



666 Shares of Series A Convertible Preferred Stock

Class A Warrants to Purchase 166,500 Shares of Common Stock

This free writing prospectus relates only to the offering described below and should be read together with the preliminary prospectus supplement dated April 4, 2019 (including the documents incorporated by reference therein and the base prospectus in respect thereof) relating to the offering of Series A convertible preferred stock (the “Series A preferred stock”) and Class A warrants to purchase common stock (the “Preliminary Prospectus Supplement”). Capitalized terms used but not defined herein shall have the meanings set forth in the Preliminary Prospectus Supplement.

The following information supplements and updates the information contained in the Preliminary Prospectus Supplement.

Issuer: Syros Pharmaceuticals, Inc.

Ticker/Exchange for Common Stock: SYRS/Nasdaq Global Select Market

Series A Preferred Stock Offered: 666 shares

Public Offering Price Per Share of Common Stock and Accompanying Warrant: \$7,500.00

Warrants Offered: Warrants to purchase 166,500 shares of common stock. Each Warrant will have an exercise price per share of common stock equal to \$8.625, and will expire 42 calendar months from the date of issuance. Each Warrant will be immediately exercisable, provided that the holder will be prohibited, subject to certain exceptions, from exercising the Warrant for shares of our common stock to the extent that immediately prior to or after giving effect to such exercise, the holder, together with its affiliates and other attribution parties, would own more than 4.99% of the total number of shares of our common stock then issued and outstanding, which percentage may be changed at the holders’ election to a higher or lower percentage upon 61 days’ notice to us. This prospectus supplement also relates to the offering of the shares of our common stock issuable upon exercise of the Warrants.

For each share of Series A preferred stock purchased in the offering, the investor was entitled to receive a Class A warrant to purchase 250 shares of common stock.

The Warrants will have the following terms, in addition to those described in the Preliminary Prospectus Supplement under the heading "Description of Securities we are Offering:"

Cashless Exercise. If, at the time a holder exercises its Warrants, a registration statement registering the issuance of the shares of common stock underlying the Warrants under the Securities Act is not then effective or available for the issuance of such shares, then in lieu of making the cash payment otherwise contemplated to be made to us upon such exercise in payment of the aggregate exercise price, the holder may elect instead to receive upon such exercise (either in whole or in part) the net number of shares of common stock determined according to a formula set forth in the Warrants.

Rights as a Stockholder. Except for the rights to participate in certain dividends and distributions or by virtue of such holder's ownership of shares of our common stock, the holders of the Warrants do not have the rights or privileges of holders of our common stock, including any voting rights, until they exercise their Warrants.

Concurrent Offering:

Concurrently with the offering contemplated by the Preliminary Prospectus Supplement, we are conducting a public offering of 8,667,333 shares of our common stock and Class A warrants to purchase 1,951,844 shares of common stock. The Concurrent Offering is being conducted as a separate public offering by means of a separate prospectus supplement. This offering is not contingent upon the completion of the Concurrent Offering, and the Concurrent Offering is not contingent upon the completion of this offering.

Public Offering Price Per Share of Common Stock and Accompanying Warrant in the Concurrent Offering:

\$7.50

Proceeds from the Offering and the Concurrent Offering:

We estimate that the net proceeds to us from this offering will be approximately \$4.7 million, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. This estimate excludes the proceeds, if any, from exercise of the Warrants sold in this offering.

In addition, we estimate that the net proceeds to us from the Concurrent Offering will be approximately \$60.7 million after deducting underwriting discounts and commissions and estimated offering expenses payable by us. This offering is not contingent upon the completion of the Concurrent Offering, and the Concurrent Offering is not contingent upon the completion of this offering.

If all of the Warrants sold in this offering and the Concurrent Offering were to be exercised in cash at an exercise price per share equal to \$8.625 we would receive additional net proceeds of approximately \$18.3 million. We cannot predict when or if the Warrants will be exercised. It is possible that the Warrants may expire and may never be exercised.

Trade Date:

April 5, 2019

Settlement Date:

April 9, 2019

The issuer has filed a registration statement (including the Preliminary Prospectus Supplement and the accompanying base prospectus) with the U.S. Securities and Exchange Commission (the "SEC") for the offering to which this communication relates. Before you invest, you should read the Preliminary Prospectus Supplement and the accompanying base prospectus in that registration statement and other documents the issuer has filed with the SEC for more complete information about the issuer and this offering. You may get these documents, including the Preliminary Prospectus Supplement, for free by visiting EDGAR on the SEC Web site at <http://www.sec.gov>. Alternatively, the issuer, any underwriter or any dealer participating in the offering will arrange to send you the prospectus if you request it by contacting Cowen and Company, LLC, c/o Broadridge Financial Services, 1155 Long Island Avenue, Edgewood, NY 11717, Attention: Prospectus Department, or by telephone at (631) 274-2806; or Piper Jaffray & Co., Attention: Prospectus Department, 800 Nicollet Mall, J12S03, Minneapolis, MN 55402, or by telephone: 800-747-3924, or by email: prospectus@pjc.com.