective RARα agonist in frontline patients with higher-risk myelodysplastic syndrome with *RARA* gene overexpression. For more information, visit www.syros.com and follow us on X (@SyrosPharma) and LinkedIn.

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develop a diagnostic test to identify patients with the *RARA* biomarker; obtain and maintain patent protection for its drug candidates and the freedom to operate under third party intellectual property; obtain and maintain necessary regulatory approvals; identify, enter into and maintain collaboration agreements with third parties; manage competition; manage expenses; raise the substantial additional capital needed to achieve its business objectives; attract and retain qualified personnel; and successfully execute on its business strategies; risks described under the caption "Risk Factors" in Syros' Annual Report on Form 10-K for the year ended December 31, 2023 and Quarterly Report on Form10-Q for the quarters ended March 31, 2024 and June 30, 2024, each of which is on file with the Securities and Exchange Commission; and risks described in other filings that Syros makes with the Securities and Exchange Commission in the future.

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