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# Syros' Drug Discovery Research in Immuno-Oncology Highlighted in Oral Presentation at American College of Surgeons Clinical Congress

*Analysis of Regulatory Genomes of Cells Isolated from Pancreatic Cancer Patient Tumors Leads to Identification of New Drug Targets*

*Findings Underscore Promise of Syros' Gene Control Platform to Yield Important Insights for Discovering and Developing Drugs that Activate the Body's Immune Response Against Cancer*

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 identified alterations in regulatory regions of the genome in immune, tumor and stromal cells isolated from pancreatic cancer patient tumors, leading to the identification of new drug targets. These findings, which were made as part of a research collaboration with the Lowy laboratory at the University of California San Diego (UCSD) Moores Cancer Center, were highlighted in an oral presentation at the American College of Surgeons (ACS) 2017 Clinical Congress.

"One of the biggest challenges in treating cancer is its ability to manipulate and evade the body's immune response to fuel its growth," said Andrew Lowy, M.D., Professor of Surgery and Chief of the Division of Surgical Oncology at the Moores Cancer Center. "Syros' gene control platform provides a unique lens for understanding the regulatory mechanisms cancers use to govern cells within the tumor microenvironment. Through investigation of immune, tumor and stromal cells from patient tumors, our hope is to develop medicines that can unleash the body's natural defenses to fight cancer."

Together with the Lowy laboratory, Syros used its proprietary gene control platform to analyze and compare highly specialized regulatory regions of the genome, known as super-enhancers, in cells from pancreatic cancer patient tumors to those in cells from normal pancreatic tissues. Because super-enhancers control the expression of genes that determine cell function, their analysis can point to disease-driving changes in the expression of genes most critical to a given cell, as well as potential drug targets. The data presented at ACS showed that:

- Leukemia inhibitory factor (LIF) gene demonstrated one of the most significant changes in enhancer size from pancreatic tumors in comparison to normal pancreatic tissue. In preclinical mouse models, LIF enhanced the anti-tumor activity of chemotherapy and produced a survival benefit when inhibited using a monoclonal antibody.
- Many of the super-enhancers associated with cells in pancreatic tumor tissue are

associated with genes involved in immune signaling pathways, including antigen presentation, IL10 signaling and macrophage activation, suggesting the importance of the immune system in the development and growth of pancreatic cancer and the identification of potential therapeutic targets.

- Immunosuppressive tumor-associated macrophages had a distinct super-enhancer profile, pointing to genes critical for driving the immunosuppressive state and potential drug targets to reactivate immune cells. Tumor-associated macrophages are of significant interest in immuno-oncology because they play a key role in the immune response to cancer, with M1 macrophages promoting immune-mediated tumor regression and M2 macrophages promoting tumor immune evasion.

“These findings underscore the promise of Syros’ gene control platform to glean important biological insights that can lead to the identification of new drug targets and pave the way for medicines to increase killing of tumor cells by the immune system,” said Eric Olson, Ph.D., Chief Scientific Officer of Syros. “We believe our focus on analyzing the regulatory genomes of immune, tumor and stromal cells isolated from patients’ tumors represents a distinct approach to immuno-oncology with the potential to lead to novel therapies that provide a profound and durable benefit for subsets of cancer patients.”

Syros has a broader immuno-oncology drug discovery effort outside of the Lowy collaboration, which is focused on identifying and drugging novel targets to control the function of immune cells within the tumor microenvironment. Syros has identified a drug target that, when inhibited, may reduce the immunosuppressive capacity of tumor-associated macrophages and has a program based on this discovery in preclinical development. Syros’ immuno-oncology research is focused on cancers in which the tumor microenvironment is known to play a key role in disease progression, including glioblastoma and pancreatic, triple negative breast and ovarian cancers. By analyzing immune and tumor cells directly in patient tumors, Syros aims to better understand the heterogeneity of immune responses among patients and identify subsets of patients most likely to respond to specific immunotherapy strategies.

### **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 $\alpha$  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 benefits of Syros' gene control platform, including the ability of its platform to lead to a better understanding of immune responses in cancer as well as novel therapies in immunology. 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 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' Quarterly Report on Form 10-Q for the quarter ended June 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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