January 11, 2021

Syros Announces Strategic Priorities and Expected Milestones

On Track to Initiate Three Clinical Trials in 2021 Across Franchise of Targeted Hematology Therapies, Including Phase 3 Trial for SY-1425 in MDS

Additional Data from Dose-Escalation Trial of SY-5609 Expected in Q3 2021, with Expansion Phase of Trial Expected to Begin in 2H 2021

Cash Runway into Second Half of 2022, Through Multiple Potential Value Drivers

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Syros Pharmaceuticals (NASDAQ:SYRS), a leader in the development of medicines that control the expression of genes, today outlined its strategic priorities and expected upcoming milestones.

“Syros is rapidly accelerating toward becoming a commercial-stage company through three strategic priorities: advancing franchises in targeted hematology and selective CDK inhibition, as well as leveraging a robust gene control discovery engine to fuel our long-term growth,” said Nancy Simonian, M.D., Syros’ Chief Executive Officer. “As we enter the new year, we are well-positioned to execute against each of these strategic priorities. We plan to launch three clinical trials across our portfolio of targeted hematology therapies in patients with higher-risk MDS, AML and APL, indications where we have the opportunity to set new standards of care.”

“In parallel, we continue to build on our leadership in selective CDK inhibition, where we believe we can deliver highly selective product candidates with transformative potential for difficult-to-treat cancers. We are on track to report additional dose-escalation data, including clinical activity, from our Phase 1 trial of SY-5609 in the third quarter and move into the expansion phase of the trial in the second half of the year. These milestones bring us closer to our ultimate goal of bringing targeted therapies to market that provide profound benefits for patients with diseases that have eluded other approaches.”

Expected Milestones

SY-1425: Oral RARα agonist

- Initiate Phase 3 trial of SY-1425 in combination with azacitidine in the first quarter of 2021 in RARA-positive patients with newly diagnosed higher-risk myelodysplastic syndrome (HR-MDS).
- 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.

SY-2101: Oral arsenic trioxide (ATO)

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

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

- Expect to nominate next development candidate in 2022.

Financial Guidance
Syros ended the year with approximately $174 million in cash, cash equivalents and marketable securities[1], which the company believes is sufficient to fund its anticipated operating expenses and capital expenditure requirements into the second half of 2022.

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 the second half of 2022. 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, 2019 and Quarterly Report on Form 10-Q for the quarter ended September 30, 2020, each of 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.

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[1] Cash, cash equivalents and marketable securities at December 31, 2020 are unaudited and preliminary.

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