Sangamo BioSciences Presents New Data From In Vivo Protein Replacement Platform Programs For MPS I And MPS II At The 12th Annual WORLDSymposium™ Meeting

IVPRP Approach Permits Therapeutic Enzymes for Lysosomal Storage Disorders to Cross the Blood Brain Barrier Improving Cognitive Symptoms of Disease

RICHMOND, Calif., March 2, 2016 /PRNewswire/ -- Sangamo BioSciences, Inc. (NASDAQ: SGMO), the leader in therapeutic genome editing, announced the presentation of new preclinical data in disease models from its In Vivo Protein Replacement Platform™ (IVPRP) programs for MPS I (Hurler syndrome) and MPS II (Hunter syndrome). The data demonstrate that the Company’s IVPRP approach enabled stable production of therapeutic levels of replacement enzyme from the liver into the circulation and secondary tissues, including the brain, resulting in significant reduction in biomarkers of the disease and, importantly, statistically significant improvements in cognitive function in treated animals.

The data were presented by Sangamo scientists and their collaborators at the University of Minnesota in two oral presentations at the 2016 Annual WORLDSymposium™ Meeting being held in San Diego from February 29 to March 4, 2016.

"These data represent a fundamental shift in the therapeutic intervention in Hunter and Hurler syndromes. The data demonstrate that constant, stable production of both the human alpha-L-iduronidase and iduronate 2-sulfatase enzymes generated by the IVPRP strategy enables its transport from the circulation into the brain in sufficient quantities to have a therapeutic benefit on neurological aspects of the disease," said Chester Whitley, Ph.D., M.D., director of the Gene Therapy Center at the University of Minnesota Medical School. "If these outcomes can be replicated in human clinical trials it will change the way lysosomal storage disorders are treated. I look forward to working with Sangamo to initiate a clinical trial of this therapeutic in mid-2016."
"We are extremely pleased with these important new data that demonstrate the potential of our IVPRP strategy to provide a one-time treatment for lysosomal storage disorders, including MPS I and MPS II," said Edward Lanphier, Sangamo's president and chief executive officer. "If similar neurocognitive improvements are observed in our upcoming Phase 1/2 clinical trial for MPS I, this therapeutic will have profound implications for the one-time, permanent treatment of this debilitating disorder particularly in pediatric patients, who have the greatest need for this therapy and are ultimately the target population we hope to treat with our IVPRP approach."

Data were presented from mouse models of MPS I and MPS II demonstrating significantly increased levels of human alpha-L-iduronidase (hIDUA) and iduronate 2-sulfatase (hIDS) enzymes, respectively, in the plasma and in secondary tissues, including spleen, lung, muscle and heart. This was achieved after a single intravenous administration of the ZFP Therapeutic®. In both models, the increase in enzyme activity resulted in the significant reduction of glycosaminoglycan (GAG) biomarker levels in all of these tissues, effectively correcting the disease phenotype, as the accumulation of GAGs is associated with MPS I and II disease characteristics. Furthermore, expression of enzymatically active hIDUA and hIDS at therapeutic levels and reduction of tissue GAG levels were stable throughout the four-month studies.

Most importantly, behavioral data from animals tested in the Barnes Maze, a tool used to measure spatial learning and memory, demonstrated statistically significant preservation of cognitive learning in MPS I and MPS II mice treated with the ZFP Therapeutic, compared to untreated mice. Mice were assessed for their ability to learn and remember the location of a target zone using a configuration of fixed visual cues located around the testing area. The animals were tested approximately four months after receiving a single treatment with the ZFP Therapeutic. The data demonstrated that the ability of treated MPS I and MPS II mice to perform this task was similar to that of wildtype mice and significantly better than untreated mice. Supporting these data, increased levels of the hIDUA and hIDS (statistically significant at high dose) enzymes were detected in the brain tissue of treated animals. The data demonstrate that therapeutic hIDUA and hIDS produced in the liver could be transported across the blood brain barrier at levels that were able to effect meaningful change in cognitive function.

In February, Sangamo received clearance from the U.S. Food and Drug Administration (FDA) for its Investigational New Drug (IND) application to initiate a Phase 1/2 clinical trial for MPS I. The Company plans to initiate the trial in mid-2016 and Dr. Whitley is the principal investigator. Sangamo also plans to file an IND application for its MPS II program in the first half of 2016, and expects to file IND applications for its other IVPRP-based lysosomal storage disorder (LSD) programs for Gaucher and Fabry disease in the second half of 2016.

About Lysosomal Storage Disorders

Lysosomal storage disorders are a heterogeneous group of inherited genetic disorders, including MPS I (Hurler syndrome) and MPS II (Hunter syndrome), that are caused by defects in genes that encode enzymes that break down and eliminate unwanted substances in the cells of the body. These enzymes are found in structures called
lysosomes which act as recycling sites in cells, breaking down unwanted material into simple products for the cell to reuse. A defect in a lysosomal enzyme leads to the accumulation of toxic levels of the substance that the enzyme would normally break-down and results in cell damage which can lead to serious health consequences.

There are nearly 50 LSDs altogether and they may affect different parts of the body, including the skeleton, skin, heart and central nervous system. Currently, there are no cures for LSDs and treatments have not yet been developed for many of these diseases. For certain disorders, including Hunter and Hurler syndrome, costly enzyme replacement therapies (ERTs) are available, but require frequent administration in order to be effective. Over time, patients may also develop an immunogenic response to the administered enzyme, rendering the ERT less efficacious.

**About WORLD Symposium™**

The WORLD Symposium is a multidisciplinary forum presenting the latest information from basic science, translational research, and clinical trials for lysosomal diseases. Originally conceived in 2004 in response to an NIH RFP for rare diseases, the Symposium is often cited as the most important scientific meeting on lysosomal molecular biology, disorders and treatment. The meeting has become the major educational and unifying activity of lysosomal disease researchers, and has evolved into a highly interactive research activity. The underlying theme "transitioning molecular biology to human therapies" seeks to elucidate the challenges—and highlight the successes—in bringing bench discoveries into successful clinical therapies. The main emphasis of the meeting remains the same: to assess the mechanisms, and obstacles, for taking bench research into human therapy.

**About Sangamo's IVPRP**

The IVPRP approach makes use of the albumin gene locus, a highly expressing and liver-specific genomic "safe-harbor site," that can be edited with zinc finger nucleases (ZFNs) to accept and express any therapeutic gene. The platform is designed to enable the patient's liver to permanently produce circulating, therapeutic levels of a corrective protein product, such as Factor VIII or IX to treat hemophilia, or replacement enzymes to treat lysosomal storage disorders. The ability to permanently integrate the therapeutic gene in a highly specific targeted fashion significantly differentiates Sangamo's IVPRP approach from conventional adeno-associated virus (AAV)-based gene therapy approaches, which are non-integrating and may "wash out" of the liver as cells divide and turn over. Ultimately, the target population for IVPRP programs will be pediatric patients for whom it is critical to be able to produce stable levels of therapeutic protein during growth and for the lifetime of the patient. With such a large capacity for protein production (approximately 15g/day of albumin), targeting and co-opting only a very small percentage of the albumin gene’s capacity is sufficient to produce the needed replacement protein at therapeutically relevant levels with no significant effect on albumin production. The first two IVPRP clinical programs, for hemophilia B and MPS I, both received unanimous approval from the NIH Recombinant DNA Advisory Committee (RAC) and have been cleared by the FDA, enabling Sangamo to begin Phase 1/2 clinical trials in patients with the disorders.

**About Sangamo**
Sangamo BioSciences, Inc. is focused on Engineering Genetic Cures® for monogenic and infectious diseases by deploying its novel DNA-binding protein technology platform in therapeutic genome editing and gene regulation. The Company’s proprietary In Vivo Protein Replacement Platform™ (IVPRP) approach is focused on monogenic diseases, including hemophilia and lysosomal storage disorders. Based on its proprietary IVPRP approach, Sangamo is initiating Phase 1/2 clinical trials for hemophilia B, the first in vivo genome editing application cleared by the FDA, and MPS I. In addition, Sangamo has a Phase 2 clinical program to evaluate the safety and efficacy of novel ZFP Therapeutics® for the treatment of HIV/AIDS (SB-728). The Company has also formed a strategic collaboration with Biogen Inc. for hemoglobinopathies, such as sickle cell disease and beta-thalassemia, and with Shire International GmbH to develop therapeutics for Huntington’s disease. It has established strategic partnerships with companies in non-therapeutic applications of its technology, including Dow AgroSciences and Sigma-Aldrich Corporation. For more information about Sangamo, visit the Company’s website at www.sangamo.com.

ZFP Therapeutic® is a registered trademark of Sangamo BioSciences, Inc.

This press release may contain forward-looking statements based on Sangamo’s current expectations. These forward-looking statements include, without limitation, references relating to research and development of novel ZFNs and therapeutic applications of Sangamo’s ZFP technology platform; the potential of Sangamo’s ZFP technology to treat LSDs, including Hunter and Hurler syndromes, and the safety of the approach of using ZFN-mediated genome editing in vivo; the expected IND applications for Hunter, Gaucher and Fabry programs; and the applicability of Sangamo’s ZFP technology in monogenic diseases. Actual results may differ materially from these forward-looking statements due to a number of factors, including uncertainties relating to the initiation and completion of stages of our clinical trials, whether the clinical trials will validate and support the safety, tolerability and efficacy of ZFNs, technological challenges, Sangamo’s ability to develop commercially viable products and technological developments by our competitors. For a more detailed discussion of these and other risks, please see Sangamo's public filings with the Securities and Exchange Commission, including the risk factors described in its Annual Report on Form 10-K and its most recent Quarterly Report on Form 10-Q. Sangamo assumes no obligation to update the forward-looking information contained in this press release.

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