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): January 19, 2021

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.

Syros Pharmaceuticals, Inc. is supplementing the risk factors previously disclosed in its Annual Report on Form 10-K for the fiscal year ended December 31, 2019 (the "2019 Form 10-K") and its Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2020 (the "Q3 2020 Form 10-Q") with the following risk factors. These risk factors should be read in conjunction with the risk factors included in the 2019 Form 10-K and the Q3 2020 Form 10-Q.

We face certain risks related to the development, marketing and commercialization of SY-2101, which could result in substantial harm to our business.

In December 2020, we acquired assets related to SY-2101, a novel oral form of arsenic trioxide that we are developing for acute promyelocytic leukemia, or APL, a subtype of acute myeloid leukemia that is caused by a fusion of the RARA and PML genes. We are advancing SY-2101 into a dose confirmation study to be followed by a planned Phase 3 study in newly diagnosed APL patients, and the risks relating to product development, marketing and commercialization that are described in the risk factors included in the 2019 Form 10-K and the Q3 2020 Form 10-Q will also apply to our activities with respect to SY-2101.

If we are to receive FDA approval for SY-2101 prior to January 2025, we must demonstrate to the FDA that SY-2101 provides a "major contribution to patient care" relative to an approved drug with the same active moiety for the same indication, and there can be no assurance that we will be successful.

We are developing SY-2101 as an alternative to Trisenox®, an intravenously administered arsenic trioxide product. The U.S. Food and Drug Administration, or FDA, has granted Trisenox orphan drug exclusivity for the treatment of a form of APL until January 2025. A company that obtains FDA approval for a designated orphan drug receives orphan drug market exclusivity for the designated indication for a period of seven years from the date of approval in the United States. This orphan drug exclusivity approval bars the FDA from approving another drug product with the same active moiety for the same orphan drug indication, unless the sponsor of the drug product is able to demonstrate, and the FDA concludes, that the drug product is "clinically superior" to the previously approved product, due to the fact that it is safer, more effective, or provides a major contribution to patient care within the meaning of FDA regulations and guidance.

In assessing whether a sponsor has demonstrated that its candidate product provides a "major contribution to patient care" when compared to the drug product with orphan drug exclusivity, the FDA will evaluate the question on a case by case basis and may in appropriate circumstances consider such factors as convenience of treatment location, duration of treatment, patient comfort, reduced treatment burden, advances in ease and comfort of drug administration, longer periods between doses, and the potential for self-administration of the product. Such demonstration to the satisfaction of the FDA is difficult to establish with limited precedents.

SY-2101 was granted an orphan drug designation by the FDA for the treatment of APL in November 2015, after the FDA concluded that there is a plausible hypothesis for clinical superiority when compared to Trisenox. Specifically, given that SY-2101 is administered orally instead of intravenously, it could provide a major contribution to patient care by allowing for the treatment of APL patients in a more convenient outpatient setting through a self-administered delivery method, which could eliminate or significantly decrease the costs associated with IV administration, reduce the inconvenience and cost to patients and caregivers associated with frequent hospitalizations and trips to infusion centers, and reduce

the burden on the healthcare system in delivery of life-saving medicines to patients in need. We intend to seek to demonstrate to the FDA that SY-2101 is "clinically superior" to Trisenox constituting a "major contribution to patient care" within the meaning of the FDA regulations and guidance. However, there can be no assurance that we will be successful in these efforts and, if we are not, the FDA will not approve SY-2101 until orphan drug exclusivity expires for Trisenox. Any failure to demonstrate "clinical superiority" for SY-2101 could prevent or delay FDA approval or cause SY-2101 to fail to receive or maintain orphan drug exclusivity status, which could have a material adverse effect on our business, prospects, financial condition and results of operations.

We do not have composition of matter patent protection with respect to the active pharmaceutical ingredient of SY-2101.

We do not have composition of matter patent protection for arsenic trioxide, the active pharmaceutical ingredient of SY-2101. Our competitors may be able to offer and sell products so long as these competitors do not infringe any other patents that we hold, including patents with claims directed to the formulation of SY-2101 drug product and/or methods of manufacture of SY-2101. In general, method patents are more difficult to enforce than composition of matter patents because, for example, of the risks that the FDA may approve an oral formulation of arsenic trioxide that is not covered by our formulation or manufacturing method patents. FDA approval of an oral formulation of arsenic trioxide that is not covered by our patents would limit our ability to generate revenue from the sale of SY-2101, if approved for commercial sale.

We, or any future collaborators, may not be able to obtain orphan drug designation or orphan drug exclusivity for our product candidates and, even if we do, that exclusivity may not prevent the FDA or the EMA from approving competing products.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States. We have obtained orphan drug designation for SY-2101 for the treatment of APL in the United States, and for the treatment of acute myeloid leukemia, or AML, in Europe. In the future, however, we or any future collaborators may seek orphan drug designations for SY-2101 in other indications or territories or for other product candidates and may be unable to obtain such designations.

Even if we, or any future collaborators, obtain orphan drug designation for a product candidate, we, or they, may not be able to obtain orphan drug exclusivity for that product candidate. Generally, a product with orphan drug designation only becomes entitled to orphan drug exclusivity if it receives the first marketing approval for the indication for which it has such designation, in which case the FDA or the European Medicines Agency, or EMA, will be precluded from approving another marketing application for the same drug for that indication for the applicable exclusivity period. The applicable exclusivity period is seven years in the United States and ten years in Europe. The European exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or the EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

Even if we, or any future collaborators, obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition and the same drug can be approved for different conditions. Even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

For example, even if SY-2101 were to be approved and receive orphan drug exclusivity, that would not preclude a competitor from asserting a separate "major contribution to patient care" argument based on a showing of clinical superiority to SY-2101 due to, for example, a change in an inactive ingredient that results in a more favorable profile or a statistically significant improvement in an important safety parameter. In addition, since healthcare providers can prescribe approved drug products for uses outside of their approved labeling, it is possible that another drug product could be approved for a different indication, such as relapsed/refractory APL, and be used "off label" in the up-front setting. On August 3, 2017, Congress passed the FDA Reauthorization Act of 2017 which, among other things, codified the FDA's pre-existing regulatory interpretation, to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

Our internal computer systems, or those of any collaborators or contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Despite the implementation of security measures and certain data recovery measures, our internal computer systems and those of our current and any future collaborators and other contractors or consultants are vulnerable to damage from cyber-attacks, computer viruses, unauthorized access, sabotage, natural disasters, terrorism, war and telecommunication and electrical failures. We have experienced, and may experience in the future, security breaches of our information technology systems. Any system failure, accident or security breach that causes interruptions in our operations, for us or those third parties with which we contract, could result in a material disruption of our product development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions, in addition to possibly requiring substantial expenditures of resources to remedy. For example, the loss of clinical trial data from an ongoing, completed or future clinical trial could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we may incur liabilities, our competitive position could be harmed and the further development and commercialization of our product candidates may be delayed. In addition, we may not have adequate insurance coverage to provide compensation for any losses associated with such events.

We could be subject to risks caused by misappropriation, misuse, leakage, falsification or intentional or accidental release or loss of information maintained in the information systems and networks of our company, including personal information of our employees. In addition, outside parties have attempted, and may in the future attempt, to penetrate our systems or those of our vendors or fraudulently induce our employees or employees of our vendors to disclose sensitive information to gain access to our data. Like other companies, we may experience threats to our data and systems, including malicious codes and viruses, and other cyber-attacks. The number and complexity of these threats

continue to increase over time. If a material breach of our security or that of our vendors occurs, the market perception of the effectiveness of our security measures could be harmed, we could lose business and our reputation and credibility could be damaged. We could be required to expend significant amounts of money and other resources to repair or replace information systems or networks. Although we develop and maintain systems and controls designed to prevent these events from occurring, and we have a process to identify and mitigate threats, the development and maintenance of these systems, controls and processes is costly and requires ongoing monitoring and updating as technologies change and efforts to overcome security measures become more sophisticated. Moreover, despite our efforts, the possibility of these events occurring cannot be eliminated entirely.

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: January 19, 2021

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