Sangamo BioSciences Presents Phase 2 Clinical Data From Two SB-728-T HIV Studies

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Preliminary Data Suggest Adenoviral Delivery Method Superior for Immune Stimulation and Control of Viral Load in the Absence of Antiretroviral Therapy (ART)

Two of Three Subjects Remain Off ART for More Than One Year

RICHMOND, Calif., Dec. 11, 2015 /PRNewswire/ -- Sangamo BioSciences, Inc. (Nasdaq: SGMO), the leader in therapeutic genome editing, announced the presentation of Phase 2 data from two of the Company's ongoing clinical trials (SB-728-1101 Cohort 3* and SB-728-mR-1401) of SB-728-T, which is being developed for the functional control of HIV/AIDS. The preliminary comparative data suggest that adenoviral delivery of zinc finger nucleases (ZFNs) to T-cells may be uniquely immune-stimulatory for both acute control of infection, and importantly, HIV reservoir reduction.

"The preliminary Phase 2 data suggest superiority of the SB-728-T product produced using adenoviral delivery to both CD4 and CD8 cells with two of three initially treated subjects remaining off ART for over one year," stated Dale Ando, M.D., Sangamo's vice president of therapeutic development and chief medical officer. "The adenovirus used to deliver the CCR5-modifying ZFNs to the T-cells may act somewhat like an "adjuvant," providing additional immune stimulation beyond Cytoxan preconditioning, and enhancing expansion of CD8 cells once they are infused back into the subject. This expansion may improve the likelihood of viral load control in the absence of ART, particularly in HIV-infected individuals who may have only a narrow repertoire of anti-HIV activity."

"The proportion of treated subjects in the adenoviral modified Cohort 3* who have responded and established sustained control of viral load in the absence of ART is very striking and may reflect reprogramming of the immune system," stated Rafick Pierre Sékaly, Ph.D., co-director, CHAR Proteomics and Systems Biology Core, Department of Pathology, Case Western Reserve University. "These data suggest that Sangamo has developed a product that can potentially protect the immune system, restore T-cell homeostasis and CD4 T-cell function thereby enabling durable immunological control of HIV by CD8 killer T-cells."

"The observation of functional control in some Cohort 3* subjects complements the observation of significant reduction of HIV reservoir in the immunologic non-responder cohort (SB-728-0902 trial). In that study, infusion of CCR5 modified T-cells led to restoration of T-cell homeostasis and an HIV resistant subset of memory stem T-cells that effectively diluted and reduced the HIV reservoir over time," Dr. Sékaly further commented.

The data demonstrate that SB-728-T manufactured using both mRNA and adenoviral delivery of CCR5-modifying ZFNs to CD4 and CD8 T cells were safe and well-tolerated following a Cytoxan conditioning regimen. The mRNA product showed greater accumulation of total CD4, CD8 and CCR5-modified cells with 3 compared to 2 repeat doses, with persistence of modified cells in the circulation. However, preliminary data suggest that adenoviral delivery may enhance the expansion of CD8 cells compared with mRNA delivery. In addition, a higher proportion of HIV infected subjects treated with the adenoviral SB-728-T product achieved durable control of viral load during a treatment interruption (TI) of their ART than those dosed with a product generated using mRNA delivery or adenoviral delivery to only CD4 cells. Both delivery methods achieved similar levels of CCR5 modification of T-cells.

Preliminary data from the two Phase 2 studies were presented by Dr. Ando at the *7th International Workshop on HIV Persistence during Therapy*, considered to be the reference workshop on HIV reservoirs and eradication strategies, which is being held in Miami, FL, December 8-11, 2015. Analyses exploring the potential mechanism of action of SB-728-T in promoting reduction of the HIV reservoir in immune non-responder patients with HIV infection will be summarized in a presentation given by Dr. Sékaly today titled, "The Anti-inflammatory Response and the HIV Cure."

Sangamo's earlier studies of this ZFP Therapeutic®, generated using adenoviral delivery of ZFNs, used an SB-728-T product that was depleted of CD8 cells and thus enriched in CD4 cells. Previously published reports have suggested that individuals who naturally control their HIV infection, so called elite controllers, have activated CD8 cells with low CCR5 expression. For this reason, the SB-728-T product evaluated in both studies described in the presentation was manufactured to contain both ZFN-modified CD4 and CD8 T-cells.

The studies compared two cohorts of subjects that both received a Cytoxan preconditioning treatment, and similar doses of CD4 and CD8 T-cells that were ZFN-modified to disrupt expression of CCR5, a critical co-receptor for HIV entry. One group of subjects (SB-728-1101 Cohort 3*), received a single dose of cells that were modified using ZFNs delivered in an adenoviral formulation and the second group (SB-728-mR-1401, n=8) received an equivalent total dose of modified cells spread over two or three treatments that had been manufactured using electroporation of ZFNs delivered as mRNA. In Cohort 3* four subjects have been treated (of a planned total of eight subjects) and three subjects have completed the protocol's 16-week TI. Both methods generate products with similar levels of ZFN-mediated disruption of the CCR5 gene and both treatments were safe and well-tolerated. Cytoxan is a drug that is used to transiently reduce the numbers of T-cells in the body, which then rapidly repopulate once the drug is discontinued, and it is into this "growth" environment that SB-728-T is infused.

"We have previously demonstrated that delivery of ZFNs to both T-cells and hematopoietic stem cells using mRNA and electroporation results in high levels of genome editing at clinical scale and we continue to use this method for all other *ex vivo* applications," stated Geoff Nichol, M.B.,

Ch.B., Sangamo's executive vice president of research and development. "Adenoviral delivery of ZFNs to T cells may be uniquely immune-stimulatory for both acute control of infection and, based on our earlier studies, reservoir reduction, in HIV. We look forward to receiving data from an additional five Cohort 3* subjects in 2016."

Summary of Clinical Trial Design

About SB-728-1101 Cohort 3*

SB-728-1101 is an open-label, multi-center study designed primarily to evaluate safety and tolerability of SB-728-T following optimal cyclophosphamide (Cytoxan) pre-conditioning, on engraftment, viral load and total T-cell counts in peripheral blood. Subjects in Cohort 3* of the study will be treated with a preparation of up to 40 billion ZFN-modified CD4 and CD8 T-cells. The study uses an adenoviral vector to deliver the ZFNs to the isolated T-cells. Four weeks after the last SB-728-T infusion, subjects with CD4 cell counts ≥500 cells/mm^3 will undergo a 16 week TI during which time their ART will be discontinued. ART will be reinstituted in subjects whose CD4 T-cell counts drop and/or whose HIV-RNA increases to certain pre-defined levels. At the end of the TI, subjects with a sustained detectable viral load or reduced CD4 T-cell count will be reinstituted on ART. Up to eight subjects will be treated, all of which have been accrued.

About SB-728-mR-1401

SB-728-mR-1401 is an open-label, multi-center study designed primarily to evaluate safety and tolerability and the effect of repeat doses of SB-728-T containing both CD4 and CD8 cells following optimal cyclophosphamide pre-conditioning, on engraftment, viral load and total CD4 and CD8 counts in peripheral blood. The study used a new manufacturing process, using electroporation of mRNA encoding the ZFNs rather than an adenoviral vector to deliver the ZFNs to the isolated T-cells. This process enables repeat dosing of the product. Up to eight subjects have been enrolled into two cohorts. Each subject received a total of up to 40 billion ZFN-modified T-cells. The first cohort received this dose in two infusions of equal doses of SB-728mR-T, 14 days apart after a cyclophosphamide (1 g/m^2) preconditioning treatment, two days prior to the first SB-728mR-T infusion. The second cohort received three infusions of equal doses of cells. Dividing the total cell dose and administering sequentially in this manner is thought to maximize overall cell engraftment. Four weeks after the last SB-728-mR infusion, subjects with CD4 cell counts ≥500 cells/mm^3 underwent a 16 week TI during which time their anti-retroviral therapy was discontinued. ART was reinstituted in subjects whose CD4 T-cell counts dropped and/or whose HIV-RNA increased to certain pre-defined levels. At the end of the TI, subjects with a sustained detectable viral load or reduced CD4 T-cell count were reinstituted on ART.

About SB-728-T

Sangamo's drug, SB-728-T, is generated by ZFN-mediated modification of the gene encoding the CCR5 receptor in a patient's own T-cells. ZFN modification disrupts the expression of this key co-receptor for HIV entry and renders cells resistant to HIV infection. The approach is based on the observation that a naturally occurring mutation in the CCR5 gene, CCR5 delta-32, provides protection from HIV infection. Individuals in whom both copies of the CCR5 gene carry the delta-32 mutation are generally not susceptible to the most common strain of HIV.

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 has a Phase 2 clinical program to evaluate the safety and efficacy of novel ZFP Therapeutics® for the treatment of HIV/AIDS (SB-728). Sangamo's other therapeutic programs are focused on monogenic and rare diseases. The Company has 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 also 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 ZFP TFs and ZFNs and therapeutic applications of Sangamo's ZFP technology platform for the treatment of HIV/AIDS, including a potential functional cure for HIV/AIDS, the ability of a ZFP Therapeutic to control HIV infection, and projected timing of data from SB-728-T clinical trials. 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 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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