Sangamo Therapeutics Presents Recent Developments from Research and Clinical Programs at Annual Meeting of the American Society of Gene & Cell Therapy

May 15, 2017

RICHMOND, Calif., May 15, 2017 /PRNewswire/ -- Sangamo Therapeutics, Inc. (NASDAQ: SGMO) today highlighted data from research and clinical-stage programs presented over the past week at the 20th Annual Meeting of the American Society of Gene & Cell Therapy (ASGCT). Research from Sangamo scientists and collaborators was selected for 10 oral presentations and nine poster presentations during the conference.

"This year at ASGCT we showcased several exciting research and clinical programs emerging from Sangamo's laboratories," said Dr. Sandy Macrae, Sangamo's CEO. "Sangamo is known for its leading research in genome editing, and over time we have developed additional expertise in gene therapy, gene regulation and cell therapy. We are also rapidly advancing our viral and non-viral delivery capabilities which have the potential to broaden our applications of genomic therapies. Such range of expertise allows us to be selective as we pair technology platforms with therapeutic applications, and compels us to make strategic choices about our product candidates. We will develop and commercialize certain products ourselves, while others, such as our gene therapy for hemophilia A now in collaboration with Pfizer, or our CNS or oncology programs, we may advance with a partner to leverage the right disease area focus, skills and resources."

Selected Highlights from ASGCT 2017

Zinc Finger Nuclease Technology Improvements
Ed Rebar, Ph.D., Sangamo's vice president of technology, presented recent enhancements to the Company's zinc finger nuclease (ZFN) genome editing technology that substantially improve specificity while maintaining very high levels of on-target modification. These include the removal of positively charged amino acids in the zinc finger beta-sheet that make non-specific contacts with the DNA phosphate backbone, as well as the substitution of key residues within the Fok-1 cleavage domain. Dr. Rebar showed that these refinements could be applied broadly to ZFN reagents to substantially reduce off-target cleavage without sacrificing on-target cutting efficiency.

Dr. Rebar concluded with a detailed specificity analysis of a ZFN pair, in which these approaches were combined, which identified no significant off-target modification with an assay sensitivity of approximately 0.1%. Importantly, this study was performed on samples generated using clinically relevant delivery conditions, transfection scales and cell types, and with an on-target modification level of greater than 80%.

Gene Therapy for Fabry Disease
Thomas Wechsler, Ph.D., Sangamo's director and lead scientist for rare diseases, presented new data from the Company's preclinical AAV-cDNA gene therapy program for Fabry disease. Earlier in the week, Sangamo announced that it will advance this program toward human clinical development with preclinical studies enabling an Investigational New Drug Application (IND) in the second half 2018.

Fabry is an X-linked lysosomal storage disorder caused by mutations in the GLA gene that encodes for the alpha-galactosidase A enzyme (α-Gal A). This mutation results in the buildup of Gb3 and Lyso-Gb3 lipid molecules in the body's cells, resulting in a range of symptoms and life-threatening complications that affect multiple tissues and organ systems in the body.

Dr. Weschler presented data from GLAKO mouse models of Fabry disease demonstrating that a single infusion of Sangamo's AAV vector containing an α-Gal A transgene and a liver specific promoter successfully transduced the liver, resulting in episomal expression of α-Gal A in the plasma and various tissues for the duration of the study, out to 60 days. From a single treatment, the AAV-cDNA vector achieved enzyme activity levels in the plasma of up to 100 fold greater than wildtype and 10 to 100 fold greater than wildtype in tissues including the liver, heart, kidney and spleen. Importantly, α-Gal A secreted from the liver led to a significant reduction in the levels of accumulated Gb3 and Lyso-Gb3 lipid substrates, in target tissues such as the kidney and heart.

Gene Regulation Treatment for Reduction of Tau
Sangamo Scientist Bryan Zeitler, Ph.D., presented recent data demonstrating significant reduction of tau expression using Sangamo's proprietary zinc finger protein transcription factor (ZFP-TF) gene-regulation technology. The research was conducted in conjunction with Dr. Brad Hyman, Director of the Alzheimer's Disease Research Center at Massachusetts General Hospital. The reduction of tau expression has been shown to help reduce neurofibrillary tangles in the brain and provide neuronal protection and reversal of pathology in Alzheimer's disease and other tauopathy disease models.

The presentation included data from *in vivo* studies in wild-type mice demonstrating up to 90% reduction of tau mRNA and protein in the mouse hippocampus, as well as up to 70% tau reduction across all regions of the brain, including the cortex, midbrain, cerebellum, thalamus, hypothalamus and striatum.

In addition, data from *in vivo* studies in an amyloid mouse model of Alzheimer's disease suggest that a single administration of ZFP-TFs significantly reduced neuronal dystrophies in mice with established disease pathology. This is the first time that a tau lowering agent has demonstrated a reduction in neuritic dystrophy. Specificity and off-target analysis in ZFP-TF-treated primary neurons revealed that tau was the only gene suppressed out of more

than 26,000 coding transcripts analyzed. New data in Dr. Zeitler's presentation demonstrated that the effect of ZFP-TF treatment in lowering tau was durable out to the last measurement, at 11 months.

These experiments were conducted using Sangamo's novel, proprietary AAV serotype for improved CNS transduction.

Sangamo intends to seek a partner with disease area expertise for the development and commercialization of its gene regulation approach for certain central nervous system applications including Alzheimer's disease and other tauopathies.

***In Vivo* Genome Editing Treatments for MPS I and MPS II**
Sangamo Scientist Russell DeKelver, Ph.D., presented additional preclinical data from the Company's *in vivo* genome editing clinical programs in MPS I and MPS II demonstrating phenotypic correction of disease in mouse models following a single administration of Sangamo's genome editing treatments. Newly presented histopathological analysis demonstrated reduced cellular vacuolation in various secondary tissues, as well as in the bone marrow, and central nervous system tissues such as the spinal cord and pituitary gland in treated MPS I and MPS II mice, four months after dosing. Furthermore, newly presented mass spectrometry analysis confirmed significant reduction of dermatan sulfate, a type of GAG biomarker, in the brains of MPS I and MPS II mice treated with Sangamo's genome editing treatments.

Sangamo recently initiated two Phase 1/2 clinical trials evaluating SB-318 and SB-913, ZFN-mediated *in vivo* genome editing treatments for MPS I and MPS II, respectively. Data are expected in late 2017 or early 2018.

Cell Therapy
Research by Brigit Riley, Ph.D., Sangamo's director of discovery and translational research, was presented demonstrating high levels of homology driven genome editing of human B cells by ZFN mRNA and AAV6 transgene delivery. The data demonstrated robust ZFN-mediated, site-specific modification of B cells at targeted loci, including AAVS1, CCR5 and TRAC locus. The data also demonstrated high levels of targeted transgene insertion, driven by homology directed repair, using a B cell specific promoter. Analysis of AAV serotype transduction showed the superiority of AAV6 in transducing B cells compared to several other serotypes.

The data demonstrate the potential for using genome editing to genetically modify B cells *ex vivo* and harness their natural ability to produce large amounts of antibodies to generate protein production reservoirs. This novel approach for using genome editing to harness the protein production capacity of B cells could be relevant for multiple indications, including immune disorders, cancer immunotherapies and other monogenic disorders.

Delivery
Sangamo Scientist Anthony Conway, Ph.D., presented new data from the Company's research into a next-generation delivery platform using lipid nanoparticles (LNPs). ZFN mRNA delivery via LNPs allowed for accumulation of genome modification within the mouse liver following repeat administration, with progressive increases in genomic modification out to six repeat doses tested. LNP delivery of new ZFN architectures led to greater than 85% on-target modification *in vitro* and greater than 60% on-target modification *in vivo*, resulting in greater than 90% protein knockdown of TTR and PCSK9 in wildtype mice. Repeat dosing of ZFNs using LNP-mRNA in combination with a single human AAV-IDS donor vector resulted in efficient targeted insertion of the IDS gene into the albumin locus and accumulative enzymatic activity levels in mouse plasma after each subsequent dose.

About Sangamo
Sangamo Therapeutics, Inc. is focused on translating ground-breaking science into genomic therapies that transform patients' lives using the company's industry leading platform technologies in genome editing, gene therapy, gene regulation and cell therapy. The Company is advancing Phase 1/2 clinical programs in Hemophilia A and Hemophilia B, and lysosomal storage disorders MPS I and MPS II. Sangamo has a strategic collaboration with Pfizer, Inc. for Hemophilia A, with Bioverativ Inc. for hemoglobinopathies, including beta thalassemia and sickle cell disease, and with Shire International GmbH to develop therapeutics for Huntington's disease. In addition, it has established strategic partnerships with companies in non-therapeutic applications of its technology, including Sigma-Aldrich Corporation and Dow AgroSciences. For more information about Sangamo, visit the Company's website at www.sangamo.com.

Forward Looking Statements
This press release contains forward-looking statements regarding Sangamo's current expectations. These forward looking statements include, without limitation, references to the potential of novel delivery systems to broaden applications of genomic therapies, the ability to bring research and preclinical studies to clinical development, the expected timing of filing INDs and releasing data from ongoing clinical programs, the intent to seek partners and collaborators to develop and commercialize gene regulation treatment, and the research and development of ZFNs and ZFP-TFs, clinical trials and therapeutic applications of Sangamo's ZFP technology. These statements are not guarantees of future performance and are subject to certain risks, uncertainties and assumptions that are difficult to predict. Factors that could cause actual results to differ include, but are not limited to, the dependence on the success of clinical trials of lead programs, the lengthy and uncertain regulatory approval process, uncertainties related to the timing of initiation and completion of clinical trials, whether clinical trial results will validate and support the safety and efficacy of Sangamo's therapeutics, and the ability to establish strategic partnerships. Further, there can be no assurance that the necessary regulatory approvals will be obtained or that Sangamo and its partners will be able to develop commercially viable gene-based therapeutics. Actual results may differ from those projected in forward-looking statements due to risks and uncertainties that exist in Sangamo's operations and business environments. These risks and uncertainties are described more fully in Sangamo's Annual Reports on Form 10-K and Quarterly Reports on Form 10-Q as filed with the Securities and Exchange Commission. Forward-looking statements contained in this announcement are made as of this date, and Sangamo undertakes no duty to update such information except as required under applicable law.

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Released May 15, 2017