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Sangamo presents immunological data from SB-728-T HIV clinical study at CROI 2016

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Sangamo BioSciences, Inc. (Nasdaq: SGMO), the leader in therapeutic genome editing, announced the presentation of immunological data from the Company's clinical trials of SB-728-T, a ZFP Therapeutic® designed to provide functional control of HIV. Analysis of data from Sangamo's most recent SB-728-1101 study suggests key, potentially interrelated mechanisms for viral load (VL) control in treated subjects during a treatment interruption (TI) from their antiretroviral therapy (ART). The analysis was presented by Sangamo's collaborator, Rafick-Pierre Sékaly, Ph.D., Richard Fasenmeyer Chair in Immunopathogenesis, Case Western Reserve University, at the 2016 Annual Conference on Retroviral and Opportunistic Infections (CROI 2016). The meeting is being held in Boston from February 22-26, 2016.

"A significant number of subjects treated with SB-728-T have experienced a striking control of their viral load for a sustained period in the absence of ART," stated Dr. Sékaly. "This is particularly notable in cohorts treated with optimal doses of Cytoxan® in the SB-728-1101 study. Immunological and HIV reservoir analyses suggest that the best predictors for post-treatment viral control are higher levels of SB-728-T engraftment, specifically long-lived memory T-cells, evidence of polyfunctional antiviral CD8 responses during TI and lower HIV reservoir levels prior to TI. This may provide a model mechanism of action for SB-728-T and help identify HIV-infected individuals who will benefit most from this novel immune-based therapy."

"The evidence of sustained viral load control in subjects enrolled in the 1101 study is very encouraging," said Dale Ando, M.D., Sangamo's vice president of therapeutic development and chief medical officer. "Four of nine subjects treated at Cytoxan doses of 1.0 and 1.5 g/m^2 remain on extended TI, including two of three treated subjects in Cohort 3* who were included in this analysis and have viral loads under 1,000. The data suggest that by mimicking the characteristics of the 'elite controller' HIV subpopulation it may be possible to develop a functional cure for HIV/AIDS. Based on our extensive clinical studies, we believe that we have identified both an SB-728-T manufacturing method and patient characteristics that will aid us and a future partner in the development of this therapeutic through pivotal studies."

Of the nine subjects pre-conditioned with Cytoxan doses of 1.0 and 1.5 g/m^2 (Cohorts 3, 3* and 5) six subjects demonstrated durable control of viremia (VL<10,000) during an extended TI (14-26 months duration), with two subjects showing consistent ongoing VL measurements less than 1,000 (17 and 20 months at the time of analysis). Using a univariate linear regression model, the analysis demonstrated that greater levels of engrafted CCR5-modified cells before TI ($p=0.03$) and higher frequencies of long-lived CD4 memory T-cells (TSCM) during TI ($p=0.01$) correlated with lower VLs. The data suggest that an HIV resistant, long-lived CD4 TSCM compartment is likely to be critical in establishing VL control possibly by restoring immune homeostasis and providing help to HIV-specific CD8 T-cells. Multivariate analyses were used to determine parameters that further predict VL control during TI. Results indicate that higher CD4 TSCM levels, as well as a more robust polyfunctional anti-HIV gag CD8 response during TI ($p=0.04$) were associated with reduced VL. Furthermore, the analysis demonstrated that HIV reservoir size prior to TI showed a significant interaction with CD8 response in this model ($p=0.03$). These data suggest that a smaller HIV reservoir at the beginning of the TI coupled with a strong CD8 response resulted in better VL control.

In late 2015, Sangamo enrolled five additional subjects in Cohort 3* and expects to present that data at the end of 2016. Pending the data readout for SB-728-1101 Cohort 3*, the Company intends to partner the HIV program for pivotal studies and commercialization.

Source:
Sangamo BioSciences, Inc.