November 3, 2016

Syros Pharmaceuticals to Present New Data on SY-1425, Its First-in-Class Potent and Selective RARα Agonist, at the ASH Annual Meeting

Data to Further Support the Potential of SY-1425 in AML by Showing Similar Biological Responses in Preclinical Models of AML and APL, the Approved Indication in Japan

Presentation to Describe Pharmacodynamic Markers to Measure Early Signs of Biological Activity in Ongoing Phase 2 Clinical Trial

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Syros Pharmaceuticals (NASDAQ: SYRS) today announced that new data on its lead candidate, SY-1425, a selective retinoic acid receptor alpha (RARα) agonist currently in Phase 2 clinical development in genomically defined subsets of patients with acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS), will be highlighted in two presentations at the 58th American Society of Hematology (ASH) Annual Meeting and Exhibition taking place December 3-6, 2016, in San Diego.

The new preclinical data will demonstrate that SY-1425 produces a biologic response in *in vitro* models of AML with high levels of*RARA* gene expression similar to that seen in models of acute promyelocytic leukemia (APL), while having little effect on AML cells with low levels of *RARA* gene expression. APL is a form of AML with a distinct genetic alteration in the *RARA* gene. SY-1425 is approved in Japan for the treatment of APL, with a well-established efficacy and safety profile. The consistent biological responses suggest that SY-1425 may provide a clinical benefit for subsets of AML patients whose tumors are driven by high levels of *RARA* as it does in APL patients. In both diseases, RARα is a key oncogenic driver directly targeted by SY-1425.

The presentations also will detail the identification of pharmacodynamic markers to measure the biological activity of SY-1425 in an ongoing Phase 2 clinical trial in order to provide an early indicator that the drug is affecting the targeted biology in AML and MDS patients. Lastly, the preclinical data will show that SY-1425 increases the anti-tumor activity of chemotherapy and hypomethylating agents, supporting the potential development of SY-1425 as a combination therapy with these standard-of-care treatments for AML and MDS patients.

Details on the presentations are as follow:

Date & Time: Saturday, December 3, from 5:30 - 7:30 p.m. PST
Presentation Title: SY1425 (tamibarotene) Induces Profound Transcriptional Changes in AML Tumors with High Retinoic Acid Receptor Alpha
Session: 602. Disordered Gene Expression in Hematologic Malignancy, including

Disordered Epigenetic Regulation: Poster I
Presenter: Christopher Fiore, Ph.D., Scientist, Syros Pharmaceuticals
Abstract Number: 1523
Location: San Diego Convention Center, Hall GH

Date & Time: Sunday, December 4, 2016, from 6 - 8 p.m PST
Presentation Title: Clinical Pharmacodynamic Markers and Combinations with SY-1425 (tamibarotene) in a Genomically Defined Subset of Non-APL AML
Session Title: 617. Acute Myeloid Leukemia: Biology, Cytogenetics, and Molecular Markers in Diagnosis and Prognosis: Poster II
Presenter: Michael R. McKeown, Ph.D., Senior Scientist, Syros Pharmaceuticals
Abstract Number: 2898
Location: San Diego Convention Center, Hall GH

Using its gene control platform, Syros discovered subsets of AML and MDS patients whose tumors have a highly specialized regulatory region of non-coding DNA, known as a super-enhancer, that is associated with the *RARA* gene, which codes for the RARα transcription factor. The super-enhancer is believed to lead to over-expression of the RARα transcription factor, locking cells in an immature, undifferentiated and proliferative state. Syros further investigated this unique biology directly in patient tissues and conducted preclinical studies showing that the *RARA* super-enhancer is predictive of response to treatment with SY-1425 in preclinical AML models, providing a strong rationale for developing SY-1425 in subsets of AML and MDS patients with the *RARA* super-enhancer. Syros in-licensed SY-1425 for development and commercialization in North America and Europe in cancer.

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 RARα 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 with potential in a range of solid tumors and blood 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 potential therapeutic benefits of treatment with SY-1425 in genomically defined subsets of AML and MDS patients as well as treatment with SY-1425 in combination with other agents in AML and MDS patients. 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-1425, under the timelines it projects in current and future clinical trials; obtain and maintain patent protection for its drug candidates and the freedom to operate under third party intellectual property; 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 biomarkers associated with the *RARA* super-enhancer; 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 the company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2016, which is on file with the Securities and Exchange Commission; and risks described in other filings that the company 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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Media Contact:
Syros Pharmaceuticals, Inc.
Naomi Aoki, 617-283-4298
naoki@syros.com
or
Investor Contact:
Stern Investor Relations, Inc.
Hannah Deresiewicz, 212-362-1200
hannahd@sternir.com

Source: Syros Pharmaceuticals