# 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): October 24, 2020**

# 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**<br>**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 October 24, 2020, Syros Pharmaceuticals, Inc. (the "**Company**") issued a press release announcing initial data from its Phase 1 clinical trial evaluating SY-5609 in patients with select solid tumors. A copy of this press release is filed as Exhibit 99.1 to this 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 Form 8-K contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995 that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Form 8-K, including statements regarding the Company's strategy, research and clinical development plans, future operations, prospects, plans and objectives of management, are forward-looking statements. 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 SY-5609 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 SY-5609; sustain the response rates seen to date with SY-5609; replicate scientific and non-clinical data in clinical trials; successfully establish a patient selection strategy and develop a companion diagnostic test to identify patients most likely to benefit from SY-5609; 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, 2019 and Quarterly Report on Form 10-Q for the quarter ended June 30, 2020, 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. In addition, the extent to which the COVID-19 outbreak continues to impact our workforce and our research, supply chain and clinical trial operations activities, and the operations of the third parties on which we rely, will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the duration and severity of the outbreak, additional or modified government actions, and the actions that may be required to contain the virus or treat its impact. Any forward-looking statements contained in this press release speak only as of the date hereof, and the Company expressly disclaims any obligation to update any forward-looking statements, whether because of new information, future events or otherwise.

**Item 9.01 Financial Statements and Exhibits.**

| Exhibit No. | Description |
|---|---|
| 99.1 | Press release dated October 24, 2020. |
| 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: October 26, 2020

By: /s/ Gerald E. Quirk
Gerald E. Quirk
Chief Legal & Administrative Officer

# Syros Presents Initial Data from Phase 1 Clinical Trial of SY-5609, Its Selective Oral CDK7 Inhibitor, at EORTC-NCI-AACR Meeting

*Early Dose-Escalation Data Demonstrate Proof of Mechanism and Support Ongoing Development of SY-5609 for Difficult-to-Treat Cancers*

*On Track to Report Additional Data, including Clinical Activity Data, in Mid-2021*

CAMBRIDGE, Mass., October 24, 2020 – Syros Pharmaceuticals (NASDAQ:SYRS), a leader in the development of medicines that control the expression of genes, today announced initial safety, pharmacokinetics (PK) and pharmacodynamics (PD) data from the ongoing dose-escalation portion of its Phase 1 clinical trial of SY-5609 in patients with select solid tumors. SY-5609 is a highly selective and potent oral cyclin-dependent kinase 7 (CDK7) inhibitor. These early data demonstrate proof of mechanism in patients with advanced solid tumors and establish a maximum tolerated dose (MTD) for continuous daily dosing. The data are being presented in a poster session at the 32nd EORTC-NCI-AACR Symposium.

"These early findings from our Phase 1 trial of SY-5609 reinforce our conviction in CDK7 inhibition as a potentially transformative targeted approach for difficult-to-treat cancers," said David A. Roth, M.D., Chief Medical Officer of Syros. "As we move forward in this trial, we are committed to fully exploring the potential of SY-5609. To that end, we opened the trial to pancreatic cancer patients, expanded a cohort to focus on lung cancer patients, and also expanded the combination cohort in treatment-resistant breast cancer patients. Additionally, we opened cohorts evaluating alternate dosing regimens, all with the goal of identifying optimal next steps for pursuing single-agent and combination development opportunities and ultimately delivering the greatest benefit to patients."

**Early Data Demonstrate Proof-of-Mechanism at Tolerable Doses**

Syros presented initial data from its ongoing Phase 1 multi-center, open-label, dose-escalation study of SY-5609 in patients with advanced breast, colorectal, lung, ovarian or pancreatic cancer, or other solid tumors with Rb pathway alterations. The study also includes a cohort evaluating SY-5609 in combination with fulvestrant in CDK4/6 inhibitor-resistant HR-positive breast cancer patients.

As of August 21, 17 patients had been enrolled in the trial and were eligible for safety, PK and PD analysis. Patients were either treated with continuous daily dosing of single-agent SY-5609 at 1, 3, 4 or 5 mg, or for three weeks on and one week off at 3 mg in combination with fulvestrant. The median age of the patients enrolled in the study was 64. Patients were heavily pretreated with a median of four prior therapies. The MTD for continuous daily dosing was achieved at 3 mg. The data showed that:

- SY-5609 demonstrated dose-dependent increases in POLR2A mRNA expression, a PD marker being used in the trial to measure CDK7 biological activity.
    - Notably, increases in POLR2A in patients treated at 3 mg daily reached levels associated with tumor regressions in preclinical models, as well as with levels of CDK7 target engagement at which a clinical response and apoptosis were observed in a trial of patients treated with a first-generation IV CDK7 inhibitor.
- SY-5609 demonstrated approximately dose-proportional PK as both a single agent and in combination, minimal accumulation with repeat dosing, and a steady state half-life compatible with once-daily dosing.
- The majority of adverse events reported with SY-5609 as a single agent were low grade. The most common AEs were nausea, diarrhea, fatigue, platelet count decrease, and vomiting.
- The safety profile of SY-5609 in combination with fulvestrant was consistent with that of single-agent SY-5609.
- Five of the 13 patients treated with single-agent SY-5609 were response evaluable, and of those, three achieved stable disease and two had progressive disease; one of the four patients treated in the combination cohort was response evaluable and had progressive disease.

The Phase 1 trial continues to actively enroll patients with select solid tumors, including the recently expanded single-agent cohort in lung cancer patients and combination cohort in breast cancer patients, to further evaluate the 3 mg daily dose in focused patient populations. The trial has also been opened to patients with advanced pancreatic cancer, another tumor type that has demonstrated sensitivity to SY-5609 in preclinical models. Additional cohorts are evaluating alternate regimens, supported by preclinical data showing that intermittent regimens of SY-5609 induced tumor regressions.

Syros expects to report additional dose-escalation data, including clinical activity data, in mid-2021. Additional details about the Phase 1 trial of SY-5609 can be found using the identifier NCT04247126 at www.clinicaltrials.gov.

**About Syros Pharmaceuticals**

Syros is redefining the power of small molecules to control the expression of genes. Based on its unique ability to elucidate regulatory regions of the genome, Syros aims to develop medicines that provide a profound benefit for patients with diseases that have eluded other genomics-based approaches. Syros is advancing a robust pipeline, including SY-1425, a first-in-class oral selective RARÎ± agonist in a Phase 2 trial in a genomically defined subset of acute myeloid leukemia patients, and SY-5609, a highly selective and potent oral CDK7 inhibitor in a Phase 1 trial in patients with select solid tumors. Syros also has multiple preclinical and discovery programs in oncology and monogenic diseases. For more information, visit www.syros.com and follow us on Twitter (@SyrosPharma) and LinkedIn.

**Cautionary Note Regarding Forward Looking Statements**

This press release contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995, including without limitation statements regarding the timing for reporting additional dose-escalation data, including clinical activity data,

from the Phase 1 clinical trial of SY-5609, the future expansion of such trial to include additional cohorts and dosing regimens, and the ability ofSY-5609 to have a benefit for patients. Moreover, there can be no assurance that the initial clinical data generated to date in the ongoing Phase 1 clinical trial of SY-5609 are predictive of the ability of any cohort of such trial to meet any of its endpoints or to continue comparing favorably with other treatments or treatment regimens. 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 Syros’ ability to: advance the development of SY-5609 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 SY-5609; sustain the response rates seen to date withSY-5609; replicate scientific and non-clinical data in clinical trials; successfully establish a patient selection strategy and develop a companion diagnostic test to identify patients most likely to benefit from SY-5609; 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, 2019 and Quarterly Report on Form 10-Q for the quarter ended June 30, 2020, 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. In addition, the extent to which the COVID-19 outbreak continues to impact our workforce and our research, supply chain and clinical trial operations activities, and the operations of the third parties on which we rely, will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the duration and severity of the outbreak, additional or modified government actions, and the actions that may be required to contain the virus or treat its impact. Any forward-looking statements contained in this press release speak only as of the date hereof, and Syros expressly disclaims any obligation to update any forward-looking statements, whether because of new information, future events or otherwise.

**Media Contact:**
Naomi Aoki
Syros Pharmaceuticals
617-283-4298
naoki@syros.com

**Investor Contact:**
Hannah Deresiewicz
Stern Investor Relations, Inc.
212-362-1200
hannah.deresiewicz@sternir.com