



Syros Announces New Preclinical Data on SY-1365 at San Antonio Breast Cancer Symposium

SY-1365 Shows Synergistic Activity in Combination with Fulvestrant in HR-Positive Breast Cancer Cells Resistant to Treatment with a CDK4/6 Inhibitor, Supporting Ongoing Clinical Investigation of the Combination

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Syros Pharmaceuticals (NASDAQ: SYRS), a leader in the development of medicines that control the expression of genes, today announced new preclinical data on SY-1365, its first-in-class selective cyclin-dependent kinase 7 (CDK7) inhibitor, showing that it inhibits tumor cell growth in hormone receptor-positive (HR-positive) breast cancer cell lines that are resistant to treatment with CDK4/6 inhibitors and that it has synergistic activity in combination with fulvestrant in these treatment-resistant cells. These data are being presented by Syros' collaborators from Dana-Farber Cancer Institute at the San Antonio Breast Cancer Symposium (SABCS).

"While CDK4/6 inhibitors have emerged as an important class of treatments for HR-positive metastatic breast cancer, patients eventually develop resistance," said Rinath M. Jeselsohn, M.D., Instructor in Medicine at Dana-Farber and principal investigator of the research presentation. "These data shed light on potential mechanisms behind resistance to CDK4/6 inhibitors, pointing to CDK7 as one of the genes critical to the growth of treatment-resistant HR-positive breast cancer cells and selective CDK7 inhibition as a promising new approach for the treatment of HR-positive breast cancer. I look forward to the continuing to evaluate SY-1365 in the ongoing Phase 1 trial focused on breast and ovarian cancers."

Researchers from Dana-Farber characterized an HR-positive breast cancer cell line that is resistant to treatment with CDK4/6 inhibitors, and they demonstrated that these cells have alterations in the RB-pathway, including loss of the retinoblastoma (Rb) protein, higher levels of p107, CDK2 and cyclin E2, and lower levels of the estrogen receptor.

The aim of this study was to identify genes critical for the growth and survival of these cells by evaluating both resistant and sensitive cell lines. The researchers also tested SY-1365 in these resistant cell lines as a single agent and in combination with fulvestrant, an estrogen receptor degrader. The data, highlighted in a Spotlight poster discussion session, show that:

- *CDK7* and *ESR1* are critical for *in vitro* cell growth in both CDK4/6 inhibitor-sensitive and CDK4/6 inhibitor-resistant cells.
- SY-1365 significantly arrests cell cycle progression and reduces the expression of cancer-promoting genes in both CDK4/6 inhibitor-sensitive and -resistant cell lines.
- SY-1365 in combination with fulvestrant demonstrates synergistic activity in CDK4/6 inhibitor resistant cells.

“We are encouraged by these new preclinical data, which speak both to the importance of CDK7 inhibition in HR-positive breast cancer and to the specific potential of this approach in patients who develop resistance to CDK 4/6 inhibitors.,” said David Roth, M.D., Chief Medical Officer of Syros. “We are particularly pleased by the data for SY-1365 in combination with fulvestrant, which demonstrate synergistic activity in CDK4/6 inhibitor-resistant HR-positive breast cancer cells. These data support the ongoing clinical evaluation of SY-1365 in combination with fulvestrant in HR-positive breast cancer patients who progress after treatment with a CDK 4/6 inhibitor. We are actively enrolling patients in the Phase 1 trial and are committed to exploring the full potential of CDK7 inhibition with SY-1365 for people with difficult-to-treat cancers.”

The ongoing Phase 1 trial of SY-1365 is a multi-center, open-label trial designed to evaluate the safety, tolerability and anti-tumor activity of SY-1365 in patients with advanced solid tumors. Following completion of the dose escalation portion of the trial, Syros opened expansion cohorts to further assess the potential of SY-1365 in multiple ovarian and breast cancer patient populations. The expansion cohorts are evaluating SY-1365: as a single agent in primary platinum-refractory ovarian cancer patients; as a single agent in ovarian cancer patients who have relapsed after three or more therapies; in combination with carboplatin in ovarian cancer patients who have relapsed after one or more prior therapies; and in combination with fulvestrant in patients with HR+ metastatic breast cancer who have progressed after treatment with a CDK4/6 inhibitor. An additional cohort is enrolling patients with any solid tumor accessible for biopsy to further evaluate the mechanism of action of SY-1365. Additional details about the trial can be found using the identified NCT03134638 at www.clinicaltrials.gov.

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

About Syros Pharmaceuticals

Syros is pioneering the understanding of the non-coding regulatory region of the genome to advance a new wave of medicines that control the expression of genes. Syros has built a proprietary platform that is designed to systematically and efficiently analyze this unexploited region of DNA 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 monogenic 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 ovarian and breast cancers. Syros is also developing a deep preclinical and discovery pipeline, including SY-5609, an oral CDK7 inhibitor, as well as programs in immuno-oncology and sickle cell disease. 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 potential benefits of CDK7 inhibition and of SY-1365, alone or in combination with

fulvestrant; the ability to successfully enroll the ongoing Phase 1 clinical trial of SY-1365 and conduct further investigation of SY-1365; and the benefits of Syros' gene control platform. 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-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; 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, 2017, as updated in its Quarterly Reports on Form 10-Q for the quarters ended March 31, June 30 and September 30, 2018, 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.

View source version on businesswire.com:

<https://www.businesswire.com/news/home/20181207005018/en/>

Naomi Aoki
Syros Pharmaceuticals
617-283-4298
naoki@syros.com

Investor Contact:

Hannah Deresiewicz
Stern Investor Relations, Inc.
212-362-1200
hannahd@sternir.com

Source: Syros Pharmaceuticals