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Syros Pharmaceuticals Announces FDA Acceptance of IND to Advance SY-1425 Into Phase 2 Clinical Trial

Company On Track to Initiate Study in Mid-2016 in Genomically Defined Subsets of Patients with Acute Myeloid Leukemia and Myelodysplastic Syndrome

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Syros Pharmaceuticals today announced that the U.S. Food and Drug Administration (FDA) accepted the Company's Investigational New Drug (IND) application to advance its lead drug candidate, SY-1425, a potent and selective retinoic acid receptor alpha (RARα) agonist, into a Phase 2 clinical trial in genomically defined subsets of patients with relapsed or refractory acute myeloid leukemia (AML) and relapsed high-risk myelodysplastic syndrome (MDS) identified through its platform. Syros is on track to initiate the Phase 2 clinical trial in mid-2016.

"We're delighted to reach this important milestone for patients and for Syros," said Nancy Simonian, MD, Chief Executive Officer of Syros. "SY-1425 represents a promising therapeutic approach for subsets of AML and MDS patients with a novel biomarker that we discovered using our proprietary gene control platform, and our goal is to rapidly advance this first-in-class therapy for these currently underserved patients. The achievement of this milestone marks our evolution into a clinical-stage company just three years since our founding. Our progress is a testament to our team and to our pioneering approach of systematically analyzing the non-coding region of the genome to advance a new wave of medicines designed to control the expression of disease-driving genes."

Using its gene control platform, Syros identified subsets of AML and MDS patients whose tumors have a highly specialized regulatory region of non-coding DNA, known as a super-enhancer, associated with the *RARA* gene. Syros then identified a biomarker for the *RARA*-associated super-enhancer, which it found in approximately 25 percent of AML and MDS patient tissue samples. Preclinical studies show the *RARA* biomarker is predictive of response to treatment with SY-1425 in AML cell lines and patient-derived xenograft (PDX) models of AML. Treatment with SY-1425 was observed to inhibit cancer growth and prolong survival in PDX models of AML with the *RARA* biomarker but not in models of AML without the biomarker. These data provide meaningful evidence that patients with the *RARA* biomarker may be promising candidates for treatment with SY-1425 and support further development of SY-1425 in these genomically defined patient populations.

The Phase 2 clinical trial will be a multi-center, open-label trial exploring safety and efficacy in relapsed or refractory AML and relapsed high-risk MDS patients who have been prospectively selected using the Company's *RARA* biomarker. The trial is expected to enroll approximately 40 patients. The primary endpoint of the trial will be overall response rate. The trial will also assess pharmacodynamic markers, duration of response, safety and tolerability, survival and biomarker predictability.

Syros in-licensed SY-1425 to develop and commercialize SY-1425 in North America and Europe for all cancers. SY-1425 is approved in Japan as Amnolake (tamibarotene) to treat a different form of AML known as acute promyelocytic leukemia (APL), in which it has a well-established efficacy and safety profile. Syros continues to research the role of the *RARA* super-enhancer in other cancers and plans to pursue additional indications upon achieving clinical proof-of-concept in AML and MDS.

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, the Company's gene control platform has broad potential to achieve profound and durable benefit across a range of diseases. Syros is focused on cancer and immune-mediated diseases and is advancing a growing pipeline, including its lead drug candidates SY-1425, a selective RARα agonist for genomically defined subsets of patients identified by its platform, for a range of cancers including acute myeloid leukemia and myelodysplastic syndrome, and SY-1365, a selective CDK7 inhibitor for a range of blood cancers and solid tumors. Led by a team with deep experience in drug discovery, development and commercialization, Syros is located in Cambridge, Mass.

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Media Contact:
Ten Bridge Communications, Inc.
Naomi Aoki, 617-283-4298
naomi@tenbridgecommunications.com
or
Investor Contact:
Stern Investor Relations, Inc.
Jesse Baumgartner, 212-362-1200
jesse@sternir.com

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