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Syros Announces Clinical Supply Agreement with Janssen to Evaluate SY-1425, Its First-in-Class Selective RARα Agonist, in Combination with Daratumumab in Genomically Defined AML and MDS Patients

Cohort Added to Ongoing Phase 2 Trial of SY-1425 to Evaluate Safety and Efficacy of the Combination in Biomarker-Selected Relapsed or Refractory AML or Higher-Risk MDS Patients

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Syros Pharmaceuticals (NASDAQ:SYRS), a biopharmaceutical company pioneering the development of medicines to control the expression of disease-driving genes, today announced that it has entered into a clinical supply agreement with Janssen Research and Development, LLC. Under the agreement, Janssen will supply daratumumab for a recently added combination dosing cohort in Syros' ongoing Phase 2 clinical trial of SY-1425, a first-in-class selective retinoic acid receptor alpha (RARα) agonist, in genomically defined subsets of patients with acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS). Daratumumab (DARZALEX®) is an anti-CD38 antibody approved for use in various multiple myeloma populations.

"We are delighted to work with Janssen to investigate the potential of SY-1425 in combination with daratumumab to benefit AML and MDS patients with the *RARA* or *IRF8* biomarkers," said Nancy Simonian, M.D., Chief Executive Officer of Syros. "By inducing expression of CD38 in these patients' tumors, we believe SY-1425 may sensitize them to treatment with daratumumab, which is believed to induce tumor cell death in CD38-positive cells through multiple immune-mediated mechanisms. Based on preclinical data supporting this hypothesis as well as CD38 induction seen in the bone marrow of AML and MDS patients treated with SY-1425, we added a cohort to our ongoing Phase 2 clinical trial of SY-1425 and look forward to starting to enroll patients early this year."

In exchange for providing daratumumab, Janssen will receive access to data from the cohort evaluating the safety and efficacy of SY-1425 in combination with daratumumab for its research and development programs related to daratumumab. The study will continue to be sponsored solely by Syros.

Syros is assessing the safety and efficacy of SY-1425 in combination with azacitidine in newly diagnosed AML patients who are not suitable candidates for standard chemotherapy, and in combination with daratumumab in patients with relapsed or refractory AML or higher-risk MDS, in an ongoing Phase 2 clinical trial. All patients enrolled or to be enrolled in this

clinical trial are prospectively selected using the Company's proprietary *RARA* and *IRF8* biomarkers. Enrollment in the combination cohort with azacitidine began last year and is ongoing. Syros expects to begin enrolling patients in the combination cohort with daratumumab in early 2018. Syros expects to present initial clinical data on both combinations in 2018.

Analysis of bone marrow biopsies from relapsed or refractory AML and higher-risk MDS patients enrolled in the ongoing clinical trial showed increased CD38 expression in 11 out of 13 (85 percent) of evaluable patients. Preclinical studies showed that SY-1425 induced CD38 in *RARA* biomarker-positive AML cells comparable to levels of CD38 seen in multiple myeloma cells that are known to be responsive to daratumumab, as well as in an *in vivo* model of biomarker-positive AML. Notably, AML cells do not normally express high levels of CD38. Preclinical studies also showed that SY-1425 in combination with daratumumab triggered robust activation of natural killer cells and immune-cell mediated tumor cell death in biomarker-positive AML cells.

DARZALEX is the first CD38-directed monoclonal antibody approved to treat patients with multiple myeloma. It was first approved by the U.S. Food and Drug Administration (FDA) in November 2015 for patients with multiple myeloma who have received at least three prior lines of therapy, including a proteasome inhibitor (PI) and an immunomodulatory agent or who are double refractory to a PI and immunomodulatory agent. DARZALEX is also approved in Europe, Canada and several other countries for a similar patient population. DARZALEX was more recently approved by the FDA in November 2016 for use in combination with lenalidomide (an immunomodulatory agent) and dexamethasone, or bortezomib (a PI) and dexamethasone, for multiple myeloma patients who have received at least one prior therapy. Daratumumab received Breakthrough Therapy Designation from the FDA for this indication in July 2016. In June 2017, the FDA approved a supplement for DARZALEX use in combination with pomalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor. Janssen licensed daratumumab from Genmab A/S in August 2012 and is responsible for all global development, marketing and manufacturing.

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 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 mechanism of action of SY-1425, the timing for initiation of patient enrollment in the daratumumab combination cohort of the ongoing clinical trial of SY-1425, the timing for the reporting of data from such clinical trial, and the promise of Syros' pipeline and gene control platform. The words ''anticipate,'' ''believe,'' ''continue,'' ''could,'' ''estimate,'' ''expect,'' ''intend,'' ''may,'' ''plan,'' ''potential,'' ''predict,'' ''project,'' "aim," ''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; 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; replicate scientific and non-clinical data in clinical trials; successfully develop a companion diagnostic test to identify patients with the *RARA* and *IRF8* 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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