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Sangamo BioSciences Presents Clinical Data From Key SB-728-T HIV Studies: Proof Of Concept For Ongoing Sustained Functional Control Of HIV Viral Load; Cytoxan Preconditioning Successfully Enhances Engraftment

Undetectable Viral Load Sustained Over 20 Weeks in SB-728-902 Study; Data Demonstrate Dose Response in SB-728-1101 Cytoxan Study; Reduction of Viral Reservoir Observed in All Immune Non-Responders Over Three Years

RICHMOND, Calif., Dec. 6, 2013 /PRNewswire/ -- Sangamo BioSciences, Inc. (Nasdaq: SGMO) announced today the presentation of data from all dose cohorts in the Company's ongoing clinical trials (SB-728-1101 and SB-728-902 Cohort 5) of SB-728-T, which is being developed for the functional control of HIV/AIDS. The data are being presented at the Sixth 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 3-6 2013.

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"The results announced today represent a major milestone," stated Geoff Nichol, M.B., Ch.B., Sangamo's executive vice president of research and development. "We have succeeded in achieving sustained control of HIV with SB-728-T in CCR5 delta-32 heterozygotes, and we have shown that we can safely use Cytoxan to potentially achieve threshold levels of engraftment for all patients with HIV. Collectively, data from our clinical studies suggest that protection of CD4 T-cells by ZFN mediated CCR5 disruption may provide helper function to CD8 cells enabling the immune system to mount an anti-HIV response that can also erode the HIV reservoir. The reservoir is a compartment of the HIV-infected immune system that is not addressed by antiretroviral medication and its depletion is key to the goal of complete eradication of HIV infection."

Sangamo's Phase 1 data suggested that if a threshold level of engraftment of SB-728-T was achieved, specifically of CD4 cells fully protected from HIV entry by zinc finger nuclease (ZFN)-mediated modification of both CCR5 genes (biallelic modification), then functional control of HIV infection may be possible. New data from the SB-728-1101 study demonstrating a clear relationship between increasing the dose of Cytoxan and increased levels of both engrafted SB-728-T and total CD4 T-cell counts further support this hypothesis and suggest that with these, or higher doses, levels of SB-728-T that will enable functional control of the virus may be reliably attained.

Each of the two trials addressed a different approach to maximizing engraftment of infused SB-728-T that had undergone biallelic modification of the CCR5 gene. Inclusion of newly eligible subjects in the analysis strengthened previous data demonstrating a statistically significant correlation (p=0.008) between estimated number of engrafted biallelically modified cells and the reduction in viral load (VL) during a treatment interruption (TI) from antiretroviral therapy (ART).

"The decreases observed in viral load in several subjects on both of these trials have been very impressive and are not something that one would expect to happen by chance," stated Gary Blick, M.D., AAHIVS, Medical & Research Director, CIRCLE CARE Center and an investigator on both studies. "Furthermore, the data that have been generated in the course of the clinical investigation of this novel therapy on reductions in viral load and the levels of viral reservoir, as well as the increases in total CD4 cells, demonstrate that a single SB-728-T treatment has the unique ability to enable sustained immunological functional control of HIV in the absence of ART."

In the **SB-728-902 Cohort 5 study**, bialleic modification of the infused CD4 cells could be approximately doubled by treating subjects heterozygous for the naturally occurring CCR5 delta-32 mutation. Three of eight evaluable CCR5 delta-32 heterozygous subjects with high levels of engraftment achieved a VL at or below the limit of quantification during a TI. This includes two of seven subjects that had initiated TI in the SB-728-902 Cohort 5 study and an additional CCR5 delta-32 heterozygote subject from an earlier Phase 1 clinical trial of SB-728-T. One SB-728-902 Cohort 5 subject, who had the highest levels of estimated biallelically modified cells and measurable immunological responses to the virus (polyfunctional anti-gag response), demonstrated sustained control of VL at or below the limits of detection, which is ongoing for more than 20 weeks into the TI.

The **SB-728-1101 study** aimed to demonstrate enhanced engraftment of SB-728-T modified CD4 cells following cyclophosphamide (Cytoxan) preconditioning. 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. This study was successful in showing a Cytoxan-dose dependent increase in both SB-728-T and total CD4 T-cells at the beginning of the treatment interruption, which in the top dose tested (1g/m^2) approached the engraftment levels observed in CCR5 delta 32 heterozygote VL responders, and resulted in up to a two-log decrease in VL in one of three subjects who remains on TI and a 0.8-log decrease in a second subject. In the study, a total of twelve subjects were treated in three cohorts of escalating doses of Cytoxan (three subjects at 200 mg, six subjects at 500 mg/$m^2$and three subjects at 1000 mg/m^2). All doses tested were safe and well-tolerated although two of the first three subjects in the second cohort experienced Grade 2 nausea, which was reversed using an improved anti-emetic regimen that was further tested with an additional three subjects (total of six subjects at this dose level). Cytoxan dose-dependent increases were observed in both SB-728-T and total CD4 T-cells. The study has been expanded to test an additional six subjects in two cohorts of three at Cytoxan doses of 2.0 and 3.0 g/m^2.

The viral reservoir is a source of chronic HIV infection that is not addressed by current ART. All nine subjects enrolled in Sangamo's Phase 1 study (**SB-728-902 Cohorts1-3**) experienced a long term reduction in the reservoir over three years, as measured by HIV DNA in peripheral blood mononuclear cells (median 0.9 log decrease at Month 36). In addition, a reduction in the viral reservoir, as measured by integrated HIV DNA in sorted CD4 cells, correlated with increased numbers of functional HIV gag-responsive CD8 T-cells, suggesting that these cells can mount an anti-HIV response with the help of ZFN modified CD4 T-cells (SB-728-T).

Collectively, data from clinical studies demonstrate that in all trial subjects, SB-728-T treatment results in a durable increase in total CD4 T-cells and sustained levels of SB-728-T which correlate with ZFN-modification of long lived central memory and memory stem cell subsets. Data from immunological analyses of subjects in both Phase 1 and Phase 2 studies of SB-728-T suggest that certain cell surface marker and gene expression profiles may predict which patients will likely respond best to SB-728-T treatment.

"We are very encouraged by our data to date and by our continued progress in understanding the factors required to maximize the potential of this novel immunologic approach to functional control of HIV," said Edward Lanphier, Sangamo's president and CEO. "We look forward to continuing to update on our progress in the coming months as we complete treatment in our expanded SB-728-1101 study. We will also present preclinical data from several of Sangamo's programs in monogenic diseases and other indications at the upcoming Annual Meeting of the American Society of Hematology (ASH)."

Summary of Clinical Trial Design
About SB-728-902
Cohorts 1-3
The study is an open-label Phase 1 clinical trial to evaluate the safety and tolerability of single infusions of an escalating dose of an autologous (a patient's own) CD4+ T-cell product genetically modified at the CCR5 gene by CCR5-specific ZFNs (SB-728-T). Nine HIV-infected subjects (three cohorts of three subjects each) classified as immune non-responders (INR) with sub-optimal T-cell levels and no detectable viral load on long-term ART were enrolled into the trial. Subjects received SB-728-T at doses of approximately 5, 20 or 30 billion cells and remained on their existing antiviral therapy throughout the study without undergoing a TI.
Cohort 5
Ten HIV-infected subjects heterozygous for the CCR5 delta-32 mutation (i.e. with one CCR5 gene that is naturally modified) who are currently on ART have been enrolled and have received a single intravenous infusion of SB-728-T (12.6 to 23.5 billion cells). Two months after SB-728-T treatment, subjects underwent a 16 week TI during which time their ART was discontinued. ART was reinstituted in subjects whose CD4 T-cell counts dropped to < 350 cells/ mm^3 and/or whose HIV-RNA increased to > 100,000 /mL for three consecutive weekly measurements. At the end of the TI, subjects with a sustained detectable HIV viral load were reinstituted on ART. Subjects with an undetectable viral load can remain off ART until HIV RNA levels are > 10,000 copies/mL for three consecutive weekly measurements or their CD4 T-cell count drops below 500 cell/mm^3 for two consecutive weekly measurements.

About SB-728-1101
SB-728-1101 is an open-label, dose escalation, multi-center study designed primarily to evaluate the safety and tolerability of escalating doses of cyclophosphamide (Cytoxan) administered prior to SB-728-T infusion. 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. Such lymphodepletive treatment has been used to enhance engraftment of adoptively transferred T-cells in the treatment of cancer and as therapy for numerous autoimmune diseases. The drug has been previously used in HIV-infected individuals and studies demonstrate that, while the drug was transiently lymphodepleting, it did not significantly reduce total CD4 T-cell counts over the long term and was adequately tolerated.

In addition to safety, the study is evaluating the effect of escalating doses of Cytoxan on SB-728-T engraftment, the effect of SB-728-T treatment on viral load following ART interruption, the change in CD4+ T-cell counts in peripheral blood and the long-term persistence of SB-728-T.

By protocol, nine HIV-infected subjects on ART were enrolled into three dose-escalating cohorts (three subjects/cohort), and

received intravenous Cytoxan (200 mg, 500 mg/m^2 or 1000 mg/m^2). In cohort two, an additional three subjects were evaluated on an improved anti-emetic protocol due to an adverse event of Grade 2 nausea observed in two subjects at that dose level. Within each cohort, treatment was staggered so that each subsequent subject was infused with Cytoxan two weeks after the preceding subject. One to three days after receiving Cytoxan, subjects were infused with SB-728-T (8.2 to 36.2 billion cells). Six weeks after SB-728-T infusion, subjects with CD4 cell counts ≥500 cells/mm^3underwent a 16 week TI during which time their anti-retroviral therapy was discontinued. ART was reinstituted in subjects whose CD4 T-cell counts dropped to < 500 cells/$mm^3$and/or whose HIV-RNA increased to > 100,000 copies/ mL for three consecutive measurements. At the end of the TI, subjects with a sustained detectable viral load > 10,000 copies/ mL or CD4 T-cell count < 500 cells/mm^3 were reinstituted on ART. Subjects with a viral load > 10,000 copies/ mL and CD4 T-cell count > 500 cells/mm^3 can remain off ART until HIV RNA levels are > 10,000 copies/ mL for three consecutive weeks or their CD4 T-cell count drops below 500 cells/mm^3 for two consecutive weekly measurements.

Two additional cohorts of three subjects each will be treated at doses of 2000mg/m^2 and 3000mg/m^2, respectively.

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 research and development of novel DNA-binding proteins for therapeutic gene regulation and genome editing. The Company has ongoing Phase 2 and Phase1/2 clinical trials to evaluate the safety and efficacy of a novel ZFP Therapeutic® for the treatment of HIV/AIDS. As part of its acquisition of Ceregene Inc., Sangamo acquired a fully-enrolled and funded, double-blind, placebo-controlled Phase 2 trial to evaluate NGF-AAV (CERE-110) in Alzheimer's disease. Sangamo's other therapeutic programs are focused on monogenic diseases, including hemophilia, Huntington's disease and hemoglobinopathies such as beta-thalassemia and sickle cell anemia. Sangamo's core competencies enable the engineering of a class of DNA-binding proteins known as zinc finger DNA-binding proteins (ZFPs). Engineering of ZFPs that recognize a specific DNA sequence enables the creation of sequence-specific ZFP Nucleases (ZFNs) for gene modification and ZFP transcription factors (ZFP TFs) that can control gene expression and, consequently, cell function. Sangamo has entered into a strategic collaboration with Shire AG to develop therapeutics for hemophilia, Huntington's disease and other monogenic diseases and has 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.

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, projected timing of release of SB-728-T clinical data and preclinical data from Sangamo's monogenic disease programs, the expansion of clinical studies for HIV-infected individuals and the initiation of additional preclinical studies of ZFN-gene modification. 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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