



## Sangamo BioSciences Presents New Clinical Data at CROI 2015 From Trial of ZFP Therapeutic® Designed to Provide Functional Control of HIV

February 26, 2015

**Data Demonstrate Cytoxin Preconditioning Combined with CD4/CD8 ZFN-modified T-cell Product Reduces Viral Load to Limit of Quantification in One Subject of Three; Delays Onset of Viremia in Another Subject**

**Company Also Announces FDA Acceptance of IND Application for New HIV/AIDS Clinical Trial Using ZFN-modification of Hematopoietic Stem Cells**

RICHMOND, Calif., Feb. 26, 2015 /PRNewswire/ -- Sangamo BioSciences, Inc. (Nasdaq: SGMO) announced the presentation of new clinical data from its Phase 1/2 clinical trial (SB-728-1101). The study is designed to evaluate SB-728-T, a ZFP Therapeutic® generated by ZFN-mediated genome editing of T-cells to knockout the CCR5 gene, which encodes a critical co-receptor for HIV infection. SB-728-T is being developed as a potential 'functional cure' for HIV/AIDS. The data were presented at the Conference on Retroviruses and Opportunistic Infections (CROI 2015) which is being held in Seattle from February 23 to 26, 2015.



"In our studies of SB-728-T, we have observed remarkable effects on both the viral load and the levels of the viral reservoir," said Dale Ando, M.D., Sangamo's vice president of therapeutic development and chief medical officer. "Data and models developed by other groups have defined the characteristics of so-called 'elite controllers' whose immune systems prevent their HIV infections from progressing to AIDS, without antiretroviral drugs (ART). As part of the 1101 study, we are evaluating whether an improvement in HIV control can be obtained by including CD8 T-cells in our SB-728-T product, mimicking a phenotype observed in 'elite controllers.' The data demonstrate that we can generate a CD4/CD8 SB-728-T cell product that can be successfully combined with Cytoxin preconditioning to drive robust engraftment. Moreover, in the three subjects treated we have already observed encouraging increases in total CD8 T-cells and effects on the viral load during a treatment interruption (TI)."

The 1101 study was designed to evaluate the effect of increasing doses of Cytoxin® preconditioning as a method to maximize engraftment of ZFN-modified cells (SB-728-T) in which both copies of the CCR5 gene had been disrupted, making the cells fully resistant to HIV infection. Data from Cohorts 1-5 of the 1101 study (18 subjects) demonstrated a dose-related increase in both total CD4 T-cell and ZFN modified CD4 T-cell engraftment in response to Cytoxin preconditioning up to 1.0 g/m<sup>2</sup>. In addition, all subjects underwent a TI and were taken off ART at sixteen weeks post infusion. Four subjects from Cohort 1-5 remain on long-term TI and have remained off ART for at least 40 weeks.

New data reported at CROI also included a further cohort (3\*) of three subjects who received a ZFN-mediated CCR5 modified SB-728-T product containing both CD4 and CD8 T-cells. Among the three subjects treated in Cohort 3\*, one displayed a reduction in viral load below the limit of quantification (LOQ). Another subject displayed a markedly delayed onset of viremia for over 8 weeks from the start of TI. TI is ongoing in all three subjects. CD8 cells are the cells that are directly involved in clearance of the virus with "help" from CD4 cells. 'Elite controllers' have been shown to have elevated levels of CD8 T-cells that express low levels of CCR5 and have good anti-viral responses, a characteristic shared by those SB-728-T treated subjects in which the greatest effects on the virus have been seen to date.

"Data generated in these studies support our conviction that an immunologic approach to a 'functional cure' of HIV infection is likely to be the most successful," said Geoff Nichol, M.B., Ch.B., Sangamo's executive vice president of research and development. "This new mixed CD4/CD8 SB-728-T cell product not only has the potential to improve the antiviral effect of the treatment, but significantly simplifies the manufacturing process as we have eliminated the step of removing CD8 T-cells from the modified product. Sangamo continues to evaluate these modifications in our ongoing study (SB-728-mR-1401), which reflects our best understanding of the potential mechanism of this novel therapeutic. We believe that this trial, combined with our ongoing evaluations of previous studies, will yield data that will provide a clear path to pivotal studies."

Sangamo has an ongoing Phase 2 clinical trial, SB-728-mR-1401, designed to provide further evidence of functional control of HIV in additional subjects. The protocol incorporates a number of methods to increase the engraftment of CD4 T-cells that have undergone biallelic CCR5 gene modification, including certain criteria for subject selection, Cytoxin preconditioning and a number of process improvements such as mRNA delivery of the ZFNs, which will allow the administration of multiple doses. The Company completed patient accrual for this study in 2014 and expects to report preliminary data by the end of 2015.

"In addition, subsequent to the U.S. Food and Drug Administration's (FDA) recent acceptance of an Investigational New Drug (IND) application, Sangamo, with our collaborator, City of Hope, expects to initiate a Phase 1 clinical trial of this same approach in hematopoietic stem progenitor cells in the first half of 2015," continued Dr. Nichol.

### Clinical Data Summary

#### Abstract #434: Cytoxin Enhancement of SB-728-T Engraftment: A Strategy to Improve Anti-HIV Response

Wednesday, February 25, 2015

HIV-infected subjects were enrolled in a Phase 1/2 clinical trial (SB-728-1101) in six cohorts. Cohorts 1-5, (18 subjects) designed primarily to evaluate

the safety and tolerability of escalating doses of cyclophosphamide (Cytoxan<sup>®</sup>) (doses tested: 200 mg, 500 mg/m<sup>2</sup>, 1.0g/m<sup>2</sup>, 1.5g/m<sup>2</sup> or 2.0g/m<sup>2</sup>) administered prior to an infusion of SB-728-T (CD4 cell enriched). The sixth cohort, Cohort 3\*, (3 subjects) was designed to evaluate a CD4/CD8 SB-728-T product post-administration of Cytoxan at the optimal dose of 1.0g/m<sup>2</sup>.

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.

All subjects were on ART and had stably controlled undetectable levels of HIV in their blood. Each subject received a single dose of SB-728-T (8 to 36 billion cells) after a dose of Cytoxan.

The study evaluated safety and tolerability of escalating doses of Cytoxan preconditioning, changes in CD4+ T-cell counts and the ratio of CD4+ to CD8+ T-cells, as well as levels of SB-728-T in the blood and levels of viral load during a 16 week TI beginning six weeks after subjects received the SB-728-T treatment.

Analysis of the data from subjects in the study presented, demonstrated:

- Cytoxan preconditioning at doses up to 1.0 gm/m<sup>2</sup> safely enhanced total CD4 and CCR5 modified CD4 T-cells (Cohorts 1-5, 18 subjects)
- Four subjects who received either 1.0 or 1.5 gm/m<sup>2</sup> remain on long-term TI, (40-71 weeks).
- CD8 repletion in Cohort 3\* did not affect the safety profile of SB-728-T
- In Cohort 3\* increased levels of CCR5 modified CD8 T-cells were observed post infusion, suggesting expansion of CD8 T-cells
- Three subjects from Cohort 3\* have shown a doubling of their CD8 T-cells, with one subject displaying control of viral load below the LOQ during TI, and another displaying delayed onset of viremia during TI

#### **About SB-728-T**

Sangamo's drug, SB-728-T, is generated by ZFN-mediated modification of the gene encoding CCR5 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<sup>™</sup> for monogenic and infectious diseases by deploying its novel DNA-binding protein technology platform in therapeutic gene regulation and genome editing. The Company has clinical stage programs to evaluate the safety and efficacy of novel ZFP Therapeutics<sup>®</sup> for the treatment of HIV/AIDS (SB-728-T), beta-thalassemia (SB-BCLmR-HSPC), and NGF-AAV for Alzheimer's disease (CERE-110). Sangamo's other therapeutic programs are focused on monogenic and rare diseases. The Company has formed a strategic collaboration with Shire International GmbH to develop therapeutics for hemophilia, Huntington's disease and other monogenic diseases, and with Biogen Idec for hemoglobinopathies, such as sickle cell disease and beta-thalassemia. 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](http://www.sangamo.com).

*ZFP Therapeutic<sup>®</sup> 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, projected timing of release of SB-728-T clinical data and the expansion of clinical studies for HIV-infected individuals. 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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SOURCE Sangamo BioSciences, Inc.

Released February 26, 2015