Syros Presents New Preclinical Data on SY-5609, Its Highly Selective Oral CDK7 Inhibitor, at AACR-NCI-EORTC International Conference

SY-5609 Shows Robust Anti-Tumor Activity in Lung, Breast and Ovarian Cancer Models
 Deeper and More Sustained Responses Associated with RB Pathway Alterations

Preclinical Data Support Planned Clinical Trial Strategy for SY-5609; Phase 1 Initiation Expected Q1 2020

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Syros Pharmaceuticals (NASDAQ: SYRS), a leader in the development of medicines that control the expression of genes, today presented new preclinical data for SY-5609, its highly-selective and potent oral inhibitor of cyclin-dependent kinase 7 (CDK7). The data demonstrate that SY-5609 induces deep and sustained anti-tumor activity, including complete regressions, in multiple preclinical models of solid tumors at doses below the maximum tolerated dose (MTD). These data were presented at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics in Boston.

“We are excited to share these new preclinical data for SY-5609, which speak to its potential as a best-in-class oral CDK7 inhibitor and reinforce our conviction in CDK7 inhibition as a potentially transformative approach for difficult-to-treat cancers,” said Eric R. Olson, Ph.D., Syros’ Chief Scientific Officer. “We are particularly encouraged that SY-5609 as a single agent induced rapid and dose-dependent tumor growth inhibition in preclinical models of lung, breast and ovarian cancers, and by the observation that sustained regressions are associated with RB pathway alterations. These data support the focus of our planned Phase 1 trial on those patient populations, which we believe are most likely to benefit from treatment with SY-5609, and we look forward to initiating the study early next year.”

New Preclinical Data on SY-5609 Highlight Broad Potential Across Solid Tumor Types

Researchers from Syros conducted a series of preclinical studies to characterize the in vitro and in vivo profile of SY-5609. The data show that SY-5609 induced:

- Dose-dependent tumor growth inhibition in ovarian and breast cancer models, with tumor regressions observed at doses as low as one-fifth of the MTD.
- Rapid, sustained and dose-dependent transcriptional pharmacodynamic responses in xenograft tumor tissue that correlated with tumor growth inhibition.
- Substantial tumor growth inhibition in 100% (12/12) of triple negative breast cancer, small cell lung cancer and high grade serous ovarian cancer models tested, including
deep and sustained regressions in 58% (7/12) of these models, at well-tolerated doses.
  - RB pathway alterations were associated with deeper and more sustained responses.
- Robust anti-tumor activity in combination with fulvestrant in treatment-resistant models of estrogen receptor-positive breast cancer, including models that were resistant to both fulvestrant and a CDK4/6 inhibitor.

Additionally, the data suggest that SY-5609 plasma exposures are dose proportional and do not accumulate with repeated daily dosing at therapeutic doses and that the overall pharmacokinetic profile supports a daily dosing regimen.

Syros expects to complete investigational new drug application-enabling studies for SY-5609 by year-end. The Company plans to initiate a Phase 1 trial in patients with select solid tumors, including breast, lung and ovarian cancers, and in solid tumors of any histology harboring RB pathway alterations, in the first quarter of 2020.

The poster presented at AACR-NCI-EORTC is now available on the Publications and Abstracts section of the Syros website at www.syros.com.

**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. Currently focused on cancer and monogenic diseases, Syros is advancing a robust pipeline of development candidates, including SY-1425, a first-in-class oral selective RARα agonist in a Phase 2 trial in a genomically defined subset of acute myeloid leukemia patients, and SY-5609, a highly selective and potent oral CDK7 inhibitor in investigational new drug application-enabling studies in cancer. Syros also has multiple preclinical and discovery programs in oncology and sickle cell disease. 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’ ability to complete IND-enabling preclinical studies of SY-5609 by year end and begin clinical development of SY-5609 in the first quarter of 2020; the potential of SY-5609 to be a best-in-class CDK7 inhibitor; Syros’ ability to replicate preclinical data with SY-5609 in clinical trials; and the potential for selective CDK7 inhibition to be a transformative approach for difficult-to-treat cancers. 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-5609, under the timelines it projects; demonstrate in clinical trials the requisite safety, efficacy and combinability of SY-5609; successfully progress SY-5609 through IND-enabling preclinical
and toxicology studies; replicate scientific and non-clinical data in clinical trials; demonstrate in clinical trials the association of RB pathway alterations and clinical responses; obtain and maintain patent protection for SY-5609 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, 2018 and Quarterly Report on Form 10-Q for the quarter ended June 30, 2019, 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. 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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