August 9, 2017

Syros Reports Second Quarter 2017 Financial Results and Highlights Accomplishments and Upcoming Milestones

Initiated Phase 1 Clinical Trial for SY-1365, Its First-in-Class CDK7 Inhibitor, Adding a Second Clinical-Stage Program to Syros' Pipeline

Presented Preclinical Data Supporting Rational Combination Strategy for SY-1425, Including Ongoing Clinical Development in Combination with Standard-of-Care Therapy and Planned Future Development in Combination with Anti-CD38 Therapy

Announced Cancer Discovery Publication Highlighting Platform as New Approach for Stratifying Patients with Potential to Lead to Improved Treatment

On Track to Present Initial Phase 2 Clinical Data for SY-1425 in Fourth 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 quarter ended June 30, 2017 and provided an update on recent accomplishments and upcoming events.

"Syros made significant progress during the second quarter by dosing the first patient in our Phase 1 clinical trial of SY-1365 and driving toward the planned initial data readout from our Phase 2 trial of SY-1425 in the fourth quarter," said Nancy Simonian, M.D., Chief Executive Officer of Syros. "We presented data at key medical meetings supporting our rationale for the ongoing and planned future development of SY-1425 as both a monotherapy and combination agent in defined subsets of AML and MDS patients. We also presented data on our identification of 14 new drug targets for triple negative breast cancer and our discovery of key genes controlling the autoimmune response in lupus. The depth of our programs, from discovery to development, is a testament to the promise of our gene control platform to generate a sustainable pipeline across a range of diseases to support our long-term goal of building an enduring company that makes a profound difference for patients."

Syros also announced that Kyle Kuvalanka, Chief Operating Officer, has resigned effective September 22, 2017. Syros has initiated a search to appoint a chief financial officer.

"Kyle has been instrumental in charting our strategic course and maturing Syros into a publicly-traded entity with robust investor support and sufficient funding to enable operations through key inflection points," said Dr. Simonian. "The Syros team and our board of directors thank Kyle for his many contributions, and we wish him much success in the future."

Upcoming Milestones

- Syros expects to report initial clinical data from its ongoing Phase 2 clinical trial of SY-1425, an oral first-in-class selective retinoic acid receptor alpha (RARα) agonist, in the fourth quarter of 2017. The Phase 2 trial is assessing the safety and efficacy of SY-1425 as a monotherapy in four acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS) patient populations, as well as in combination with azacitidine, a standard-of-care therapy, in newly diagnosed AML patients who are not suitable candidates for standard chemotherapy. All patients in the trial are prospectively selected using biomarkers for high expression of *RARA* or *IRF8*, which are genes associated with the *RARA* pathway.
- Syros expects to report preliminary clinical data from its ongoing Phase 1 clinical trial of SY-1365, a first-in-class selective cyclin-dependent kinase 7 (CDK7) inhibitor, in 2018. The Phase 1 trial is evaluating the safety and tolerability of SY-1365 in patients with advanced solid tumors, including transcriptionally dependent cancers such as triple negative breast, small cell lung and ovarian cancers.

Recent Platform and Pipeline Highlights

- In July 2017, Syros published data providing the foundation of its clinical development strategy for SY-1425 in *Cancer Discovery*, a peer-reviewed journal of the American Association of Cancer Research (AACR), supporting the ongoing Phase 2 clinical trial of SY-1425. The publication highlights Syros' discovery of subsets of AML and MDS patients with altered regulation of the *RARA* gene, which was shown in preclinical studies to be predictive of response to SY-1425. The findings underscore the promise of Syros' gene control platform to provide a new approach for stratifying patients with the potential to lead to improved treatment for defined subsets of patients.
- In June 2017, Syros presented preclinical data on SY-1425 at the European Hematology Association (EHA) 22nd Congress. The data demonstrate the synergistic activity of SY-1425 with standard-of-care AML and MDS therapies and targeted anti-CD38 therapies, strengthening the rationale for ongoing and planned future clinical investigation of SY-1425 as both a monotherapy and combination agent. Additional preclinical data presented at EHA elucidate SY-1425's mechanism of action, demonstrating that SY-1425 regulates genes associated with the proliferation of AML cells and normal myeloid differentiation.
- In June 2017, Syros presented on its discovery of key genes controlling the autoimmune response in lupus in a late-breaking oral presentation at the 17th Annual Meeting of the Federation of Clinical Immunology Societies (FOCIS). Using its proprietary gene control platform, Syros discovered alterations in regulatory regions of the genome in T cells from patients with systemic lupus erythematosus (SLE), revealing genes critical for activating T cells and driving disease. These findings provide important biological insights that could lead to the identification of novel drug targets and therapeutic approaches to treat SLE.
- In May 2017, Syros dosed the first patient in a Phase 1 clinical trial of SY-1365, its first-in-class selective CDK7 inhibitor, in patients with advanced solid tumors, including transcriptionally dependent cancers such as triple negative breast, small cell lung and ovarian cancers.

- In May 2017, Syros presented new preclinical data further detailing the mechanism of action of SY-1425 in an oral plenary session at the AACR Hematologic Malignancies: Translating Discoveries to Novel Therapies conference. These data demonstrate that SY-1425 represses genes known to be associated with the proliferation of AML cells, while activating genes critical for driving normal cell differentiation.
- In May 2017, Syros presented new data demonstrating the power of its gene control platform to identify novel drug targets at the IMPAKT 2017 Breast Cancer Conference. Using its platform to systematically analyze regulatory regions of the genome, Syros identified 14 new drug targets for triple negative breast cancer across a range of druggable target types.
- In April 2017, Syros presented new data on its clinical and preclinical development programs at the AACR Annual Meeting. These data showed:
    - High *IRF8* expression is predictive of response to SY-1425 in preclinical models of AML, supporting the utilization of this biomarker in the ongoing trial;
    - SY-1365 induces anti-proliferative and pro-apoptotic effects, including complete regressions, in solid tumor cell lines and preclinical models of difficult-to-treat transcriptionally dependent solid tumors; and
    - Selective inhibition of cyclin-dependent kinase 12 (CDK12) and cyclin-dependent kinase 13 (CDK13) exhibits distinct transcriptional changes and anti-proliferative effects in subsets of ovarian and breast cancer cells compared with the relatively indiscriminate effects of pan-CDK and selective CDK9 inhibitors, supporting Syros' rationale for optimizing selective CDK12 and CDK13 inhibitors that may be suitable for clinical development.

Recent Corporate Highlights

- In June 2017, Syros announced the appointment of Srinivas Akkaraju, M.D. Ph.D., to its board of directors.
- In April 2017, Syros completed a private financing with a select group of existing and new institutional investors, raising approximately $35 million in gross proceeds through the sale of 2,592,591 shares of its common stock at a purchase price of $13.50 per share.

Second Quarter 2017 Financial Results

Cash, cash equivalents and marketable securities as of June 30, 2017 were $91.5 million, compared with $83.6 million on December 31, 2016. The increase in cash is primarily due to gross proceeds of approximately $35.0 million from the April 2017 private placement of our common stock, partially offset by cash used to fund operations during the six-months ended June 30, 2017.

For the second quarter 2017, Syros reported a net loss of $13.4 million, or $0.52 per share, compared to a net loss of $12.0 million, or $5.42 per share, for the same period in 2016. The change in net loss per share reflects the significant increase in shares of common stock outstanding in July 2016 relating to the Company's initial public offering and the conversion of the Company's convertible preferred stock into common stock. Stock-based

compensation included in the net loss was $1.2 million for the second quarter 2017, compared to $1.1 million for the same period in 2016.

- Research and development (R&D) expenses were $10.0 million for the second quarter 2017, as compared to $9.5 million for the same period in 2016. This increase was primarily attributable to an increase in clinical development expenses for SY-1425 as well as an increase in personnel related expenses due to the hire of research and development personnel, partially offset by a decrease in SY-1365 expenses due to the completion of toxicology studies in 2016, as well as a decrease in stock-based compensation. Stock-based compensation included in R&D expenses was $0.4 million for the second quarter 2017, compared to $0.9 million for the same period in 2016. This decrease in stock-based compensation is primarily due to the vesting of restricted stock awards in 2016.
- General and administrative (G&A) expenses were $3.5 million for the second quarter 2017, as compared to $2.5 million for the same period in 2016. This increase was primarily attributable to an increase of employee-related costs, including salary and benefits as a result of the increase in headcount to support growth as a public company. Stock-based compensation included in G&A expenses was $0.7 million for the second quarter 2017, compared to $0.2 million for the same period in 2016.

Financial Guidance

Syros expects that its operating expenses for 2017 will be approximately $55.0 million. This amount includes approximately $5.0 million in non-cash expenses, primarily consisting of stock-based compensation and depreciation, resulting in an estimated cash burn of approximately $50.0 million for the year.

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 in a Phase 1 clinical trial for patients with advanced solid tumors, including transcriptionally dependent cancers such as triple negative breast, small cell lung and ovarian 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: the timing for presentation of initial clinical data for SY-1425 and SY-1365; plans for future clinical development of SY-1425 in combination with an anti-CD38 antibody; the ability to

replicate pre-clinical data of Syros' product candidates in clinical trials; the ability to identify inhibitors of CDK12 and CDK13 suitable for clinical development, the ability of drug targets identified by Syros to result in product candidates; Syros' anticipated operating expenses and cash burn for the year ended December 31, 2017; the ability to recruit a chief financial officer; and the promise of Syros' gene control platform. 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' Quarterly Report on Form 10-Q for the quarter ended June 30, 2017, 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)

	June 30, 2017	December 31, 2016
Cash, cash equivalents and marketable securities	$ 91,521	$ 83,593
Working capital (1)	86,174	75,941
Total assets	99,031	91,323
Total stockholders' equity	91,081	80,602

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

Syros Pharmaceuticals, Inc.

Condensed consolidated statements of operations

(in thousands, except share and per share data)

(unaudited)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2017	**2016**	**2017**	**2016**
Revenue (2)	$ —	$ —	$ 1,101	$ —
Operating expenses:				
Research and development	10,041	9,525	19,669	17,790
General and administrative	3,472	2,540	6,558	4,911
Total operating expenses	13,513	12,065	26,227	22,701
Loss from operations	(13,513)	(12,065)	(25,126)	(22,701)
Other income, net	145	44	243	92
Net loss	$ (13,368)	$ (12,021)	$ (24,883)	$ (22,609)
Accrued dividends on preferred stock	—	(1,823)	—	(3,560)
Net loss applicable to common stockholders	$ (13,368)	$ (13,844)	$ (24,883)	$ (26,169)
Net loss per share applicable to common stockholders - basic and diluted	$ (0.52)	$ (5.42)	$ (1.02)	$ (10.57)
Weighted-average number of common shares used in net loss per share applicable to common stockholders - basic and diluted	25,584,147	2,553,146	24,511,205	2,475,576

(2) Under a research agreement we entered into with a multinational pharmaceutical company, we recognized revenue of $1.1 million during the six months ended June 30, 2017. The research agreement expired on March 31, 2017, and we do not expect to recognize revenue from this agreement in the future. We did not earn any revenue during the six months ended June 30, 2016.

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