Sangamo Therapeutics Announces Data From Novel Proprietary Neurotropic AAV Capsid Demonstrating Industry-leading Blood-brain Barrier Penetration and Brain Transduction in NHPs

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- *Novel AAV capsid engineered by Sangamo showed robust penetration of blood-brain barrier (BBB) and widespread transgene expression throughout brain in non-human primates (NHPs) following intravenous administration.*
- *Demonstrated industry-leading brain tropism and enrichment in NHPs, resulting in 700-fold higher transgene expression than benchmark capsid AAV9.*
- *Capsid-enabled delivery of zinc finger payloads targeting prion disease and tauopathies resulted in robust and widespread repression of target genes.*
- *STAC-BBB capsid could potentially unlock multiple neurology epigenetic regulation programs paused by Sangamo pending identification of suitable capsid and could be advanced either internally or with a collaborator.*
- *Sangamo expects to file up to three neurology Investigational New Drug (IND) submissions and/or Clinical Trial Applications (CTA) by end of 2025.*
- *Sangamo to discuss results in conference call scheduled for Wednesday, March 13 at 4:30pm Eastern Time.*

RICHMOND, Calif.--(BUSINESS WIRE)--Mar. 13, 2024-- Sangamo Therapeutics, Inc. (Nasdaq: SGMO), a genomic medicine company, today announced preclinical data from its proprietary adeno-associated virus (AAV) capsid variant, STAC-BBB, that demonstrated robust penetration of the blood-brain barrier (BBB) and strong transgene expression throughout the central nervous system (CNS) of NHPs when administered intravenously at clinically-relevant doses, outperforming results obtained by Sangamo for other known neurotropic capsid variants evaluated in the study. Importantly, potent repression of target genes was observed in brain cells expressing the zinc finger cargo, indicating that STAC-BBB could enable development of genomic medicines to potentially treat a wide range of neurological diseases.

“The advancement of neurological medicines has long been limited by the inability to achieve widespread CNS delivery, an essential attribute for an effective treatment for devastating neurological disorders. We are extremely encouraged that STAC-BBB, a potentially game-changing capsid variant engineered using our SIFTER capsid platform, demonstrated results that outperformed other known neurotropic capsid variants, achieving widespread brain delivery and transgene expression, desired de-targeting of liver and other peripheral tissues and a favorable safety profile,” said Sandy Macrae, Chief Executive Officer of Sangamo. “Furthermore, these data demonstrated that delivery of our zinc finger epigenetic regulators using STAC-BBB could result in a meaningful repression of disease-relevant target genes throughout the brain, which we believe may result in profound improvements in disease pathology and progression. These data further support our transformation into a neurology-focused genomic medicine company focused on combining potent epigenetic regulation capabilities with innovative capsid delivery technology to develop best-in-class neurology medicines.”

Sangamo intends to use the novel STAC-BBB capsid in its wholly owned prion disease and tauopathy programs. In addition, STAC-BBB could potentially unlock multiple neurology epigenetic regulation programs that were paused by Sangamo pending the identification of a suitable capsid, including programs previously in development under Sangamo’s former collaboration agreements with Biogen and Novartis. Sangamo is exploring avenues to resume development of these programs internally, subject to receipt of adequate funding, or with new potential collaborators.

Summary of STAC-BBB Preclinical Data

In NHP studies when administered intravenously at clinically relevant doses, STAC-BBB demonstrated its potential to be a leading neurotropic capsid.

Highlights include:

- **Broad brain coverage.** Robust penetration of the BBB and widespread transgene expression throughout the brain, including key regions integral to human neurological diseases such as Alzheimer’s disease, Parkinson’s disease, Amyotrophic Lateral Sclerosis (ALS), Huntington’s disease and prion disease.
- **Industry-leading brain tropism.** Exhibited 700-fold higher transgene expression in neurons compared to the benchmark capsid AAV9 and outperformed all other known published neurotropic capsid variants evaluated in the study.
- **Widespread neuronal transduction across all animals.** STAC-BBB mediated robust expression of zinc finger cargo in neurons, the key cell type to target for treatment of neurological diseases. Moreover, results were dose-dependent and consistent across all NHPs in the study.
- **Potent and widespread repression of target genes.** Capsid-enabled delivery of zinc finger payloads resulted in the repression of prion and tau genes across key brain regions, demonstrating the potential for modification of disease progression in prion disease and various tauopathies. Visualization of gene expression in individual brain cells by RNAscope revealed highly potent repression of tau in neurons expressing the zinc finger cargo across multiple brain regions.
- **Desired de-targeting of the liver and other peripheral organs.** Capsid biodistribution was shown to be enriched in the CNS and de-targeted from the liver, dorsal root ganglia (DRG) and other peripheral organs. This biodistribution profile demonstrated by STAC-BBB is optimal for an AAV-based treatment of neurological diseases.

- **Favorable safety profile.** STAC-BBB was well tolerated in NHPs, with no notable treatment related pathological findings in brain, spinal cord or peripheral tissues.
- **Manufacturable using standard processes and at scale.** We believe STAC-BBB is manufacturable at commercial scale using standard cell culture and purification processes, is soluble using known excipients, and can be characterized using available analytics.

Sangamo expects to file an IND submission for its Nav1.7 program addressing chronic neuropathic pain, which leverages an intrathecally administered capsid, in the fourth quarter of 2024, and a CTA submission for its prion disease program, which is expected to leverage the STAC-BBB capsid, in the fourth quarter of 2025, each subject to additional funding. Sangamo also intends to resume development of its tau program leveraging the STAC-BBB capsid, with an IND submission expected as early as the fourth quarter of 2025.

The Sangamo management team will discuss these results on a conference call on Wednesday, March 13 at 4:30pm Eastern Time.

Participants should register for, and access, the call using this link. While not required, it is recommended you join 10 minutes prior to the event start. Once registered, participants will be given the option to either dial into the call with the number and unique passcode provided or to use the dial-out option to connect their phone instantly.

An updated corporate presentation is available in the Investors and Media section under Presentations.

The link to access the live webcast can also be found on the Sangamo website in the Investors and Media section under Events. A replay will be available following the conference call, accessible at the same link.

About Sangamo Therapeutics

Sangamo Therapeutics is a genomic medicine company dedicated to translating ground-breaking science into medicines that transform the lives of patients and families afflicted with serious neurological diseases who do not have adequate or any treatment options. Sangamo's zinc finger epigenetic regulators are ideally suited to potentially address devastating neurological disorders and Sangamo's capsid discovery platform is expanding delivery beyond currently available intrathecal delivery capsids, including in the central nervous system. Sangamo's pipeline also includes multiple partnered programs and programs with opportunities for partnership and investment. To learn more, visit www.sangamo.com and connect with us on LinkedIn and Twitter/X.

Forward-Looking Statements

This press release contains forward-looking statements regarding our current expectations. These forward-looking statements include, without limitation, statements relating to: expectations regarding the therapeutic potential of Sangamo's technologies, including the delivery of zinc finger epigenetic regulators using STAC-BBB to result in the repression of disease-relevant target genes in the brain, to result in profound improvements in disease pathology and progression, to modify disease progression in prion disease and various tauopathies, to be manufacturable at commercial scale using standard cell culture and purification processes, to be soluble using known excipients, and to be characterized using available analytics; Sangamo's intentions to use STAC-BBB in two of its epigenetic regulation product candidates under development internally; expectations that preclinical data from STAC-BBB will support Sangamo's transformation into a neurology-focused genomic medicine company; expectations regarding STAC-BBB's potential to unlock multiple neurology epigenetic regulation programs that have been paused by Sangamo pending the identification of a suitable capsid, and plans to either resume their development internally, with receipt of additional funding, or with a new potential collaborator; Sangamo's plans to file INDs submissions and/or CTAs and the expected timing of such regulatory submissions; and other statements that are not historical fact. These statements are not guarantees of future performance and are subject to certain risks and uncertainties that are difficult to predict. Factors that could cause actual results to differ include, but are not limited to, risks and uncertainties related to the uncertain and costly research and development process, including the risk that preclinical results may not be indicative of results in any future clinical trials; Sangamo's lack of capital resources to fully develop, obtain regulatory approval for and commercialize its product candidates, including Sangamo's ability to secure a partnership or the funding required to initiate planned IND and/or CTA submissions in a timely manner or at all; Sangamo's need for substantial additional funding to execute its operating plan and to continue to operate as a going concern, including the risk that Sangamo will be unable to obtain the funding necessary to advance Sangamo's Nav1.7, prion disease and tau programs and to otherwise continue to operate as a going concern, in which case, Sangamo may be required to cease operations entirely, liquidate all or a portion of its assets, and/or or seek protection under applicable bankruptcy laws; the effects of macroeconomic factors or financial challenges, including as a result of the ongoing overseas conflict, current or potential future bank failures, inflation and elevated interest rates, on the global business environment, healthcare systems and business and operations of Sangamo and our collaborators; the research and development process; the potential for technological developments that obviate technologies used by Sangamo; Sangamo's reliance on collaborators and its potential inability to secure additional collaborations, and Sangamo's ability to achieve expected future operating results.

There can be no assurance that we and our current or potential future collaborators will be able to develop commercially viable products. Actual results may differ materially from those projected in these forward-looking statements due to the risks and uncertainties described above and other risks and uncertainties that exist in the operations and business environments of Sangamo and its collaborators. These risks and uncertainties are described more fully in Sangamo's Securities and Exchange Commission, or SEC, filings and reports, including in its Annual Report on Form 10-K for the year ended December 31, 2023, filed with the SEC, and future filings and reports that Sangamo makes from time to time with the SEC. 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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