Sangamo Therapeutics Logo

Sangamo Therapeutics Presents New Preclinical Data Demonstrating Significant Reduction In Tau Expression With Gene Regulation Technology

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- Sangamo's gene regulation platform technology fuses zinc finger proteins with transcription factors (ZFP-TFs)
- Data presented at ADPD show that tau-targeted ZFP-TFs delivered with AAVs in mice and nonhuman primates have significant activity
- Tau was reduced by greater than 80% in the brains of mice and nonhuman primates

BRISBANE, Calif., March 29, 2019 /PRNewswire/ -- Sangamo Therapeutics, Inc. (NASDAQ: SGMO), a genomic medicine company, presented new preclinical data demonstrating significant (>80%) reduction of tau expression in the nonhuman primate brain following administration of zinc finger protein transcription factors (ZFP-TFs). Tau pathology is strongly linked to the progression of several neurodegenerative diseases, called tauopathies, including Alzheimer's disease. The data, reported in a podium presentation at the 14thInternational Conference on Alzheimer's & Parkinson's Diseases (ADPD) held in Lisbon, Portugal, described the effects of tau-targeted ZFP-TFs delivered with adeno-associated viruses (AAVs) in the mouse and nonhuman primate (NHP) brain.

Sangamo™ THERAPEUTICS

Sangamo's ZFP-TF technology acts at the DNA level to selectively repress or activate the expression of specific genes to achieve a desired therapeutic effect. Gene regulation differs from other genome editing approaches as it is designed to enable precise, robust, and long-term repression of a selected gene following a single administration of AAV and does not cut or modify the target DNA.

Tauopathies are characterized by the accumulation of toxic tau protein in the brain that leads to widespread neuronal dysfunction and loss. Reducing the total amount of tau expressed within neurons has been shown to provide benefit in animal models of tauopathies.

"There are currently no disease modifying therapies approved for the treatment of tauopathies. While many tau-targeted approaches are currently being explored, a key challenge has been the incomplete understanding of the toxic tau proteins that drive disease progression, which are complex and vary between tauopathies. Sangamo's proprietary ZFP-TF gene regulation technology provides a differentiated approach to this problem by focusing on lowering all forms of tau at the DNA level and has the potential to provide significant therapeutic benefits for tauopathy patients," said Adrian Woolfson, BM., B.Ch., Ph.D., Executive Vice President of Research and Development at Sangamo. "These results also demonstrate the high degree of precision, efficiency and specificity of our zinc finger protein transcription factor platform and demonstrate how gene specific transcriptional regulation may play a key role in the future treatment of central nervous system diseases."

The goal of the preclinical studies presented at ADPD was to assess the pharmacology of tau gene repression in the mouse and NHP brain. AAV vectors were used to deliver tau-targeted ZFP-TFs *in vitro* to neurons and *in vivo* to vulnerable brain regions that are impacted by tauopathies. The data demonstrate that ZFP-TFs selectively reduced mouse and human tau by up to 98% *in vitro* in both primary mouse and induced pluripotent stem cell-derived human neurons. Intrahippocampal ZFP-TF delivery to adult mice resulted in more than 80% tau reduction, and intravenous ZFP-TF administration reduced tau levels by 50-70% across the entire mouse brain. ZFP-TF expression and mouse tau reduction were sustained for at least six months following a single administration. Furthermore, in APP/PS1 mice, tau-targeted ZFP-TFs reduced dystrophic neurites by approximately 50% across the cerebral cortex.

AAV ZFP-TFs targeting tau were administered to the adult NHP hippocampus using real-time MRI-guided stereotaxic infusion. ZFP-TF treatment resulted in more than 80% lowering of tau in the hippocampus and entorhinal cortex, and transgene expression levels were strongly correlated with tau reduction. The treatment was well tolerated for the duration of the study. Together these data from mice and NHPs highlight the potential for a single administration of ZFP-TF to lower tau as a treatment for tauopathies, including Alzheimer's disease.

Preclinical development of tau-targeted ZFP-TFs is ongoing, and Sangamo plans to present additional data at a future scientific meeting.

Sangamo is also developing potential ZFP-TF gene therapies for amyotrophic lateral sclerosis (ALS) and Huntington's disease, which are linked to mutations in the C9ORF72 gene and CAG repeat expansion in the HTT gene respectively. The ALS research is being performed in collaboration with Pfizer, while the Huntington's disease research is being performed in collaboration with Takeda.

About Sangamo Therapeutics
Sangamo Therapeutics, Inc. is focused on translating ground-breaking science into genomic medicines with the potential to transform patients' lives using the Company's platform technologies in genome editing, gene therapy, gene regulation and cell therapy. For more information about Sangamo, visit www.sangamo.com.

Forward-Looking Statements
This press release contains forward-looking statements based on Sangamo's current expectations. These forward-looking statements include, without limitation, statements relating to the potential therapeutic applications for Sangamo's ZFP-TF platform technology, the ability of ZFP-TFs to potentially lower all forms of tau levels at the DNA level and provide significant therapeutic benefits to treat tauopathies, including Alzheimer's disease and other central nervous system diseases, Sangamo's plans for the ongoing development of tau-targeted ZFP-TFs and plans to present additional data, and other statements that are not historical fact. 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, risks and uncertainties related to early preclinical data, including the risk that the early preclinical data may not warrant regulatory approvals to conduct human clinical trials, and may not be representative of results of any such human clinical trials; that ZFN-TFs may not produce any beneficial therapeutic effect in humans; Sangamo's reliance on partners and other third-parties to further develop its technology; Sangamo's ability to develop commercially viable products; and the potential for technological developments by Sangamo's competitors that will be better than Sangamo's ZFN-TF technology. These risks and uncertainties and other risks are described more fully in Sangamo's Annual Report on Form 10-K for the year ended December 31, 2018 as filed with the Securities and Exchange Commission. Forward-looking statements contained in this press release 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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