

CONFIDENTIAL TREATMENT REQUEST UNDER RULE 83**The entity requesting confidential treatment is:**

Syros Pharmaceuticals, Inc.
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Suite 300
Cambridge, Massachusetts 02139-4815
Attn: Nancy Simonian, M.D.
Chief Executive Officer
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June 10, 2016

VIA EDGAR SUBMISSION

Securities and Exchange Commission
 Division of Corporation Finance
 100 F Street, NE
 Washington, DC 20549

Attention: Suzanne Hayes

Re: Syros Pharmaceuticals, Inc.
 Registration Statement on Form S-1
File No. 333-211818

Ladies and Gentlemen:

In connection with the filing by Syros Pharmaceuticals, Inc. (the "Company") on June 3, 2016 of the above-referenced Registration Statement on Form S-1 (File No. 333-211818) (the "Registration Statement"), on behalf of the Company, we are providing the staff (the "Staff") of the Securities and Exchange Commission with further supplemental information for the Staff's consideration regarding the anticipated price range for the Company's initial public offering. The supplemental response set forth below is based upon information provided to Wilmer Cutler Pickering Hale and Dorr LLP by 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 Washington

Determining the Fair Value of Common Stock Prior to the IPO

As disclosed in the Registration Statement, the Company historically determined the fair value of its common stock on each option grant date based on a variety of factors, including contemporaneous and, in certain instances, retrospective valuations with the assistance of third-party valuation specialists, using a hybrid of the option pricing method ("OPM") and the probability-weighted expected return method and, prior to January 1, 2015, the OPM. The valuation analyses included judgments regarding the determination of an appropriate valuation method at each grant date, and other judgments and estimates including the time to completing an initial public offering ("IPO") or other liquidity event, the probabilities assigned to such events, and the related valuations under each scenario, and an assessment of the Company's development pipeline, market conditions and progress towards undertaking an IPO, among other factors.

The Company obtained a third-party valuation of its common stock as of May 27, 2016 which resulted in an estimated fair value of common stock of \$3.11 per share. This valuation was considered by the Board of Directors (the "Board") in its determination of the fair value of its common stock for 243,000 stock options granted on June 1, 2016. The valuation analysis was prepared using a hybrid method which probability weighted the IPO and OPM scenarios. Management and the Board determined the probability weighting for the IPO and OPM model scenarios was 80% and 20%, respectively. For the OPM scenario, the Company (1) estimated the time to liquidity as 1.51 years; (2) assumed volatility of 97%, based on historical trading volatility for its publicly traded peer companies; and (3) used a risk-free rate of return of 0.8%, based on a pro-rated U.S. Treasury yield curve. For the OPM scenario, equity value was estimated using a backsolve approach. For the IPO scenario, equity value was based on an analysis of guideline public companies. The selected guideline public companies are biopharmaceutical companies which have recently completed IPOs. For the IPO scenario, the Company estimated time to completion of the IPO as one month and applied a risk-adjusted discount rate of 23% to the common stock and 18% to the preferred stock, based on studies that indicated rates of return required by venture investors for bridge financing or IPO-stage companies. The Company then applied a discount for lack of marketability of 29% under the OPM scenario and 7% under the IPO scenario.

The increase in the estimated fair value of the Company's common stock from \$2.27 per share as of March 21, 2016 to \$3.11 per share at May 27, 2016 was the result of the following factors:

- Increased probability of an IPO to 80% as of May 27, 2016 from 65% as of March 21, 2016.
- There has been recent improvement in market prices of publicly traded shares of generally comparable companies and in the demand for such shares.
- The Company continued to advance its research and development activities. In April 2016, the Company filed an IND for SY-1425 and on May 27, 2016, the FDA accepted the Company's IND to proceed with the Phase 2 clinical trial.
- Decreased discount for the lack of marketability under the IPO scenario to 7% as of May 27, 2016 from 12% as of March 21, 2016.

Most Recent Common Stock Valuation Compared to Estimated IPO Price Range

Rule 83 Confidential Treatment Request by Syros Pharmaceuticals, Inc. Request #1

The Company has taken into consideration guidance from its underwriting team that has been presented to and reviewed by the Board on June 1, 2016. To provide further information for the Staff's consideration, the Company supplementally advises the Staff that the Company currently anticipates that the price range for this offering will be within the range of \$[**] to \$[**] per share (before giving effect to a [**] for 1 reverse stock split that the Company plans to implement prior to effectiveness of the Registration Statement resulting in a range of \$[**] to \$[**]). This anticipated price range is based on a number of factors, including the Company's future prospects and those of the Company's industry in general, the Company's financial and operating information in recent periods, the market prices of securities of companies engaged in activities similar to the Company's, existing conditions in the public capital markets and preliminary discussions with the underwriters regarding potential valuations of the Company. The actual price range to be included in a subsequent amendment to the Registration Statement (which will comply with the Staff's interpretation regarding the parameters of a bona fide price range) has not yet been determined and remains subject to adjustment based on factors outside of the Company's control. However, the Company believes that the foregoing indicative price range will not be subject to significant change.

The estimated price range for this offering was determined with reference to several quantitative and qualitative factors, each of which contributed to the difference between the Company's most recent determination of the value of its common stock as of May 27, 2016 of \$3.11 per share and the midpoint of the anticipated offering price range of \$[**] per share. Specifically, the Company believes that the difference between the fair value of its common stock determined as of May 27, 2016 and the midpoint of the anticipated price range for this offering is primarily the result of the following factors:

Syros Pharmaceuticals, Inc. respectfully requests that the information contained in Request #1 be treated as confidential information and that the Commission provide timely notice to Nancy Simonian, M.D., Chief Executive Officer, Syros Pharmaceuticals, Inc., 620 Memorial Drive, Suite 300, Cambridge, Massachusetts 02139-4815, (617) 744-1340, before it permits any disclosure of the bracketed information in Request #1.

- The estimated price range for this offering necessarily assumes that the Company's IPO has occurred and a public market for the Company's common stock has been created, and therefore excludes any discount for lack of marketability of the Company's common stock, which was appropriately taken into account in the Company's prior determinations of the fair value of its common stock.
- The estimated price range for this offering necessarily assumes that all of the Company's preferred stock has converted into common stock in connection with this offering. The Company's preferred stock currently has substantial economic rights and preferences over the Company's common stock. Upon the closing of this offering, all outstanding shares of the Company's preferred stock will convert into common stock, thus eliminating the superior rights and preferences of the preferred stock as compared to the common stock.
- The estimated price range is based only upon a scenario in which the Company completes this offering and is not probability weighted, in contrast to the Company's prior valuations of its common stock, which considered multiple potential outcomes, some of which would have resulted in a lower value of the Company's common stock than an initial public offering.
- In recent "testing-the-waters" meetings, the Company received positive feedback from potential investors.
- The Company has taken further steps towards the completion of an IPO, including on June 3, 2016, the Company publicly filed the Registration Statement with the Commission.
- The proceeds of a successful IPO would substantially strengthen the Company's balance sheet by increasing its cash resources. In addition, the completion of this offering would provide the Company with more ready access to the public company equity and debt markets. These projected improvements in the Company's financial position influenced the increased common stock valuation indicated by the midpoint of the anticipated price range.
- In the public markets, the Company believes there are investors who may apply more qualitative and subjective valuation criteria to certain of its clinical assets than the valuation methods applied in the Company's valuations, although there can be no assurance

that this will in fact be the case. As a private company, the Company used a more quantitative methodology to determine the fair value of its common stock and this methodology differs from the methodology used to determine the estimated price range for this offering. The estimated price range for this offering was not derived using a

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formal determination of fair value, but rather was determined by negotiation between the Company and the underwriters. In particular, the estimate of fair value of the Company's common stock as of May 27, 2016 was not a factor in setting the estimated price range for this offering.

The price that investors are willing to pay in this offering, for which the price range is intended to serve as an estimate, may take into account other factors that have not been expressly considered in the Company's prior valuations, such as the value of the Company's patent portfolio, its additive manufacturing technology and capabilities, and clinical and economic study data, that are not objectively determinable and that valuation models are not able to quantify.

The Company respectfully requests that the Staff return to the undersigned this letter pursuant to Rule 418 of the Securities Act of 1933, as amended, once the Staff has completed its review. For the convenience of the Staff, we have provided a self-addressed stamped envelope for this purpose. We respectfully reserve the right to request that this letter be returned to us at an earlier date.

In addition, the Company requests confidential treatment under 17 C.F.R. § 200.83 for the contents of this letter and has submitted a separate request for confidential treatment in accordance therewith to the Commission's Office of Freedom of Information and Privacy Act Operations.

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If you have any further questions or comments, or if you require any additional information, please contact the undersigned by telephone at (617) 526-6393. Thank you for your assistance.

Very truly yours,

/s/ Cynthia T. Mazareas
Cynthia T. Mazareas

cc: Nancy Simonian, M.D.
Kyle D. Kovalanka
Colleen E. DeSimone

Office of Freedom of Information and Privacy Act Operations
Securities and Exchange Commission
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