Sangamo Therapeutics Announces Presentation of New Data Demonstrating Significant Reduction of Tau Expression Using Proprietary ZFP Gene Regulation Technology

Engineered Zinc Finger Protein Transcription Factors Lowered Tau Levels by More Than 90% in Human Neurons In Vitro and Reduced Neuritic Dystrophy in Amyloid Mouse Model of Alzheimer's Disease

RICHMOND, Calif., March 29, 2017 /PRNewswire/ -- Sangamo Therapeutics, Inc. (NASDAQ: SGMO), the leader in therapeutic genome editing, announced today the presentation of new human in vitro and animal model data demonstrating significant reduction of tau mRNA and tau protein expression using the Company's zinc finger protein transcription factor (ZFP-TF)-mediated gene regulation technology. These results are the first evidence of a tau lowering agent demonstrating efficacy on neuritic dystrophy in an amyloid mouse model of Alzheimer's disease. The data were presented by Sangamo's collaborators from Massachusetts General Hospital Alzheimer's Disease Research Center and Harvard Medical School at the 13th International Conference on Alzheimer's & Parkinson's Diseases. The meeting is being held in Vienna, Austria from March 29th to April 2nd.

"Tau protein plays a critical role in certain devastating neurodegenerative diseases, including dementias such as Alzheimer's disease, and studies point to the potential for tau reduction to prevent neuronal loss and possibly even reverse Alzheimer's disease pathology," said Bradley Hyman, M.D., Ph.D., Director, Massachusetts Alzheimer's Disease Research Center and Alzheimer's Unit Director, MassGeneral Institute for Neurodegenerative Disease at Massachusetts General Hospital, and John B. Penney Jr., Professor of Neurology, Harvard Medical School. "Of the many approaches to reduce tau expression that we've studied, zinc finger protein gene regulation technology is especially promising for its exquisite specificity, its potent reduction of tau protein expression, and its potential to provide a durable, long-lasting effect with only a single administration."
Sangamo's ZFP-TF gene regulation technology is designed either to selectively repress (down-regulate) or activate (up-regulate) the expression of a specific endogenous gene or gene sequence for a desired therapeutic effect. This approach enables targeting of a broad range of diseases requiring regulation of endogenous gene expression and differs from other approaches such as genome editing or gene therapy, which are designed to correct or replace a missing or mutated gene or gene sequence.

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

The March 29th presentation included data from in vitro studies conducted using induced pluripotent stem cell (iPSC) derived neurons demonstrating that a single administration of ZFP-TFs, via adeno-associated virus (AAV) vectors, resulted in greater than 90% reduction of human tau mRNA and protein. These data were consistent with a separate in vitro study using cortical neurons from wild-type mice, in which greater than 90% reduction in tau mRNA and protein was achieved. Furthermore, 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.

Additionally, data from in vivo studies of wild-type mice demonstrated greater than 80% reduction of tau mRNA and protein in the hippocampus, as well as sustained and well-tolerated ZFP-TF expression with minimal impact on inflammatory markers. Finally, data from in vivo studies in an amyloid mouse model of Alzheimer's disease demonstrated significantly reduced neuritic dystrophy after a single administration of ZFP-TFs in mice with established disease pathology.

"Our zinc finger protein transcription factor technology continues to demonstrate great potential as a highly differentiated, best-in-class genomic therapy platform for neurodegenerative diseases," said Michael Holmes, Ph.D., Sangamo's vice president and head of research. "Zinc finger proteins provide unparalleled precision and potency, which are especially critical for gene-targeting in neurons. Our ZFP-TFs allow us to selectively repress the tau gene which results in significant reduction of all forms of the tau protein, in contrast to other monoclonal antibody-based approaches to Alzheimer's and tauopathies that bind only to specific forms of tau."

The repression of tau in both mouse and human neurons is another demonstration of preclinical proof-of-concept for Sangamo's gene regulation approach for neurodegenerative diseases, which has also been applied to selectively repress the mutant huntingtin allele that causes Huntington's disease. Sangamo's huntingtin ZFP-TF specifically targets the mutant CAG-repeat expansion on the disease-causing allele, while preserving the expression of the wild-type huntingtin allele, and has been shown to correct molecular, histopathological and behavioral Huntington's phenotypes in mouse models of the disease. Sangamo's ZFP-TF technology is being developed for Huntington's disease in partnership with Shire.

**About Alzheimer's Disease and Tauopathies**

Alzheimer's disease and other tauopathies are characterized by the accumulation of hyper-phosphorylated tau protein and neurofibrillary tangles in the brain leading to
widespread neuronal dysfunction and loss. Intracellular tau protein aggregates and extracellular amyloid plaques are histopathological hallmarks of Alzheimer's disease. The reduction of tau expression has been shown to provide neuronal protection and reversal of pathology in Alzheimer's disease and tauopathy models.

About Sangamo Therapeutics

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. Sangamo 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 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 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 therapeutic applications of Sangamo's zinc finger protein transcription factor technology, the potential of Sangamo's technology to treat neurodegenerative diseases, including Alzheimer's and Huntington's disease, the application of ZFP-TF gene regulation technology to a broad range of diseases, and the ability of Sangamo to enter into partnerships for the development of its technology. Actual results may differ materially from these forward-looking statements due to a number of factors, including 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 SEC filings, including the risk factors described in its Annual Report on Form 10-K and its most recent Quarterly Report on Form 10-Q. Sangamo Therapeutics, Inc. assumes no obligation to update the forward-looking information contained in this press release.


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