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Syros Announces New Preclinical Data on SY-1365, Its First-in-Class Selective CDK7 Inhibitor, Pointing to a Potential Biomarker of Response and Combination Approach

SY-1365 Shows Anti-Tumor Activity in Leukemia and Lymphoma Cell Lines and In Vivo Models of AML

Sensitivity to SY-1365 Associated with Low Expression of BCL2L1 Across a Range of Leukemia Cell Lines

SY-1365 Shows Synergistic Activity with BCL2 Inhibitor in AML Cells and In Vivo Models

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Syros Pharmaceuticals (NASDAQ: SYRS), a biopharmaceutical company pioneering the discovery and development of medicines to control the expression of disease-driving genes, today announced that new preclinical data on SY-1365, its first-in-class selective cyclin-dependent kinase 7 (CDK7) inhibitor currently in a Phase 1 clinical trial in advanced solid tumors, show anti-tumor activity in *in vitro* and *in vivo* models of blood cancers. Additionally, the data point to a potential biomarker of response to SY-1365 and synergistic activity with a BCL2 inhibitor in preclinical models of acute myeloid leukemia (AML). These data are being presented at the 59th American Society of Hematology (ASH) Annual Meeting and Exposition.

“We believe SY-1365 represents a promising therapeutic approach across a number of solid tumors and blood cancers,” said Eric R. Olson, Ph.D., Chief Scientific Officer of Syros. “These new preclinical data underscore the power of our gene control platform to elucidate the underlying biology and mechanism of action of SY-1365, furthering our ability to identify biomarkers to select the patients most likely to respond and to identify rational combination approaches with the potential to provide a profound benefit for patients.”

Syros scientists analyzed the anti-tumor activity of SY-1365 in a broad panel of leukemia and lymphoma cell lines, as well as in primary cell cultures from leukemia patients. They then grouped the cell lines according to sensitivity to SY-1365 and looked for markers of response using Syros’ gene control platform. Based on the findings, Syros evaluated SY-1365 in combination with venetoclax, a BCL2 inhibitor, in preclinical studies. The data showed that:

- SY-1365 inhibited proliferation *in vitro* in leukemia and lymphoma cells, as well as in leukemia cells from primary patient cultures.
- SY-1365 induced cell death in the majority of AML, leukemia and lymphoma cell lines tested.

- SY-1365 inhibited tumor growth, including inducing tumor regression, using biweekly dosing in preclinical mouse models of AML.
- Sensitivity to SY-1365 was associated with low expression of the mitochondrial apoptosis antagonist *BCL2L1* in AML and other leukemia cell lines.
- SY-1365 lowered expression of *MCL1*, a gene in the mitochondrial apoptosis pathway that is known to inhibit apoptosis.
- SY-1365 synergized with venetoclax in AML cell lines *in vitro* and increased tumor growth inhibition when combined with venetoclax, compared to either SY-1365 or venetoclax alone.

The Phase 1 trial of SY-1365 is a multi-center, open-label trial enrolling patients with advanced solid tumors. The primary objective of the trial is to assess the safety and tolerability of escalating doses of SY-1365, with the goal of establishing a maximum tolerated dose and a recommended Phase 2 dose and regimen. The dose-escalation phase is open and expected to enroll approximately 35 solid tumor patients for whom standard curative or palliative measures do not exist or are no longer effective. Following the dose-escalation phase, expansion cohorts are planned to further evaluate the safety and anti-tumor activity of SY-1365 in patients with transcriptionally driven tumors and to enroll patients with tumors of any histology in a cohort focused on analyzing biopsied tumor tissue. Additional details about the trial can be found using the identifier NCT03134638 at www.clinicaltrials.gov. Syros expects to present initial clinical data from this study in 2018.

About Syros Pharmaceuticals

Syros Pharmaceuticals is pioneering the understanding of the non-coding region of the genome to advance a new wave of medicines that control expression of disease-driving genes. Syros has built a proprietary platform that is designed to systematically and efficiently analyze this unexploited region of DNA in human disease tissue to identify and drug novel targets linked to genomically defined patient populations. Because gene expression is fundamental to the function of all cells, Syros' gene control platform has broad potential to create medicines that achieve profound and durable benefit across a range of diseases. Syros is currently focused on cancer and immune-mediated diseases and is advancing a growing pipeline of gene control medicines. Syros' lead drug candidates are SY-1425, a selective RAR α agonist in a Phase 2 clinical trial for genomically defined subsets of patients with acute myeloid leukemia and myelodysplastic syndrome, and SY-1365, a selective CDK7 inhibitor in a Phase 1 clinical trial for patients with advanced solid tumors, including transcriptionally dependent cancers such as triple negative breast, small cell lung and ovarian cancers. Led by a team with deep experience in drug discovery, development and commercialization, Syros is located in Cambridge, Mass.

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 therapeutic benefit of SY-1365 in solid tumors and blood cancers; the utility of any predictive biomarker of response to SY-1365; the reporting of initial clinical data from the ongoing Phase 1 clinical trial of SY-1365 in 2018; the ability to identify an appropriate dose and schedule to support expansion of the Phase 1 clinical trial of SY-1365, and the benefits of Syros' gene control platform. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "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-1365, 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; replicate scientific and non-clinical data in clinical trials; successfully develop a companion diagnostic test to identify patients with predictive biomarkers; 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’ Quarterly Report on Form 10-Q for the quarter ended September 30, 2017, 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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