May 15, 2017

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

– Dosed First Patient in Phase 1 Clinical Trial of SY-1365 in Patients with Advanced Solid Tumors –

– Expanded Phase 2 Clinical Trial of SY-1425 to Include Combination Dosing Arm; On Track to Report Initial Clinical Data in Fall 2017 –

– Closed Private Placement for $35 Million in Gross Proceeds –

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 first quarter ended March 31, 2017 and provided an update on recent accomplishments and upcoming events.

“Syros is building a strong track record for successful execution as we deliver on the ambitious goals set forth during our IPO in June of last year,” said Nancy Simonian, M.D., Chief Executive Officer of Syros. “Our recent accomplishments strongly position Syros with two clinical-stage product candidates, a rich preclinical pipeline, and a leading gene control platform capable of meeting our goal of generating, on average, one IND every other year. Our strong balance sheet, fortified by the recent private financing from a select group of top-tier investors, gives us the financial strength to fund our planned operations through key value inflection points, including expected clinical data readouts for our two lead product candidates with the first of those being initial clinical data from our Phase 2 proof-of-concept study for SY-1425, our first-in-class selective RARα agonist, in the fall of this year.”

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 fall of 2017. The Phase 2 study is exploring the safety and efficacy of SY-1425 as a monotherapy in four acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS) patient populations. The study also includes a combination dosing arm, which is evaluating the 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. All patients in the trial are prospectively selected using biomarkers for super-enhancers linked to *RARA*-pathway associated genes, *RARA* and *IRF8*.

Recent Platform and Pipeline Highlights

- In May 2017, Syros dosed the first patient in a Phase 1 clinical trial of SY-1365, its first-in-class selective cyclin-dependent kinase 7 (CDK7) inhibitor, in patients with advanced solid tumors, including transcriptionally dependent cancers such as triple negative breast, small cell lung and ovarian cancers. The enrollment of the first patient followed about a month after the acceptance of the Investigational New Drug (IND) application in April by the U.S. Food and Drug Administration (FDA) to advance SY-1365 into the Phase 1 trial.
- In May 2017, Syros presented new preclinical data further detailing the mechanism of action of SY-1425 in an oral plenary session at the American Association for Cancer Research (AACR) Hematologic Malignancies: Translating Discoveries to Novel Therapies conference. The 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 in Brussels, Belgium. 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:
    - SY-1425 increases the anti-tumor activity of hypomethylating agents, including azacitidine, in *in vitro* and *in vivo* models of AML with high levels of *RARA* expression, supporting Syros' rational combination strategy for SY-1425 in the ongoing Phase 2 trial;
    - SY-1425 sensitizes *RARA*-high AML cells to daratumumab, an anti-CD38 monoclonal antibody that flags CD38-positive tumor cells for immune cell-mediated killing, by inducing expression of CD38, supporting future clinical investigation of this combination;
    - 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 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 common stock at a purchase price of $13.50 per share.

First Quarter 2017 Financial Results

Cash, cash equivalents and marketable securities as of March 31, 2017 were $70.5 million, excluding the proceeds from the April 2017 private financing, compared with $83.6 million on December 31, 2016. The decrease in cash was primarily the result of cash used to fund our operations during the three months ended March 31, 2017.

For the first quarter 2017, Syros reported a net loss of $11.5 million, or $0.49 per share, compared to a net loss of $10.6 million, or $5.15 per share, for the same period in 2016. Stock-based compensation included in the net loss was $0.9 million for the first quarter 2017, compared to $0.7 million for the same period in 2016.

- Research and development (R&D) expenses were $9.6 million for the first quarter 2017, as compared to $8.3 million for the same period in 2016. This increase was primarily attributable to clinical trial expenses associated with advancing SY-1425. Stock-based compensation included in R&D expenses was $0.3 million for the first quarter 2017, compared to $0.6 million for the same period in 2016.
- General and administrative (G&A) expenses were $3.1 million for the first quarter 2017, as compared to $2.4 million for the same period in 2016. This increase was primarily attributable to increased personnel-related expenses as a result of an increased headcount. Stock-based compensation included in G&A expenses was $0.6 million for the first quarter 2017, compared to $0.1 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: Syros' ability to execute on its annual goals and reach value inflection points, Syros' ability file one IND every other year on average, the timing for presentation of initial clinical data for SY-1425; initiation of combination dosing of SY-1425 with an anti-CD38 therapeutic antibody; the ability to identify a CDK12/CDK13 inhibitor suitable for clinical development, the benefits of Syros' gene control platform; Syros' anticipated operating expenses and cash burn 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' Quarterly Report on Form 10-Q for the quarter ended March 31, 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)

	March 31, 2017	December 31, 2016
Cash, cash equivalents and marketable securities	$ 70,494	$ 83,593
Working capital (1)	65,640	75,941
Total assets	78,023	91,323
Total stockholders' equity	70,136	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 March 31,	
	2017	**2016**
Revenue (2)	$ 1,101	$ —
Operating expenses:		
Research and development	9,628	8,265
General and administrative	3,086	2,371
Total operating expenses	12,714	10,636
Loss from operations	(11,613)	(10,636)
Other income , net	98	48
Net loss	$ (11,515)	$ (10,588)
Accrued dividends on preferred stock	—	(1,737)
Net loss applicable to common stockholders	$ (11,515)	$ (12,325)
Net loss per share applicable to common stockholders - basic and diluted	$ (0.49)	$ (5.15)
Weighted-average number of common shares used in net loss per share applicable to common stockholders - basic and diluted	23,393,448	2,394,470

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

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Media Contact:
Syros Pharmaceuticals
Naomi Aoki, 617-283-4298
naoki@syros.com
or
Investor Contact:

Stern Investor Relations, Inc.
Hannah Deresiewicz, 212-362-1200
hannahd@sternir.com

Source: Syros Pharmaceuticals