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Syros Announces Agreement with Roche to Evaluate SY-5609 as Part of a Novel Combination for Treatment of Colorectal Cancer

Clinical Trial Cohort to Evaluate SY-5609 in Combination with Atezolizumab, a PD-L1 Checkpoint Inhibitor

Marks First Clinical Investigation of Selective CDK7 Inhibitor with Immunotherapy

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Syros Pharmaceuticals (NASDAQ:SYRS), a leader in the development of medicines that control the expression of genes, today announced that it has entered into a clinical supply agreement with Roche. Under the agreement, Syros will supply SY-5609, its highly selective and potent oral inhibitor of cyclin-dependent kinase 7 (CDK7), for a combination dosing cohort in Roche's ongoing Phase 1/1b INTRINSIC trial, which is evaluating multiple targeted therapies or immunotherapy, including atezolizumab, as single agents or in rational specified combinations in molecularly defined subsets of colorectal cancer (CRC) patients.

"We are pleased that Roche has chosen to study SY-5609 as part of its broader strategy to explore atezolizumab in combination with other targeted agents in defined colorectal cancer patient populations," said Nancy Simonian, M.D., Chief Executive Officer of Syros, "We believe SY-5609 is a potentially transformative targeted approach for difficult-to-treat cancers. Preclinical data has shown that CDK7 inhibition enhances the anti-tumor activity of PD-L1 inhibition, providing a strong rationale for combining SY-5609 and atezolizumab. Notably, this trial marks the first clinical investigation of a CDK7 inhibitor with an immunotherapy, and we look forward to working with Roche to evaluate the potential of this novel combination in patients with BRAF-mutant colorectal cancer."

Under the terms of the agreement, Roche will sponsor and conduct the Phase 1/1b study to evaluate the safety, tolerability and preliminary efficacy of the combination and will assume all costs associated with the study. In exchange for providing SY-5609, Syros will receive access to the data on SY-5609 in combination with atezolizumab. Syros retains all rights to SY-5609.

Selective CDK7 inhibition has been shown to target two fundamental processes in cancer: transcription and cell cycle control. Additionally, published peer-reviewed research has shown that CDK7 inhibition induces DNA replication stress and genome instability in preclinical cancer models, triggering immune-response signaling, which is further enhanced by the addition of immune-checkpoint blockade.[1]

In May 2020, Syros presented preclinical data at the American Society of Clinical Oncology

Virtual Scientific Program demonstrating that SY-5609 inhibited tumor growth, including inducing sustained regressions at well-tolerated doses in CRC models. In preclinical studies, SY-5609 resulted in ≥ 50 percent tumor growth inhibition in 67 percent (20/30) of patient-derived xenograft models of CRC, and ≥ 90 percent tumor growth inhibition in 23 percent (7/30) of models. Deeper responses were observed more frequently in models with BRAF mutations (50 percent, 5/10) relative to wild-type models (10 percent, 1/10).

Syros is evaluating SY-5609 in an ongoing, multi-center, open-label Phase 1 dose-escalation study in patients with advanced breast, colorectal, lung, ovarian or pancreatic cancers, or with solid tumors of any histology that harbor Rb pathway alterations. Initial data from the dose escalation showed proof of mechanism at tolerable doses. Syros expects to report additional dose-escalation data, including clinical activity data, at the ESMO Congress in September and initiate the expansion portion of the trial in the second half of 2021.

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. 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.

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 and collaborations with respect to SY-5609, the evaluation of SY-5609 in combination with other therapies, the ability of SY-5609 to have a benefit for patients, the plans for reporting additional dose-escalation data, including clinical activity data, from Syros' Phase 1 clinical trial of SY-5609, and the future expansion of such trial. 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 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 SY-5609; sustain the response rates seen to date with SY-5609; replicate scientific and non-clinical data in clinical trials; successfully establish a patient selection strategy and develop a companion diagnostic test 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, 2020 and Quarterly Report on Form 10-Q for the quarter ended June 30, 2021, 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 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.

[1] Zhang et al., 2020, Cancer Cell 37, 1-18

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