Syros Presents Data from Phase 1/1b Clinical Trial of SY-5609 in Advanced Solid Tumors at ASCO Annual Meeting

-- New data support further evaluation of SY-5609 for PDAC and HR+ breast cancer and demonstrate significant potential for SY-5609 in a wide range of tumor types and combinations --

-- Consistent with prior guidance, exploring partnership opportunities to advance development of SY-5609 --

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Syros Pharmaceuticals (NASDAQ:SYRS), a biopharmaceutical company committed to advancing new standards of care for the frontline treatment of hematologic malignancies, today announced new clinical data from the Phase 1/1b clinical trial evaluating SY-5609, its highly selective and potent inhibitor of CDK7, in patients with relapsed/refractory pancreatic ductal adenocarcinoma (PDAC), HR+ breast cancer and other solid tumors. The data will be presented in two posters at the 2023 American Society for Clinical Oncology (ASCO) Annual Meeting, taking place June 2-6, in Chicago, Illinois.

“We are pleased to share data from our Phase 1/1b clinical trial of SY-5609, which further reinforce the potential of selective CDK7 inhibition as a potentially transformative approach for difficult-to-treat solid tumors,” said David A. Roth, M.D., Chief Medical Officer of Syros. “SY-5609’s best in class selectivity and potency produce a predictable, well-managed tolerability profile, and we have optimized an intermittent dosing schedule that we believe enables broad combination potential. Data from both combination cohorts – evaluating SY-5609 in combination with chemotherapy in PDAC and SY-5609 with fulvestrant in HR+ breast cancer – demonstrate an acceptable tolerability profile, as well as promising clinical activity in heavily pre-treated populations that are unlikely to respond to standard of care. Based on these results, we continue to believe that SY-5609 could play a meaningful role in the evolving treatment landscape and are continuing to explore partnership opportunities to maximize the potential of this program.”

Syros’ Phase 1/1b trial of SY-5609 is a multi-center, open-label study, consisting of two parts: Part 1 is a dose escalation study, evaluating single agent SY-5609 in patients with select advanced solid tumors and in combination with fulvestrant in HR+ breast cancer. Part 2 included a combination safety lead-in designed to inform a dose expansion study, evaluating the doublet regimen of SY-5609 and gemcitabine and the triplet regimen of SY-5609, gemcitabine and nab-paclitaxel in patients with PDAC in their second or third line of treatment.

Data Demonstrate Encouraging Clinical Activity in Patients with PDAC
Syros will present updated data from the single agent dose escalation portion and the gemcitabine/nab-paclitaxel combination safety lead-in portion of the Phase 1/1b trial. The maximum tolerated dose (MTD) of SY-5609 as a single-agent was 10 mg using a 7 day on/7 day off dosing schedule. For the doublet, the MTD was 5 mg SY-5609 plus 1000 mg gemcitabine. A MTD was not established using the triplet cohort of SY-5609, gemcitabine and nab-paclitaxel. Each of the single-agent, doublet and the triplet regimens were generally well-tolerated with mostly low-grade events.

Encouraging clinical activity was observed at the MTDs with SY-5609 both as a single-agent (10 mg) and in combination (4 or 5 mg plus gemcitabine). Among the three response evaluable patients with select solid tumors, which included one patient with PDAC, data demonstrated a 100% disease control rate (DCR) with 10 mg SY-5609 monotherapy, with the PDAC patient experiencing a 10% tumor reduction. Of the nine PDAC patients treated with 4 or 5 mg of SY-5609 in combination with gemcitabine, the data demonstrated a 44% DCR (four patients). The single-agent DCR of 100% is superior to results observed with lower doses of SY-5609 on the 7 day on/7 day off schedule and the doublet DCR of 44% is comparable to current second-line benchmarks.

These data will be presented in a poster titled, “Phase 1/1b study of SY-5609, a selective and potent CDK7 inhibitor, in advanced solid tumors and in 2L/3L pancreatic ductal adenocarcinoma (PDAC) in combination with gemcitabine +/- nab-paclitaxel,” on June 3, 2023, 8:00 – 11:00 am CT (9:00 am – noon ET) (Abstract# 3080).

Data Show Promising Early Activity in Patients with Advanced HR+, HER2- Breast Cancer

Syros will present data from the fulvestrant combination cohort. Patients enrolled in this cohort presented with advanced disease: 78.6% (11 of 14 patients) had liver metastases and were heavily pre-treated: 78.6% (11 of 14 patients) had received ≥5 prior therapies, 100% (14 of 14 patients) had progressed on CDK4/6 therapy, and 85.7% (12 of 14 patients) had received prior fulvestrant. The data show that the combination of SY-5609 and fulvestrant demonstrated an acceptable safety profile across a variety of dosing schedules. The adverse event profile of the combination was generally consistent with the safety profile of single agent SY-5609 or fulvestrant, with no new safety signals emerging from the combination at evaluated doses and dosing schedules. An MTD was not established.

Twelve patients were evaluable for response across a range of doses and dosing schedules. Five of 12 achieved stable disease for a DCR of 42%; three of these five patients achieved target lesion regression. Three patients remained on treatment with SD for greater than six months, including patients with the TP53 mutation, prior fulvestrant exposure and/or liver disease.

These data will be presented in a poster titled, “Tolerability and preliminary activity of the potent, selective, oral CDK7 inhibitor SY-5609 in combination with fulvestrant in patients with advanced hormone receptor-positive (HR+), HER2- breast cancer (BC),” on June 3, 2023, 8:00 – 11:00 am CT (9:00 – noon ET) (Abstract# 3081).

Both posters are now available on the Publications and Abstracts section of the Syros website at [www.syros.com](http://www.syros.com).
About Syros Pharmaceuticals

Syros is committed to developing new standards of care for the frontline treatment of patients with hematologic malignancies. Driven by the motivation to help patients with blood disorders that have largely eluded other targeted approaches, Syros is advancing a robust late-stage clinical pipeline, including tamibarotene, an oral selective RARα agonist in patients with higher-risk myelodysplastic syndrome and acute myeloid leukemia with RARA gene overexpression, and SY-2101, a novel oral form of arsenic trioxide in patients with acute promyelocytic leukemia. Syros is also seeking partnerships for SY-5609, a highly selective and potent CDK7 inhibitor in clinical development for the treatment of select solid tumors, and multiple preclinical programs in oncology. For more information, visit [www.syros.com](http://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 the commercial potential of SY-5609, its ability to benefit various patient populations, and Syros’s partnership plans with respect to the SY-5609 program. 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: secure a partnership to support the further development of the SY-5609 program; demonstrate in any future clinical trials the requisite safety, efficacy and combinability of SY-5609; sustain the response rates and durability of response seen to date with SY-5609; successfully establish a patient selection strategy to identify patients most likely to benefit from SY-5609; 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, 2022 and Quarterly Report on Form 10-Q for the quarter ended March 31, 2023, 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.

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