February 4, 2016

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Via EDGAR Submission

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

Attention: Scot Foley
Suzanne Hayes

Re: Syros Pharmaceuticals, Inc.
Draft Registration Statement on Form S-1
Submitted November 20, 2015
CIK No. 0001556263

Ladies and Gentlemen:

On behalf of Syros Pharmaceuticals, Inc. (the "Company"), we are responding to the comments contained in the letter dated December 21, 2015 from the staff (the "Staff") of the Securities and Exchange Commission to Nancy Simonian, M.D., the Company's President and Chief Executive Officer, relating to the Confidential Draft Registration Statement on Form S-1 referenced above (the "Registration Statement"). In response to the Staff's comments, the Company has revised the Registration Statement and is submitting herewith for filing a revised Registration Statement on Form S-1 (the "Revised Registration Statement") with this response letter.

The responses set forth below are based upon information provided to Wilmer Cutler Pickering Hale and Dorr LLP by the Company. For convenience, the responses are keyed to the numbering of the comments and the headings used in the Staff's letter. Where appropriate, the Company has responded to the Staff's comments by making changes to the disclosure in the Registration Statement as set forth in the Revised Registration Statement.

On behalf of the Company, we advise you as follows:

Prospectus Summary

1. *Please briefly explain the terms "transcription factors "transcriptional kinases, "proprietary assays" and "agonist."*

Response: In response to the Staff's comment, the Company has revised the disclosure on pages 1, 2, 3, 92, 93 and 94 of the Revised Registration Statement.

2. *Please explain here, and wherever else relevant in your filing, the reason(s) you are initiating clinical testing of SY-1425 with a Phase 2 trial, and not a Phase 1 trial designed to assess safety and tolerability, and indicate whether you have communicated with the Food and Drug Administration about the clinical pathway you intend to follow.*

Response: In response to the Staff's comment, the Company has revised the disclosure on pages 4 and 108 of the Revised Registration Statement.

Risks Associated with Our Business, page 5

3. *Please include a bullet point summarizing the risk factor on pages 17 – 18 that relates to the possible failure of clinical trials for your product candidates to demonstrate safety and efficacy and cite the failure of tamibarotene to achieve its primary endpoint in trials conducted by a third-party. Please also cite this failed clinical trial in your disclosure on pages 104 – 105.*

Response: In response to the Staff's comment, the Company has revised the disclosure on pages 6 and 109 of the Revised Registration Statement. The Company respectfully notes that it has added the requested additional disclosure to page 109, in the relevant discussion of previous clinical trials of tamibarotene, rather than on pages 104 – 105 of the Registration Statement (pages 107 – 108 of the Revised Registration Statement).

4. *In your last bullet point, please note that you do not have composition of matter patent protection for SY-1425 and also state this in your Intellectual Property discussion on page 112.*

Response: In response to the Staff's comment, the Company has revised the disclosure on pages 7 and 117 of the Revised Registration Statement.

Risk Factors
Risks Related to the Discovery, Development and Commercialization of Product Candidates
"Adverse events or undesirable side effects caused by, or other unexpected properties of, product candidates . . .," page 18

5. *Please amend this risk factor to note the adverse effects and the serious adverse event identified from the use of SY-1425 as a treatment for APL cited on page 103.*

Response: In response to the Staff's comment, the Company has revised the disclosure on page 19 of the Revised Registration Statement.

6. *Please amend this risk factor to provide examples of the retinoids similar to SY-1425 that cause birth defects.*

Response: In response to the Staff's comment, the Company has revised the disclosure on page 19 of the Revised Registration Statement.

7. *Please include a bullet point summarizing this risk factor in your prospectus summary and cite the propensity of retinoids to cause birth defects in it.*

Response: In response to the Staff's comment, the Company has revised the disclosure on page 6 of the Revised Registration Statement.

Use of Proceeds, page 63

8. *To the extent practicable, please separate the amount of offering proceeds you intend to allocate toward the development of SY-1425 for the AML indication from that to be allocated for the MDS indication.*

Response: In response to the Staff's comment, the Company has revised the disclosure on page 63 of the Revised Registration Statement.

9. *To the extent practicable, please separate the amount of offering proceeds you intend to allocate toward development of SY-1425 for additional indications from that to be allocated toward the CDK7 inhibitor program for other indications.*

Response: In response to the Staff's comment, the Company has revised the disclosure on page 63 of the Revised Registration Statement.

Management's Discussion and Analysis of Financial Condition and Results of Operations
Critical Accounting Policies and Estimates
Stock-Based Compensation, page 77

10. *We may have additional comments on your accounting for equity issuances including stock compensation and beneficial conversion features. Once you have an estimated offering price, please provide us an analysis explaining the reasons for the differences between recent valuations of your common stock leading up to the IPO and the estimated offering price.*

Response: The Company acknowledges the Staff's request and undertakes to comply with it. Once the Company has determined an estimated offering price range, the Company will inform the Staff of such range and explain the reasons for any differences

between recent valuations of the Company's common stock leading up to the IPO and the estimated offering price range.

Business, page 90

11. *We note your intention to use proceeds of the offering for companion diagnostic development; your references to the need to successfully validate, develop and obtain regulatory approval for companion diagnostics; and your dependence on third party collaborators to develop companion diagnostics. Please describe your agreements with these collaborators and describe these agreements. Additionally, either files the agreements as exhibits to the registration statement or provide your analysis supporting your determination that you are not substantially dependent on these agreements.*

Response: In response to the Staff's comment, the Company informs the Staff that the Company has entered into one agreement with a third party to continue developing a validated laboratory test under Clinical Laboratory Improvement Amendment, or CLIA, guidelines to prospectively enroll *RARA* biomarker-positive patients in the Company's Phase 2 clinical trial of SY-1425. The Company has determined that such agreement is not material to the Company and is not required to be filed as an exhibit to the Revised Registration Statement pursuant to Item 601(b)(10)(ii)(B) of Regulation S-K. The Company is not substantially dependent on this agreement. The Company submits that if such agreement were terminated, the Company would be able to replace such agreement without incurring material expense or delay, and that it would be able to find a replacement collaborator

upon reasonable commercial terms before any such termination would disrupt the Company's business. The total financial obligation of the Company under the agreement is immaterial, at approximately $400,000.

The Company is evaluating third parties to lead the development of a companion diagnostic to measure the *RARA* biomarker for future commercial purposes, but has not yet entered into any such agreement.

The Company has revised the disclosure on pages 107 – 108 of the Revised Registration Statement to clarify its current and planned arrangements with regard to a companion diagnostic.

Our Clinical Programs, page 101

12. *In your discussion of the preclinical data relating to the SY-1075 compound on page 108, please revise your description of its biochemical and cellular potency and selectivity to express the results in layman's language.*

Response: In response to the Staff's comment, the Company has revised the disclosure on page 113 of the Revised Registration Statement.

Intellectual Property, page 111

13. *With respect to issued patents that you license from third parties, please disclose when they expire.*

Response: In response to the Staff's comment, the Company has revised the disclosure on page 117 of the Revised Registration Statement.

Other Comments

14. *Please supplementally provide us with copies of all written communications, as defined in Rule 405 under the Securities Act, that you, or anyone authorized to do so on your behalf, present to potential investors in reliance on Section 5(d) of the Securities Act, whether or not they retain copies of the communications.*

Response: In response to the Staff's request, the Company confirms that it will provide to the Staff on a supplemental basis all of the written communications, as defined in Rule 405 under the Securities Act, that it presents to potential investors in reliance on Section 5(d) of the Securities Act. The Company is separately providing the Staff with all such communications presented to potential investors to date. Investors will not be permitted to retain copies of any such communications.

15. *Please confirm that the graphics included in your registration statement are the only graphics you will use in your prospectus. If those are not the only graphics, please provide any additional graphics prior to their use for our review.*

Response: The Company does not currently intend to include any additional graphics other than those graphics included in the Revised Registration Statement. If the Company determines to include any other graphic in the prospectus, prior to its use the Company will provide such material to the Staff.

* * *

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., *Syros Pharmaceuticals, Inc.*
Kyle Kuvalanka, *Syros Pharmaceuticals, Inc.*
Divakar Gupta, *Cooley LLP*