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Syros Presents Discovery of Key Genes Controlling the Autoimmune Response in Lupus in Late-Breaking Oral Presentation at FOCIS Meeting

Analysis of Regulatory Genome of T Cells from Lupus Patients Reveals Disease-Driving Alterations in Transcriptional Circuitry

Findings Underscore the Promise of Syros' Gene Control Platform to Identify Novel Drug Targets and Therapeutic Approaches for Autoimmune Diseases

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Syros Pharmaceuticals (NASDAQ:SYRS), a biopharmaceutical company pioneering the discovery and development of medicines to control the expression of disease-driving genes, today announced that the Company has discovered alterations in regulatory regions of the genome in T cells from patients with systemic lupus erythematosus (SLE), revealing genes critical for activating T cells and driving disease. These findings provide important biological insights into the autoimmune response in lupus that could lead to the identification of novel drug targets and therapeutic approaches to treat SLE. The research was highlighted in a late-breaking oral presentation at the 17th Annual Meeting of the Federation of Clinical Immunology Societies (FOCIS).

"Syros' gene control platform provides a unique lens for understanding the abnormal immune response in lupus that causes the body to attack itself and for developing medicines to control the expression of genes to dampen that auto-immune response," said Eric Olson, Ph.D., Syros' Chief Scientific Officer. "Regulatory regions of the genome are known to play a key role in the activation of T cells, but these findings are the first to elucidate disease-driving alterations in those regions in T cells from lupus patients. We believe our focus on the regulatory genome of immune cells has the potential to lead to better treatments for lupus patients, as well as the ability to identify subsets of patients most likely to respond to specific therapeutic approaches."

Using its proprietary gene control platform to analyze and compare the regulatory genomes of T cells from lupus patients and healthy donors, Syros scientists identified changes in highly specialized non-coding regulatory regions of DNA, known as super-enhancers, in naive, memory, and regulatory T cells. Because super-enhancers bring together large amounts of transcription factors and other regulatory proteins to drive the expression of the set of genes most critical to a given cell, their analysis sheds light on the complex transcriptional regulatory circuits that control the expression of critical genes and determine cell function. The data showed that:

- Super-enhancers found in T cells from healthy donors are associated with genes known to be important in determining cell state and function in all T cell types, including

naïve, memory and regulatory T cells, providing strong validation for this novel genomics-based approach by recapitulating known biology.

- Super-enhancer profiles of all T cell types are markedly different in SLE patients than in healthy donors, with naïve T cells in SLE displaying changes in their enhancer profiles that point to critical transcription factor networks driving disease.
- Genes regulated by activation of the SYK kinase and IRF4 transcription factor are significantly enriched in SLE naïve and memory T cells, suggesting they are key drivers of T cell activation in SLE and a core part of the transcriptional regulatory circuitry driving the disease. Notably, the activation of IRF4-driven transcriptional cirtuitry in SLE T cells points to common mechanisms driving the activation of both T and B cells in SLE.
- Super-enhancer profiles of memory T cells, especially in SLE, display considerable heterogeneity. This heterogeneity may provide an opportunity for the development of patient stratification biomarkers to better identify patient subsets and essential drivers of disease specific to these subsets.

As part of its research program in lupus, Syros has analyzed regulatory regions of the genome in both T cells and B cells from SLE patients to identify key genes controlling the activation of these immune cells in SLE with the objective of developing medicines that selectively inhibit disease-driving cells, dampening the auto-immune response. Syros has identified multiple potential drug targets in human B cells and T cells that it is investigating in preclinical studies, including a drug target that when inhibited by a small molecule inhibitor in an *in vivo* study selectively blocked the activation of antibody-producing plasma cells.

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 benefits of Syros' gene control platform, including its ability to identify novel drug targets and therapeutic approaches for SLE and to identify patient subsets more likely to respond to

therapy. 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 under the timelines it projects in current and future studies; replicate scientific and non-clinical data; 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 March 31, 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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