March 7, 2019

Syros Reports Fourth Quarter and Full Year 2018 Financial Results and Highlights Multiple Upcoming Clinical Milestones for Its First-in-Class Programs

Expects to Report Updated Data on SY-1425 in Combination with Azacitidine in Newly Diagnosed Unfit AML Patients in Second Half of 2019

Expects to Report Initial Data from Expansion Portion of Phase 1 Trial of SY-1365 in Fourth Quarter of 2019

Announces Plans to Expand Ongoing Phase 2 Trial of SY-1425 in Combination with Azacitidine to Include Biomarker-Positive Relapsed or Refractory AML Patients

Announces New Expansion Cohort to Evaluate SY-1365 in Recurrent Ovarian Clear Cell Cancer Patients

Management to Host Conference Call at 8:30 a.m. ET Today

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Syros Pharmaceuticals (NASDAQ: SYRS), a leader in the development of medicines that control the expression of genes, today reported financial results for the fourth quarter and full year ended December 31, 2018 and provided an update on recent accomplishments and upcoming events.

“Our accomplishments in 2018 position us for multiple potential clinical milestones in 2019 and 2020 that bring us closer to our vision of building a fully integrated company with medicines that provide a profound benefit for patients,” said Nancy Simonian, M.D., Chief Executive Officer of Syros. “Building on promising clinical data for both our lead programs, we plan to expand our ongoing Phase 2 trial of SY-1425 in combination with azacitidine with the addition of a cohort in *RARA* and *IRF8* biomarker-positive relapsed or refractory AML patients. We have also added a cohort of recurrent ovarian clear cell cancer patients to our ongoing Phase 1 trial of SY-1365. The unmet need in both these patient populations is significant, and we believe these cohorts could lead to rapid clinical proof-of-concept. These new cohorts, when combined with our ongoing evaluation of SY-1365 as a single agent in patients with high-grade serous ovarian cancer, give us three potential fast-to-market opportunities for our lead programs. We are focused on executing on our clinical trials with the aim of delivering much-needed therapies to patients as quickly as possible.”

Upcoming Milestones:

SY-1425

- Syros announced today that it plans to expand its ongoing Phase 2 trial to assess the safety and efficacy of SY-1425 in combination with azacitidine in *RARA* or *IRF8* biomarker-positive patients with relapsed or refractory acute myeloid leukemia (AML). The Company expects this expansion to be open for enrollment in the third quarter.
- Syros plans to complete enrollment in mid-2019 in the ongoing Phase 2 trial cohort evaluating the safety and efficacy of SY-1425 in combination with azacitidine in *RARA* or *IRF8* biomarker-positive patients with newly diagnosed AML who are not suitable candidates for standard chemotherapy.
- Syros plans to report updated data in the second half of 2019 from the ongoing Phase 2 trial of SY-1425 in combination with azaciditine in newly diagnosed unfit AML patients.

SY-1365

- Syros announced today that it has added an expansion cohort to its ongoing Phase 1 trial of SY-1365 to evaluate its safety and efficacy as a single agent in patients with recurrent ovarian clear cell cancer. The Company expects the cohort to be open for enrollment in the second quarter of 2019. This cohort will replace the cohort evaluating SY-1365 in patients with primary platinum refractory ovarian cancer.
- Syros plans to report initial clinical data in the fourth quarter of 2019 from the expansion portion of its ongoing Phase 1 trial. These data are expected to include initial efficacy and safety assessments from the cohort evaluating SY-1365 as a single agent in high-grade serous ovarian cancer patients who have had three or more prior lines of therapy; initial safety and pharmacokinetic data from the cohort evaluating SY-1365 in combination with carboplatin in high-grade serous ovarian cancer patients who have had one or more prior lines of therapy; and initial safety, efficacy and mechanistic data from the cohort evaluating SY-1365 as a single agent in patients with advanced solid tumors accessible for biopsy.

SY-5609

- Syros plans to complete investigational new drug-enabling studies of SY-5609 in 2019 to support the initiation of a Phase 1 oncology trial in early 2020.

Recent Pipeline Highlights:

- In December 2018, Syros' collaborators presented new preclinical data on SY-1365 at the San Antonio Breast Cancer Symposium (SABCS). The data showed that SY-1365 inhibits tumor cell growth in hormone receptor-positive (HR-positive) breast cancer cell lines that are resistant to treatment with CDK4/6 inhibitors and that SY-1365 has synergistic activity in combination with fulvestrant in these treatment-resistant cells.
- In December 2018, Syros presented initial clinical data from cohorts in its ongoing Phase 2 trial evaluating SY-1425 in combination with azacitidine at the 60th American Society of Hematology (ASH) Annual Meeting and Exposition. SY-1425 in

combination with azacitidine showed high response rates and rapid onset of action in biomarker-positive patients with newly diagnosed unfit AML as of an October 29, 2018 data cut-off. The data showed:

- The aggregate complete response (CR) and complete response with incomplete blood count recovery (CRi) rate was 50% in biomarker-positive patients (n=8), and the overall response rate (ORR) was 63%.
- Most initial responses in biomarker-positive patients were seen at the end of the first treatment cycle, and duration of responses ranged from 29 to 337 days, with four of five responding patients remaining on treatment.
- The ORR was 17% in biomarker-negative patients (n=6). While the data from this cohort were less mature due to the timing of patient enrollment, Syros believes that the difference in the observed ORR supports the potential predictive value of the *RARA* and *IRF8* biomarkers for identifying patients most likely to respond to SY-1425.
- The combination was generally well-tolerated, with no evidence of increased toxicities beyond what has been seen with either agent alone, including myelosuppression, which can occur when combining drugs to treat AML.

- In December 2018, Syros also presented initial clinical data from a Phase 2 study cohort evaluating SY-1425 in combination with daratumumab in biomarker-positive patients with relapsed or refractory AML and higher-risk myelodysplastic syndrome at ASH. While the data showed that SY-1425 induced CD38 expression in eight of nine evaluable patients, CD38 expression increased to levels exceeding those of a multiple myeloma cell line control in only two of these patients. Of those two, one had a morphological leukemia-free state (MLFS) response. Based on these data, Syros made a portfolio prioritization decision not to pursue further development of SY-1425 in combination with daratumumab.
- In November 2018, Syros presented clinical data from the dose escalation portion of its Phase 1 trial of SY-1365 in patients with advanced solid tumors at the 30th EORTC-NCI-AACR Molecular Targets and Cancer Therapeutics Symposium (EORTC-NCI-AACR). The data showed proof-of-mechanism and early signs of clinical activity at tolerable doses:
  - Clinical activity was observed in seven of 19 response-evaluable patients, including one patient with recurrent ovarian clear cell cancer who had a confirmed partial response (PR) and six additional patients who had stable disease (SD).
  - Dose-dependent effects on CDK7 occupancy and downstream gene expression changes in blood cells were observed.
  - At doses of 32 mg/m^2 and higher, CDK7 occupancy was greater than 50% when measured three days following dose administration, exceeding target occupancy levels in preclinical models that correlated with anti-tumor activity.
  - Adverse events were predominately low-grade, reversible and manageable.
- Also at EORTC-NCI-AACR, Syros presented preclinical data on SY-1365 showing synergistic anti-tumor activity in combination with carboplatin in ovarian cancer cell

lines and decreased expression of DNA damage response genes, providing a mechanistic rationale for the ongoing investigation of SY-1365 in combination with carboplatin in ovarian cancer patients.

- Additionally, Syros presented the first preclinical data from its oral CDK7 program, detailing the selectivity, potency and anti-tumor activity of several compounds and supporting the selection of SY-5609, an oral CDK7 inhibitor, as a development candidate.

Recent Corporate Highlights:

- In December 2018, Syros announced that it had been added to the NASDAQ Biotechnology Index® (NASDAQ: NBI), effective Monday, December 24, 2018.

Fourth Quarter 2018 Financial Results

Cash, cash equivalents and marketable securities as of December 31, 2018 were $99.7 million, compared with $72.0 million on December 31, 2017.

For the fourth quarter of 2018, Syros reported a net loss of $18.0 million, or $0.54 per share, compared to a net loss of $15.3 million, or $0.58 per share, for the same period in 2017.

- Revenues were $0.9 million for the fourth quarter of 2018, which relate entirely to Syros' target discovery collaboration with Incyte Corporation. Syros did not record revenues in the fourth quarter of 2017.
- Research and development (R&D) expenses were $15.1 million for the fourth quarter of 2018, as compared to $11.8 million for the same period in 2017. This increase was primarily attributable to an increase in SY-1365 contract manufacturing costs and professional fees in support of Syros' clinical trials, as well as an increase in employee-related expenses.
- General and administrative (G&A) expenses were $4.4 million for the fourth quarter of 2018, as compared to $3.7 million for the same period in 2017. This increase was primarily attributable to an increase in employee-related expenses.

Full Year 2018 Financial Results

For the full year ended December 31, 2018, Syros reported a net loss of $62.3 million, or $1.91 per share, compared to a net loss of $54.0 million, or $2.13 per share, for the same period in 2017.

- Revenues for the year ended December 31, 2018 were $2.1 million, as compared to $1.1 million for the same period in 2017. Revenues earned in 2018 related entirely to the Incyte collaboration. Revenues earned in 2017 were earned from a research agreement with a multinational pharmaceutical company.
- R&D expenses for the year ended December 31, 2018 were $50.2 million, as compared to $41.9 million for the same period in 2017. This increase was primarily attributable to an increase in contract manufacturing costs and professional fees in

support of Syros' clinical trials, as well as an increase in employee-related expenses.

- G&A expenses for the year ended December 31, 2018 were $16.2 million, as compared to $13.9 million for the same period in 2017. This increase was primarily attributable to an increase in employee-related expenses.

Financial Guidance

Based on its current plans, Syros believes that its existing cash, cash equivalents and marketable securities will be sufficient to fund its planned operating expenses and capital expenditure requirements into the second quarter of 2020.

Conference Call and Webcast:

Syros will host a conference call today at 8:30 a.m. ET to discuss these fourth quarter and full year 2018 financial results and provide a corporate update.

The live call may be accessed by dialing (866) 595-4538 for domestic callers or (636) 812-6496 for international callers and referencing conference ID number: 7258556. A live webcast of the conference call will be available online on the Investors & Media section of the Syros website at www.syros.com. An archived replay of the webcast will be available for approximately 90 days.

About Syros Pharmaceuticals
Syros is pioneering the understanding of the non-coding regulatory region of the genome to advance a new wave of medicines that control the expression of genes. Syros has built a proprietary platform that is designed to systematically and efficiently analyze this unexploited region of DNA 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 monogenic 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 SY-1365, a selective CDK7 inhibitor in a Phase 1 clinical trial focused on patients with ovarian and breast cancers. Syros is also developing a deep preclinical and discovery pipeline, including SY-5609, an oral CDK7 inhibitor, as well as programs in immuno-oncology and sickle cell disease. 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 Company's ability to advance its clinical-stage programs, including the of the timing and quantity of clinical data to be reported from the combination cohorts of the ongoing Phase 2 clinical trial of SY-1425 and the expansion phase of the ongoing Phase 1 clinical trial of SY-1365, as well as the opening of new cohorts in each of these trials; the ability to complete enrollment in the cohort of the ongoing clinical Phase 2 clinical trial of SY-1425 in biomarker-positive newly diagnosed unfit AML patients; the ability to achieve rapid

clinical proof of concept and take advantage of fast-to-market opportunities for SY-1425 and SY-1365; the predictive value of the Company's *RARA* and *IRF8* biomarkers; the ability to complete IND-enabling preclinical studies and begin clinical development of SY-5609; the Company's ability to fund its planned operations to the second quarter of 2020; and the benefits of Syros' gene control platform and product development pipeline. The words ''anticipate,'' ''believe,'' ''continue,'' ''could,'' ''estimate,'' ''expect,'' "hope," ''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; demonstrate in any current and future clinical trials the requisite safety, efficacy and combinability of its drug candidates; successfully progress SY-5609 through IND-enabling preclinical and toxicology studies; replicate scientific and non-clinical data in clinical trials; successfully develop a companion diagnostic test to identify patients with the *RARA* and *IRF8* biomarkers; obtain and maintain patent protection for its drug candidates and the freedom to operate under third party intellectual property; obtain and maintain necessary regulatory approvals; identify, enter into and maintain collaboration agreements with third parties, including its ability to perform under the collaboration agreement with Incyte; 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, 2018, 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, 2018	December 31, 2017
Cash, cash equivalents and marketable securities	$ 99,679	$ 72,049
Working capital (1)	82,205	60,746
Total assets	106,766	78,488
Total stockholders' equity	78,586	65,324

(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.

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

	Three Months Ended December 30,		Year Ended December 31,	
	2018	**2017**	**2018**	**2017**
Revenue	$ 893	$ —	$ 2,050	$ 1,101
Operating expenses:				
Research and development	15,128	11,780	50,182	41,896
General and administrative	4,372	3,740	16,164	13,891
Total operating expenses	19,500	15,520	66,346	55,787
Loss from operations	(18,607)	(15,520)	(64,296)	(54,686)
Other income, net	575	218	2,017	676
Net loss	$ (18,032)	$ (15,302)	$ (62,279)	$ (54,010)
Net loss per share - basic and diluted	$ (0.54)	$ (0.58)	$ (1.91)	$ (2.13)
Weighted-average number of common shares used in net loss per share - basic and diluted	33,694,756	26,316,550	32,656,237	25,406,845

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