November 14, 2016

Syros Pharmaceuticals Reports Third Quarter 2016 Financial Results and Provides Business Update

Initiated Phase 2 Trial for SY-1425 in Genomically Defined Subsets of Patients with Acute Myeloid Leukemia (AML) or Myelodysplastic Syndrome (MDS)

Highlighted Research on First Selective CDK12 and CDK13 Inhibitor as Novel Approach to Treat Range of Cancers

Closed Initial Public Offering for $57.5 Million in Gross Proceeds

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Syros Pharmaceuticals (NASDAQ:SYRS) today reported financial results for the quarter ended September 30, 2016 and provided an update on recent accomplishments and upcoming events.

“With the dosing of the first patient in our first clinical study, a Phase 2 trial of SY-1425 in genomically defined AML and MDS populations, we rapidly advanced the broad promise of our gene control platform into the clinic in less than four years since Syros’ inception,” said Nancy Simonian, M.D., Chief Executive Officer of Syros. “Our novel approach to drug discovery and development continues to produce a robust pipeline centered around identifying disease-driving genes in molecularly defined patient subsets and regulating these genes with selective small molecule inhibitors, as evidenced by the recent research published around our emerging CDK12/13 program. With a strong cash position, we are poised to deliver on multiple clinical milestones, while continuing to invest in our broader platform.”

Upcoming Milestones

- Syros plans to expand its ongoing Phase 2 trial of SY-1425, a first-in-class selective retinoic acid receptor alpha (RARα) agonist, to include newly diagnosed AML patients 60 years of age or older who are not suitable candidates for standard chemotherapy and low-risk transfusion-dependent MDS patients who test positive for a proprietary *RARA*-associated biomarker discovered using the Company’s gene control platform. Syros expects to report preliminary data from this study in the fall of 2017, approximately 12 months after enrolling the first patient in the trial.
- At the 58th American Society of Hematology Annual Meeting in San Diego, Syros will present new preclinical data on SY-1425. The data will demonstrate that SY-1425 produces a biologic response in *in vitro* models of AML with high levels of *RARA* gene expression similar to that seen in models of acute promyelocytic leukemia (APL), while having little effect on AML cells with low levels of *RARA* gene expression. APL is a form of AML with a distinct genetic alteration in the *RARA* gene. SY-1425 is approved

in Japan as Amnolake® (tamibarotene) for the treatment of APL, with a well-established efficacy and safety profile. The consistent *in vitro* biological responses suggest that SY-1425 may provide a clinical benefit for subsets of AML patients whose tumors are driven by high levels of *RARA* expression as it does in APL patients. In both diseases, RARα is a key oncogenic driver directly targeted by SY-1425. Presentations will also describe pharmacodynamic markers for use in the ongoing Phase 2 clinical trial of SY-1425, and the synergistic activity of SY-1425 in combination with other AML and MDS therapies.

- Syros remains on track to initiate the first Phase 1/2 trial of SY-1365, a first-in-class selective cyclin-dependent kinase 7 (CDK7) inhibitor, in patients with advanced solid tumors, including triple-negative breast cancer, ovarian cancer and small cell lung cancer, in the first half of 2017.

Recent Platform and Pipeline Highlights

- In October 2016, Syros announced that the U.S. Food and Drug Administration approved an investigational device exemption (IDE) for the laboratory-based blood test being used to detect the *RARA* associated biomarkers in the ongoing Phase 2 trial of SY-1425. The approval of the IDE enables the expansion of the SY-1425 clinical program into additional populations, including newly diagnosed AML and low-risk transfusion-dependent MDS patients.
- In September 2016, Syros announced that the first patient had been dosed in the Phase 2 clinical trial of SY-1425 in genomically defined subsets of patients with relapsed or refractory AML or high-risk MDS who have a *RARA*-associated biomarker.
- In August 2016, Syros announced the publication of research from its scientific founders in the peer-reviewed scientific journal *Nature Chemical Biology* demonstrating that transcriptional cyclin-dependent family kinase members CDK12 and CDK13 play a critical role in regulating gene expression and that inhibition of these targets represents a promising new approach for treating certain cancers, both as a monotherapy and in combination. Syros holds all research, development and commercial rights to the research compound described in the paper, as well as related compounds, through both ownership of the intellectual property and a license from the Dana-Farber Cancer Institute. Syros plans to leverage its unique expertise in drugging transcriptional kinases to create selective CDK12 and CDK13 inhibitors suitable for clinical development.
- During the third quarter, Syros successfully completed investigational new drug application (IND) -enabling toxicology studies for SY-1365.

Recent Corporate Highlights

- In September 2016, Syros announced the appointment of Gerald E. Quirk as Chief Legal Officer. Mr. Quirk holds broad management responsibility for all legal aspects of the business, including corporate and securities law, intellectual property matters, business development transactions and compliance.
- In July 2016, Syros completed its initial public offering (IPO), raising approximately $57.5 million in gross proceeds through the sale of 4,600,000 shares at an offering price of $12.50 per share – including 600,000 shares of common stock issued upon the

full exercise by the underwriters of their option to purchase additional shares.

Third Quarter 2016 Financial Results

- Cash and cash equivalents as of September 30, 2016 were $93.5 million, compared with $35.9 million on December 31, 2015. The increase in cash includes the net proceeds from the Company's IPO that closed in July 2016 and its Series B preferred stock offering that closed in January 2016, offset primarily by approximately $32.9 million in cash to fund operations and purchase equipment. Syros expects that its current cash and cash equivalents balance will be sufficient to fund its operating expenses and capital expenditure requirements into mid-2018.
- For the third quarter of 2016, Syros reported a net loss of $14.2 million, or $0.65 per share, compared to a net loss of $8.5 million, or $4.51 per share for the same period in 2015. Stock-based compensation included in the net loss for the third quarter of 2016 was $1.7 million, compared to $1.3 million for the same period in 2015.
- Research and development (R&D) expenses for the third quarter of 2016 were approximately $11.6 million, compared to $6.9 million for the same period in 2015. The increase was largely due to contract manufacturing and clinical development for SY-1425 and 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 IND-enabling studies for SY-1365 during the third quarter of 2016. Stock-based compensation included in R&D expenses for the third quarter of 2016 was $1.2 million, compared to $1.1 million for the same period in 2015.
- General and administrative (G&A) expenses for the third quarter of 2016 were approximately $2.6 million, compared to $1.6 million for the same period in 2015. The increase was largely due to increased professional fees associated with being a public company and 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 for the third quarter of 2016 was $0.5 million, compared to $0.2 million for the same period in 2015.

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 the potential therapeutic benefit of treatment with SY-1425 in genomically defined subsets of AML and MDS patients; Syros' strategies, plans and goals for SY-1425, including the expansion of development into additional AML and MDS patient populations; the timeline under which data are expected from clinical trials of SY-1425; the initiation of clinical development of SY-1365; the ability to generate inhibitors of CDK12 and CDK13 that are suitable for clinical development; the potential benefits of the Company's gene control platform; and the period of time for which Syros expects to have capital to fund its current 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, 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 the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2016, which is on file with the Securities and Exchange Commission; and risks described in other filings that the Company 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)

	September 30, 2016	December 31, 2015
Cash and cash equivalents	$ 93,494	$ 35,909
Working capital (1)	86,533	28,493
Total assets	100,410	43,631
Convertible preferred stock (2)	—	82,013

Total stockholders' (deficit) equity	90,781	(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 September 30,		Nine Months Ended September 30,	
	2016	**2015**	**2016**	**2015**
Collaboration revenue	$ —	$ —	$ —	$ 317
Operating expenses:				
Research and development	11,584	6,866	29,374	16,030
General and administrative	2,633	1,598	7,544	3,418
Total operating expenses	14,217	8,464	36,918	19,448
Loss from operations	(14,217)	(8,464)	(36,918)	(19,131)
Other income (expense), net	48	—	140	2
Net loss and comprehensive loss	$ (14,169)	$ (8,464)	$ (36,778)	$ (19,129)
Accrued dividends on preferred stock	(121)	(1,243)	(3,681)	(3,690)
Net loss applicable to common stockholders	$ (14,290)	$ (9,707)	$ (40,459)	$ (22,819)
Net loss per share applicable to common stockholders - basic and diluted	$ (0.65)	$ (4.51)	$ (4.44)	$ (12.21)
Weighted-average number of common shares used in net loss per share applicable to common stockholders - basic and diluted	22,012,743	2,150,274	9,110,993	1,868,182

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