March 20, 2017

Syros Reports Fourth Quarter and Full Year 2016 Financial Results and Highlights Key Accomplishments and Upcoming Milestones

– Presented Data at Key Medical Meetings Further Supporting Therapeutic Potential of SY-1425 in Genomically Defined AML, MDS and Breast Cancer Patients –

– Highlighted Data at Scientific Conferences Demonstrating Productivity of Syros' Gene Control Platform in Oncology and Immuno-oncology –

– On Track to Report Initial Clinical Data on SY-1425 in Fall 2017 –

– On Track to Initiate Phase 1 Clinical Trial of SY-1365 in Transcriptionally Driven Solid Tumors in Second Quarter of 2017 –

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Syros Pharmaceuticals (NASDAQ:SYRS), a biopharmaceutical company pioneering the discovery and development of medicines to control the expression of disease-driving genes, today reported financial results for the fourth quarter and year ended December 31, 2016, and provided an update on recent accomplishments and upcoming events.

"2016 was a year of enormous accomplishments for Syros, marked by our successful transition to a publicly traded and clinical-stage organization," said Nancy Simonian, M.D., Chief Executive Officer of Syros. "These accomplishments position us for a breakthrough 2017 with a planned clinical readout for SY-1425, our first-in-class RARα agonist, from the Phase 2 proof-of-concept trial in genomically defined AML and MDS patients, and the expected initiation of a Phase 1 clinical trial for our second program, SY-1365, a first-in-class selective CDK7 inhibitor, in patients with advanced transcriptionally driven solid tumors. We also continue to advance our preclinical pipeline in oncology and immuno-oncology keeping us on track to achieve our goal of an IND filing every other year on average. I am thrilled by our continued progress toward our vision of creating medicines that benefit patients with diseases that have eluded other genomics-based approaches."

Upcoming Milestones

- Syros expects to report initial clinical data from its ongoing Phase 2 trial of SY-1425, an oral first-in-class selective retinoic acid receptor alpha (RARα) agonist, in the fall of 2017. The Phase 2 study is exploring the safety and efficacy of SY-1425 in four acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS) patient populations with a proprietary *RARA* biomarker discovered using the Company's gene control platform.
- Syros announced its plans to expand the ongoing Phase 2 clinical trial to include

combination dosing to explore the safety and efficacy of SY-1425 when combined with azacitidine, a standard-of-care therapy, in newly diagnosed AML patients 60 years or older who are not suitable candidates for standard chemotherapy. The addition of the combination arm is part of the Company's strategy to simultaneously evaluate SY-1425 as both a single agent and in combination with other agents to facilitate its rapid and efficient development.

- Syros remains on track to initiate a Phase 1 clinical trial of SY-1365, a first-in-class selective cyclin-dependent kinase 7 (CDK7) inhibitor, in patients with transcriptionally driven solid tumors, including triple-negative breast, ovarian and small cell lung cancers, in the second quarter of 2017.
- At the American Association for Cancer Research (AACR) Annual Meeting in Washington D.C., Syros will present new data on SY-1425, SY-1365 and its CDK12/13 inhibitor program. The presentations highlight the productivity of the Company's gene control platform and the potential of its first-in-class programs both as single agents and in combination with other therapies to provide a meaningful benefit for patients with a range of aggressive cancers.

Recent Platform and Pipeline Highlights

- In February 2017, Syros presented the discovery of a novel, genomics-based approach to stratifying patients with AML at the Cold Spring Harbor Systems Biology: Global Regulation of Gene Expression conference. Through a computational analysis of regulatory regions of the genome, Syros scientists discovered a strong association between distinct super-enhancer profiles of six AML patient groups and patients' overall survival outcomes and responses to certain therapies in development.
- In February 2017, Syros' collaborators at the Lowy laboratory at the University of California, San Diego presented data on the Company's drug discovery research in immuno-oncology at the Moores Cancer Center Industry/Academia Translational Oncology Symposium. Syros scientists discovered alterations in regulatory regions of the genome in subsets of pancreatic cancer patient tissues that are associated with an immunosuppressive state. These alterations point to genes critical for driving immunosuppression in the tumor microenvironment and to potential drug targets in defined subsets of patients to reactivate the immune system to fight cancer.
- In February 2017, Syros announced the publication of research from its scientific founders in a special cancer-focused issue of *Cell* highlighting abnormal transcription as a fundamental driver of cancer. The publication underscores the growing recognition of gene control as an important area for cancer drug discovery and development, and points to transcription factors and transcriptional kinases as attractive drug targets.
- In December 2016, Syros presented new preclinical data on SY-1425 at the 39th Annual San Antonio Breast Cancer Symposium. In preclinical studies, SY-1425 inhibited tumor growth in multiple preclinical models of breast cancer driven by high levels of *RARA* gene expression, with significant anti-proliferative activity both as a single agent and in combination with standard-of-care breast cancer therapies.
- In December 2016, the Company presented new preclinical data on SY-1425 at the 58th American Society of Hematology (ASH) Annual Meeting and Exhibition. In *in vitro* models of AML cells with high levels of *RARA* gene expression, SY-1425 induced a

similar biologic response to that seen in models of acute promyelocytic leukemia (APL), for which SY-1425 is approved in Japan as Amnolake® (tamibarotene). Presentations at ASH also described pharmacodynamic markers to measure early signs of biological activity of SY-1425 in the ongoing Phase 2 trial and preclinical data showing synergistic activity of SY-1425 in combination with AML and MDS therapies, including azacitidine.

- During the fourth quarter, Syros' proprietary *RARA* biomarker test received an investigational device exemption (IDE) from the U.S. Food and Drug Administration for use in the ongoing Phase 2 trial of SY-1425. The IDE approval allowed Syros to expand the trial to include newly diagnosed AML patients 60 years of age or older who are not suitable candidates for standard chemotherapy and lower-risk transfusion-dependent MDS patients who test positive for the *RARA* biomarker.
- Also in the fourth quarter, Syros announced the inclusion of an oral CDK7 inhibitor program in its preclinical pipeline.

Recent Corporate Highlights

In January 2017, Syros announced the appointment of Peter Wirth as Chair of its Board of Directors.

Fourth Quarter 2016 Financial Results

Cash, cash equivalents and marketable securities as of December 31, 2016 were $83.6 million, compared with $35.9 million on December 31, 2015. The increase in net cash includes the net proceeds from the Company's initial public offering (IPO) that closed in July 2016 and its Series B preferred stock offering that closed in January 2016, offset primarily by approximately $42.9 million in cash used to fund operations and purchase equipment.

For the fourth quarter 2016, Syros reported a net loss of $11.0 million, or $0.47 per share, compared to a net loss of $10.7 million, or $5.14 per share, for the same period in 2015. Stock-based compensation included in the net loss was $0.7 million for the fourth quarter 2016, compared to $0.8 million for the same period in 2015.

- Research and development (R&D) expenses were $8.4 million for the fourth quarter 2016, as compared to $8.4 million for the same period in 2015. Stock-based compensation included in R&D expenses was $0.3 million for the fourth quarter 2016, compared to $0.6 million for the same period in 2015.
- General and administrative (G&A) expenses were $2.9 million for the fourth quarter 2016, as compared to $2.3 million for the same period in 2015. Stock-based compensation included in G&A expenses was $0.4 million for the fourth quarter 2016, compared to $0.2 million for the same period in 2015.

Full Year 2016 Financial Results

For the full year ended December 31, 2016, net loss was $47.7 million, or $4.05 per share, as compared to a net loss of $29.8 million, or $17.55 per share, for the same period in 2015. Stock-based compensation included in the net loss was $4.2 million for the year ended December 31, 2016, compared to $3.2 million for the same period in 2015.

- R&D expenses were $37.8 million for the year ended December 31, 2016, as compared to $24.4 million for the same period in 2015. The increase was due to contract manufacturing and clinical development for SY-1425, including a $1.0 million milestone payment made under the Company's license agreement with TMRC Co. Ltd. The increase in R&D expenses was also partially due to the conduct of preclinical activities to advance the Company's CDK7 program, including our clinical candidate SY-1365. Stock-based compensation included in R&D expenses was $3.0 million for the year ended December 31, 2016, compared to $2.7 million for the same period in 2015.
- G&A expenses were $10.5 million for the year ended December 31, 2016, as compared to $5.7 million for the same period in 2015. The increase was largely due to employee-related costs, including salary, benefits, and stock-based compensation due to the increase in G&A headcount to support the growth of the Company. Stock-based compensation included in G&A expenses was $1.2 million for the year ended December 31, 2016, compared to $0.5 million for the same period in 2015.

Financial Guidance

Syros expects that its cash-based operating expenses on a non-GAAP[i] basis will be approximately $50 million for the fiscal year 2017. In addition, Syros expects that its current cash, cash equivalents and marketable securities balance will be sufficient to fund its operating expenses and capital expenditure requirements into mid-2018.

About Syros Pharmaceuticals

Syros Pharmaceuticals is pioneering the understanding of the non-coding region of the genome to advance a new wave of medicines that control expression of disease-driving genes. Syros has built a proprietary platform that is designed to systematically and efficiently analyze this unexploited region of DNA in human disease tissue to identify and drug novel targets linked to genomically defined patient populations. Because gene expression is fundamental to the function of all cells, Syros' gene control platform has broad potential to create medicines that achieve profound and durable benefit across a range of diseases. Syros is currently focused on cancer and immune-mediated diseases and is advancing a growing pipeline of gene control medicines. Syros' lead drug candidates are SY-1425, a selective RARα agonist in a Phase 2 clinical trial for genomically defined subsets of patients with acute myeloid leukemia and myelodysplastic syndrome, and SY-1365, a selective CDK7 inhibitor with potential in a range of solid tumors and blood cancers. Led by a team with deep experience in drug discovery, development and commercialization, Syros is located in Cambridge, Mass.

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: presentation of initial clinical data for SY-1425; initiation of combination dosing of SY-1425; initiation of clinical development of SY-1365; the presentation of preclinical data on Syros' product candidates and preclinical programs; advancement of Syros' preclinical pipeline; the benefits of Syros' gene control platform; Syros' anticipated cash-based operating expenses for the year ended December 31, 2017; and the period of time for which Syros expects to

have capital to fund its planned operations. The words ‘‘anticipate,’’ ‘‘believe,’’ ‘‘continue,’’ ‘‘could,’’ ‘‘estimate,’’ ‘‘expect,’’ ‘‘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 its programs, including SY-1425 and SY-1365, under the timelines it projects in current and future clinical trials; obtain and maintain patent protection for its drug candidates and the freedom to operate under third party intellectual property; demonstrate in any current and future clinical trials the requisite safety, efficacy and combinability of its drug candidates; replicate scientific and non-clinical data in clinical trials; successfully develop a companion diagnostic test to identify patients with biomarkers associated with the RARA super-enhancer; 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, 2016, 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. 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.

Syros Pharmaceuticals, Inc.
Selected Condensed Consolidated Balance Sheet Data
(in thousands)
(unaudited)

	December 31, 2016	December 31, 2015
Cash, cash equivalents and marketable securities	$ 83,593	$ 35,909
Working capital (1)	75,941	28,493
Total assets	91,323	43,631
Convertible preferred stock (2)	—	82,013
Total stockholders' equity (deficit)	80,602	(47,964)

(1) The Company defines working capital as current assets less current liabilities. See the Company's consolidated financial statements for further details regarding its current assets and current liabilities.

(2) On July 6, 2016, upon the closing of the Company's IPO, all of the then-outstanding shares of the Company's convertible preferred stock converted into 15,988,800 shares of common stock.

Syros Pharmaceuticals, Inc.
Condensed Consolidated Statements of Operations
(in thousands, except share and per share data)
(unaudited)

	Three Months Ended December 31,		Years Ended December 31,	
	2016	**2015**	**2016**	**2015**
Revenue	$ 317	$ —	$ 317	$ 317
Operating expenses:				
Research and development	8,443	8,378	37,817	24,408
General and administrative	2,919	2,311	10,463	5,729
Total operating expenses	11,362	10,689	48,280	30,137
Loss from operations	(11,045)	(10,689)	(47,963)	(29,820)
Other income , net	80	—	220	2
Net loss	$ (10,965)	$ (10,689)	$ (47,743)	$ (29,818)
Accrued dividends on preferred stock	—	(1,244)	(3,681)	(4,934)
Net loss applicable to common stockholders	$ (10,965)	$ (11,933)	$ (51,424)	$ (34,752)
Net loss per share applicable to common stockholders - basic and diluted	$ (0.47)	$ (5.14)	$ (4.05)	$ (17.55)
Weighted-average number of common shares used in net loss per share applicable to common stockholders - basic and diluted	23,374,734	2,320,781	12,696,414	1,980,286

[i] Expected cash-based non-GAAP operating expenses exclude stock-based compensation and depreciation expense the Company anticipates recording in 2017.

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