March 4, 2021

# Syros Reports Fourth Quarter and Full Year 2020 Financial Results and Highlights Key Accomplishments and Upcoming Milestones

*Initiated Phase 3 Trial of SY-1425 in Combination with Azacitidine in RARA-Positive Newly Diagnosed Higher-Risk MDS Patients*

*On Track to Initiate Two Additional Clinical Trials Across Hematology Franchise in 2H 2021*

*On Track to Report Additional Dose-Escalation Data for SY-5609 in Select Solid Tumors in Q3 2021, with Expansion Phase of Trial Expected to Begin in 2H 2021*

*Well-funded with Cash Runway into 2023, Through Multiple Potential Value Drivers*

*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 quarter and full year ended December 31, 2020, and provided an update on recent accomplishments and upcoming events.

“2021 promises to be a pivotal year for Syros,” said Nancy Simonian, M.D., Chief Executive Officer of Syros. “We moved our lead program into our first registration-enabling study and continue to advance all three of our clinical-stage programs with the aim of setting new standards of care for targeted populations of patients with hematological malignancies and solid tumors. Following our recent financings, we are operating from a position of substantial strength, with capital to advance SY-1425, SY-2101 and SY-5609 through multiple expected data readouts while investing in our gene control platform to fuel our long-term pipeline. We are focused on executing with excellence as we accelerate toward our goal of bringing medicines to market that provide profound benefits for patients.”

**Upcoming Milestones**

*SY-1425: Oral RARα agonist*

- Initiate randomized Phase 2 trial of SY-1425 in combination with venetoclax and azacitidine in the second half of 2021 in RARA-positive newly diagnosed acute myeloid leukemia (AML) patients who are not suitable candidates for standard intensive chemotherapy.
- Report initial data from the randomized Phase 2 trial in 2022.

*SY-2101: Oral arsenic trioxide (ATO)*

- Initiate dose confirmation study of SY-2101 in the second half of 2021.
- Report confirmatory dose and pharmacokinetic data in first half of 2022.
- Initiate Phase 3 trial in 2022 in patients with newly diagnosed acute promyelocytic leukemia (APL).

*SY-5609: Oral CDK7 inhibitor*

- Report additional dose-escalation data, including clinical activity data, in the third quarter of 2021 from the ongoing Phase 1 trial of SY-5609 in patients with breast, colorectal, lung, ovarian and pancreatic cancers, as well as in patients with solid tumors of any histology harboring Rb pathway alterations.
- Initiate expansion portion of Phase 1 trial in the second half of 2021.

*Gene control discovery engine*

- Nominate next development candidate in 2022.

**Recent Pipeline Highlights**

- In February 2021, Syros opened its Phase 3 trial evaluating SY-1425 in combination with azacitidine in RARA-positive patients with newly diagnosed higher-risk myelodysplastic syndrome (HR-MDS) and is actively screening patients for enrollment. The double-blind, placebo-controlled trial is expected to enroll approximately 190 patients. Patients will be randomized 2:1 to receive SY-1425 in combination with azacitidine or placebo, respectively. The primary endpoint of the trial is complete response (CR) rate.
- In December 2020, Syros presented new clinical data from its fully enrolled Phase 2 trial evaluating SY-1425 in combination with azacitidine in RARA-positive newly diagnosed unfit AML patients. The data, presented at the 62$^{nd}$ American Society of Hematology (ASH) Annual Meeting, showed:
    - 67% overall response rate, with a composite CR rate of 61%.
    - Median time to initial response of 1.2 months.
    - Median duration of response of 10.8 months, and median overall survival among patients who achieved a CR or CR with incomplete blood count recovery of 18 months.
    - The combination was generally well-tolerated, with no evidence of increased toxicity relative to either SY-1425 or azacitidine as a single agent.
- Also at ASH, Syros presented new translational data demonstrating that most RARA-positive newly diagnosed unfit AML patients have a monocytic disease phenotype that is highly correlated with resistance to upfront treatment with venetoclax and azacitidine, suggesting that the RARA biomarker also selects for patients who are less likely to respond to treatment with venetoclax and azacitidine.

**Recent Corporate Highlights**

- In January 2021, Syros completed an underwritten public offering of 5,400,000 shares of common stock, at a public offering price of $14.00 per share, resulting in gross proceeds of approximately $75.6 million, before underwriting discounts and commissions.
- In December 2020, Syros acquired from Orsenix, LLC all of its assets related to SY-

2101, a novel oral form of ATO. SY-2101 is a targeted clinical-stage drug candidate that has the potential to dramatically reduce the treatment burden of a standard-of-care regimen for newly diagnosed APL.
- Also in December 2020, Syros announced the closing of a $90.5 million private financing with a group of institutional accredited investors. The financing was led by Bain Capital Life Sciences, with participation from new and existing investors, including Ally Bridge Group, Omega Funds, OrbiMed Advisors, EcoR1 Capital, and Samsara BioCapital.

**Fourth Quarter and Full Year 2020 Financial Results**

- Revenues were $5.7 million for the fourth quarter of 2020, consisting of $3.6 million in revenue recognized under Syros' collaboration with Global Blood Therapeutics, Inc. (GBT) and $2.1 million recognized under its collaboration with Incyte Corporation (Incyte). Revenues were $15.1 million for the year ended December 31, 2020, consisting of $11.7 million and $3.4 million from Syros' collaborations with GBT and Incyte, respectively. Syros recognized $0.5 million and $2.0 million in revenue in the fourth quarter and full year 2019, respectively. All revenues recognized in 2019 were under Syros' collaboration with Incyte.
- Research and development expenses were $29.0 million for the fourth quarter of 2020 and $76.1 million for the year ended December 31, 2020, as compared to $14.3 million for the fourth quarter of 2019 and $58.2 million for the year ended December 31, 2019. This increase was primarily attributable to $12.0 million paid for the acquisition of SY-2101 from Orsenix, LLC and continued advancement of our clinical trials and preclinical programs.
- General and administrative expenses were $5.9 million for the fourth quarter of 2020 and $21.3 million for the year ended December 31, 2020, as compared to $6.4 million for the fourth quarter of 2019 and $21.5 million for the year ended December 31, 2019.
- For the fourth quarter of 2020, Syros reported a net loss of $30.1 million, or $0.62 per share, compared to a net loss of $19.7 million, or $0.46 per share, for the same period in 2019. For the full year ended December 31, 2020, Syros reported a net loss of $84.0 million, or $1.82 per share, compared to a net loss of $75.4 million, or $1.88 per share, for the same period in 2019.

**Cash and Financial Guidance**

Cash, cash equivalents and marketable securities as of December 31, 2020 were $174.0 million, as compared with $91.4 million on December 31, 2019. This increase reflects the $20 million upfront payment received in January 2020 in connection with Syros' collaboration with GBT, $40.0 million in total that Syros drew from its senior secured loan facility with Oxford Finance, $12.3 million from the sale of common stock under Syros' at-the-market sales facility in the first quarter of 2020 and the $90.5 million that Syros received from its December private placement, partially offset by the $12.0 million paid for the acquisition of SY-2101 from Orsenix, LLC and cash used to fund its operations. Cash, cash equivalents and marketable securities as of December 31, 2020 do not include gross proceeds of $75.6 million from the January 2021 public offering.

Based on its current plans, Syros believes that its existing cash, cash equivalents and marketable securities, including proceeds from its January 2021 public offering, will be sufficient to fund its planned operating expenses and capital expenditure requirements into

2023.

**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 2020 financial results and provide a corporate update.

To access the live conference call, please dial 866-595-4538 (domestic) or 636-812-6496 (international), and refer to conference ID 4472467. A webcast of the call will also be available on the Investors & Media section of the Syros website at www.syros.com. An archived replay of the webcast will be available for approximately 30 days following the presentation.

**About Syros Pharmaceuticals**

Syros is redefining the power of small molecules to control the expression of genes. Based on its unique ability to elucidate regulatory regions of the genome, Syros aims to develop medicines that provide a profound benefit for patients with diseases that have eluded other genomics-based approaches. Syros is advancing a robust clinical-stage pipeline, including: SY-1425, a first-in-class oral selective RARα agonist in RARA-positive patients with higher-risk myelodysplastic syndrome and acute myeloid leukemia; SY-2101, a novel oral form of arsenic trioxide in patients with acute promyelocytic leukemia; and SY-5609, a highly selective and potent oral CDK7 inhibitor in patients with select solid tumors. Syros also has multiple preclinical and discovery programs in oncology and monogenic diseases. For more information, visit www.syros.com and follow us on Twitter (@SyrosPharma) and LinkedIn.

**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's clinical development plans, including with respect to SY-1425, SY-2101 and SY-5609, the timing of anticipated data readouts from its clinical trials, the timing of nomination of Syros's next development candidate, Syros's estimates regarding its balance of cash, cash equivalents and marketable securities for the year ended December 31, 2020, and the sufficiency of Syros' capital resources to fund its operating expenses and capital expenditure requirements into 2023. 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, SY-2101 and SY-5609, 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; sustain the response rates and durability of response seen to date with its drug candidates; successfully develop a companion diagnostic test to identify patients with the RARA biomarker; 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; 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, 2020, 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. In addition, the extent to which the COVID-19 outbreak continues to impact Syros’ workforce and its clinical trial operations activities, and the operations of the third parties on which Syros relies, will depend on future developments, which are highly uncertain and cannot be predicted with confidence, including the duration and severity of the outbreak, additional or modified government actions, and the actions that may be required to contain the virus or treat its impact. 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, 2020 | December 31, 2019 |
|---|---|---|
| Cash, cash equivalents and marketable securities | $ 173,984 | $ 91,416 |
| Working capital[1] | 149,933 | 90,997 |
| Total assets | 213,250 | 149,978 |
| Total stockholders’ equity | 90,553 | 79,184 |

(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 Statement of Operations**
**(in thousands, except share and per share data)**
**(unaudited)**

| | Three Months Ended December 31, | | Year Ended December 31, | |
|---|---|---|---|---|
| | 2020 | 2019 | 2020 | 2019 |
| Revenue | $ 5,698 | $ 508 | $ 15,093 | $ 1,982 |
| Operating expenses: | | | | |
| Research and development | 29,026 | 14,277 | 76,065 | 58,245 |
| General and administrative | 5,892 | 6,402 | 21,325 | 21,478 |
| Total operating expenses | 34,918 | 20,679 | 97,390 | 79,723 |
| Loss from operation | (29,220) | (20,171) | (82,297) | (77,741) |
| Interest income | 6 | 462 | 426 | 2,375 |
| Interest expense | (541) | (20) | (1,792) | (72) |

| | | | | |
|---|---|---|---|---|
| Change in fair value of warrant liability | (375) | — | (375) | — |
| Net loss applicable to common stockholders | $ (30,130) | $ (19,729) | $ (84,038) | $ (75,438) |
| Net loss per share - basic and diluted applicable to common stockholders | $ (0.62) | $ (0.46) | $ (1.82) | $ (1.88) |
| Weighted-average number of common shares used in net loss per share - basic and diluted | 48,774,598 | 42,885,208 | 46,051,617 | 40,222,182 |

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