March 15, 2022

# Syros Reports Fourth Quarter and Full Year 2021 Financial Results and Highlights Key Accomplishments and Upcoming Milestones

*On Track to Report PK and Safety Data from Ongoing Dose Confirmation Study of SY-2101 in Mid-2022*

*Expect to Report Clinical Activity from the Safety Lead-In Portions of the Ongoing SELECT-AML-1 Trial of Tamibarotene and the Expansion Cohort of SY-5609 in Pancreatic Cancer in 2H 2022*

*Expect to Initiate Phase 1 Trial of SY-5609 in Hematologic Malignancies in 2H 2022*

*New Preclinical Data on CDK12 Inhibitor to be Presented at AACR; On Track to Name Next Development Candidate in 2H 2022*

*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, 2021, and provided an update on recent accomplishments and upcoming events.

“2021 was a pivotal year for Syros, marked by the initiations of three clinical trials and one expansion cohort across our targeted hematology and CDK inhibitor portfolios, promising data from our SY-5609 program, as well as the appointments of two key leadership team members,” said Nancy Simonian, M.D., Chief Executive Officer of Syros. “We believe we are well-positioned to build on this momentum in 2022. We expect three data readouts this year, including pharmacokinetic and safety data from our dose confirmation trial of SY-2101 in APL as well as clinical activity data from the safety lead-in portions of the SELECT-AML-1 Phase 2 trial and the expansion cohort of SY-5609 in pancreatic cancer. These results have the potential to deliver important insights into each of our investigational medicines as we continue to advance towards becoming a fully integrated biopharmaceutical company with the aim to make a profound difference for patients.”

**UPCOMING MILESTONES**

**Targeted Hematology**

*Tamibarotene: Oral RARα agonist*

- Report clinical activity data from safety lead-in portion of ongoing SELECT-AML-1

Phase 2 trial in newly diagnosed unfit RARA-positive patients with acute myeloid leukemia (AML) in the second half of 2022.

- Report data from ongoing SELECT-MDS-1 Phase 3 trial in newly diagnosed RARA-positive patients with higher-risk myelodysplastic syndrome (HR-MDS) in the fourth quarter of 2023 or first quarter of 2024, with a potential new drug application (NDA) filing expected in 2024.

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

- Report pharmacokinetic (PK) and safety data from ongoing dose confirmation trial in newly diagnosed acute promyelocytic leukemia (APL) patients in mid-2022.
- Initiate Phase 3 trial in first quarter of 2023 with data expected in 2025.

**CDK Inhibition**

*SY-5609: Oral Selective CDK7 Inhibitor*

- Report clinical activity data from safety lead-in portion of ongoing expansion cohort evaluating SY-5609 in combination with chemotherapy in relapsed/refractory metastatic pancreatic cancer patients in the second half of 2022.
- Roche plans for the arm of its ongoing Phase 1/1b INTRINSIC trial investigating SY-5609 in combination with atezolizumab in BRAF-mutant colorectal cancer (CRC) to be open for enrollment in the first half of this year. Under the terms of our agreement with Roche, Roche is the sponsor of the trial and Syros is supplying SY-5609.
- Initiate Phase 1 trial evaluating SY-5609 in relapsed/refractory hematologic malignancies in the second half of 2022, with initial data expected mid-2023.

**Gene Control Discovery Engine**

- Plan to present new preclinical data on the CDK12 inhibitor program at the American Association for Cancer Research (AACR) Annual Meeting 2022, taking place from April 8-13.
- Nominate next development candidate, a CDK12 inhibitor, in the second half of 2022.

**RECENT PIPELINE HIGHLIGHTS**

- In February, the U.S. Food and Drug Administration (FDA) granted orphan drug designation to tamibarotene for the treatment of HR-MDS. The FDA's Office of Orphan Drug Products grants orphan status to support development of medicines for the treatment of rare diseases that affect fewer than 200,000 people in the United States. Orphan drug designation may provide certain benefits, including a seven-year period of market exclusivity if the drug is approved, tax credits for qualified clinical trials and an exemption from FDA application fees.

**CORPORATE**

- In March, Syros entered into a Master Collaboration Agreement with QIAGEN to develop and commercialize an assay as a companion diagnostic for Syros' proprietary RARA biomarker for use with tamibarotene in newly diagnosed HR-MDS patients. QIAGEN will also be responsible for obtaining and maintaining regulatory approvals for the commercial diagnostic test.

## FOURTH QUARTER AND FULL YEAR 2021 FINANCIAL RESULTS

- Revenues were $7.8 million for the fourth quarter of 2021, consisting of $6.5 million in revenue recognized under Syros' collaboration with Global Blood Therapeutics, Inc. (GBT) and $1.3 million recognized under its collaboration with Incyte Corporation (Incyte). Revenues were $23.5 million for the year ended December 31, 2021, consisting of $19.4 million and $4.1 million from Syros' collaborations with GBT and Incyte, respectively. Syros recognized $5.7 million in revenue in the fourth quarter of 2020, consisting of $3.6 million in revenue recognized under its collaboration with GBT and $2.1 million recognized under its collaboration with Incyte, and $15.1 million for the year ended December 31, 2020, consisting of $11.7 million and $3.4 million from its collaborations with GBT and Incyte, respectively.

- Research and development expenses were $26.8 million for the fourth quarter of 2021 and $99.9 million for the year ended December 31, 2021, as compared to $29.0 million for the fourth quarter of 2020 and $76.1 million for the year ended December 31, 2020. The decrease for the fourth quarter of 2021 compared to the same period in 2020 was primarily due to the purchase of SY-2101 in the fourth quarter of 2020. The increase for the year ended December 31, 2021 was primarily due to the increase in costs associated with the continued advancement of our clinical and preclinical programs and employee-related expenses.

- General and administrative (G&A) expenses were $6.4 million for the fourth quarter of 2021 and $23.0 million for the year ended December 31, 2021, as compared to $5.9 million for the fourth quarter of 2020 and $21.3 million for the year ended December 31, 2020.

- For the fourth quarter of 2021, Syros reported a net loss of $23.8 million, or $0.38 per share, compared to a net loss of $30.1 million, or $0.62 per share, for the same period in 2020. For the full year ended December 31, 2021, Syros reported a net loss of $86.6 million, or $1.38 per share, compared to a net loss of $84.0 million, or $1.82 per share, for the same period in 2020.

### Cash and Financial Guidance

Cash, cash equivalents and marketable securities as of December 31, 2021 were $143.4 million, as compared with $174.0 million on December 31, 2020. This change reflects cash used to fund Syros' operations during the full year ended December 31, 2021, partially offset by gross proceeds of $75.6 million that Syros received from its January 2021 public offering.

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 first quarter of 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 2021 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 9682507. 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: tamibarotene, 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 and blood cancers. 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' clinical development plans, including with respect to tamibarotene, SY-2101 and SY-5609, Syros' ability to advance towards becoming a fully integrated biopharmaceutical company and to make a profound difference for patients, the timing and impact of upcoming clinical and preclinical data readouts, the timing of nomination of Syros' next development candidate, the timing for submitting a new drug application to the FDA, the benefits of receiving an orphan drug designation, and the sufficiency of Syros' capital resources to fund its operating expenses and capital expenditure requirements into the first quarter of 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 tamibarotene, 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, 2021 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 pandemic 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 pandemic, 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, 2021 | December 31, 2020 |
|---|---|---|
| Cash, cash equivalents and marketable securities (current and noncurrent) | $ 143,407 | $ 173,984 |
| Working capital[1] | 105,077 | 149,933 |
| Total assets | 182,935 | 213,250 |
| Total stockholders’ equity | 85,218 | 90,553 |

(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, | |
|---|---|---|---|---|
| | 2021 | 2020 | 2021 | 2020 |
| Revenue | $ 7,802 | $ 5,698 | $ 23,488 | $ 15,093 |
| Operating expenses: | | | | |
| Research and development | 26,796 | 29,026 | 99,872 | 76,065 |

| | | | | |
|---|---|---|---|---|
| General and administrative | 6,429 | 5,892 | 23,036 | 21,325 |
| Total operating expenses | 33,225 | 34,918 | 122,908 | 97,390 |
| Loss from operations | (25,423) | (29,220) | (99,420) | (82,297) |
| Interest income | 31 | 6 | 87 | 426 |
| Interest expense | (986) | (541) | (3,907) | (1,792) |
| Change in fair value of warrant liability | 2,565 | (375) | 16,682 | (375) |
| Net loss applicable to common stockholders | $ (23,813) | $ (30,130) | $ (86,558) | $ (84,038) |
| Net loss per share applicable to common stockholders - basic and diluted | $ (0.38) | $ (0.62) | $ (1.38) | $ (1.82) |
| Weighted-average number of common shares used in net loss per share applicable to common stockholders - basic and diluted | 62,950,885 | 48,774,598 | 65,534,978 | 46,051,617 |

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