Sangamo Therapeutics Logo

Sangamo BioSciences Advances ZFP Therapeutic(TM) Pipeline

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Initiation of Two New Clinical Trials and Renewed JDRF Funding

RICHMOND, Calif., Jan. 11 /PRNewswire-FirstCall/ -- Sangamo BioSciences, Inc. (Nasdaq: SGMO) announced the initiation of two new clinical trials of ZFP Therapeutics, a Phase 2b study in diabetic neuropathy (DN) and a Phase 1 trial in glioblastoma, as well as the renewal of $3.0 million in funding for the Phase 2b trial by the Juvenile Diabetes Research Foundation International (JDRF). Edward Lanphier, Sangamo's president and CEO, will provide an update on the company's ZFP Therapeutic(TM) pipeline and an overview of the company's business strategy and objectives for 2010 during his presentation at the 28th Annual J.P. Morgan Healthcare Conference at 2:30 pm PT, on Wednesday, January 13, 2010.

"We enter 2010 with a strong balance sheet and a robust clinical pipeline," said Mr. Lanphier. "With the initiation of these two new clinical trials, we continue to increase the value, maturity and visibility of our novel drug development platform."

"We are developing our lead therapeutic, SB-509, for neurological indications including DN and ALS. The data generated to date in DN, our most advanced program, provide direct histologic evidence of nerve regrowth with SB-509 treatment and a mechanistic proof of concept for its neuroregenerative effects. Our enthusiasm for the potential and importance of this drug is shared by JDRF who, after extensive review of the clinical data, has committed to fund a further $3.0 million of development costs for this new Phase 2b trial. While we continue active discussions with potential corporate partners, timely initiation of this trial enables us to maximize the future value of this program. Finally, the Phase 1 glioblastoma trial is our third ZFP Therapeutic and the second zinc finger nuclease (ZFN)-based program to enter the clinic and we are pleased to have achieved this significant milestone."

"Neuropathy is a significant complication of diabetes and represents a major unmet medical need, so developing better treatments would be a tremendous near-term benefit for people with diabetes," stated Alan Lewis, Ph.D., President and Chief Executive Officer of JDRF. "JDRF is excited to move this partnership forward, particularly as it involves a drug candidate designed to harness the body's own regenerative potential to address the nerve loss characteristic of neuropathy."

The Phase 1 glioblastoma trial will be initiated by Sangamo's collaborators at City of Hope and is designed to evaluate the safety and tolerability of a modified CD8+ cytotoxic T lymphocyte (CTL) product that has been made resistant to glucocorticoid steroids using Sangamo's ZFP nuclease ZFN-based technology. The study will accrue subjects with recurrent/refractory malignant glioblastoma multiforme (GBM). The US Food and Drug Administration (FDA) has reviewed and accepted an Investigational New Drug (IND) application to initiate this open-label, multi-dosing Phase 1 clinical trial.

"We look forward to initiating this study to evaluate a promising therapeutic approach for the treatment of malignant brain tumors for which there are currently few effective therapeutic options after surgery," said Michael C.V. Jensen, M.D., Associate Chair, Department of Cancer Immunotherapeutics and Tumor Immunology, City of Hope. "In collaboration with Sangamo, we have successfully generated engineered T-cells that can destroy glioblastoma tumor cells in animals in the presence of glucocorticoids. Treatment of recurrent GBM with modified CTLs, an otherwise promising approach for this cancer, is rendered ineffective by the use of glucocorticoids to control inflammation of the brain due to the tumor and surgery. The ZFN-modification of the glucocorticoid receptor (GR) in our engineered CTLs protects the cells from the effects of steroids, which would normally inhibit T-cell function, but does not alter their cytolytic or tumor-killing properties."

"Our significant clinical, commercial and financial progress in 2009 provides us with a solid foundation upon which to build in 2010," commented Mr. Lanphier. "In the next twelve months, we expect to have final data from two Phase 2 clinical trials of SB-509, one in severe DN (SB-509-701) and one in ALS (SB-509-801). In addition, we expect to have preliminary data from our two ongoing Phase 1 trials of our ZFN-based Therapeutic, SB-728-T for the treatment of HIV/AIDS. We look forward to advancing our clinical pipeline as well as participating in the successful commercial expansion of our ZFP technology through our partnerships in plant agriculture and in the growing area of cell line engineering and transgenic animal model production."

Detail on Phase 2b Trial (SB-509-901) in Diabetic Neuropathy

Sangamo's double blind, repeat-dosing, placebo controlled Phase 2b study, SB-509-901, is designed to finalize dose, schedule and primary and secondary endpoints for pivotal Phase 3 trials. The trial will accumulate data on approvable endpoints including Neurological Impairment Score in the Lower Limb (NIS-LL), nerve conduction velocity in the sural nerve (sNCV), as well as quality of life assessments (QOL) and intraepidermal nerve fiber density (IENFD). The study will involve a total of 150 subjects who will be randomized 1:1 between placebo and treatment groups and is powered to detect statistical significance for improvements in sNCV. Inclusion criteria for the trial are based upon accumulated data from Sangamo's earlier Phase 1 and Phase 2 clinical trials in subjects with DN.

"The body of clinical data obtained in previous trials of SB-509 has enabled us to design a very focused Phase 2b study that will accrue subjects that we believe are most likely to show a significant response to SB-509 over the 180 day test period," commented Dale Ando, Sangamo's chief medical officer and vice president of therapeutics. "The data generated to date also demonstrated that SB-509 treatment resulted in statistically significant increases in nerve fiber density, nerve regeneration and an improvement in clinical outcomes such as NIS-LL and sNCV. Information collected in our Phase 2b trial will allow us to confirm eligibility criteria and primary clinical endpoints for future Phase 3 trials."

SB-509 is an injectable plasmid encoding a DNA-binding zinc finger DNA-binding protein (ZFP) transcription factor (ZFP TF) designed to upregulate the endogenous expression of the gene encoding vascular endothelial growth factor (VEGF-A). VEGF-A has been demonstrated to have direct angiogenic, neurotrophic and neuroprotective properties. Data from Phase 1 and Phase 2 clinical trials in subjects with DN have demonstrated a direct neuroregenerative effect of SB-509 treatment that resulted in a statistically significant (p value = 0.02) increase in IENFD in subjects with DN. IENFD is a validated, direct histologic measurement of small unmyelinated sensory nerve fibers in the skin, the primary sensory nerves involved in DN. IENFD also correlates with neuropathy severity in diabetes, nerve fiber densities derived from sural nerve biopsies and levels of vascular endothelial growth factor-A (VEGF-A). In subjects with more severe neuropathy, as judged by their baseline IENFD, a greater nerve regrowth response to SB-509 treatment was observed compared to regrowth responses in placebo-treated subjects. In addition, subgroup analyses using baseline severity of disease for both neurologic and vascular disease as a selection criterion demonstrated that SB-509 treatment resulted in correlative, clinically-relevant

improvements in NIS-LL and sNCV in subjects with moderate to severe disease.

Detail on Phase 1 Trial Objective in Glioblastoma Multiforme (GBM)

The Phase 1 trial is a repeat-dosing, open-label trial of a modified CD8+ cytotoxic T lymphocyte (CTL) product that has been made resistant to glucocorticoid steroids using Sangamo's ZFP nuclease ZFN-based technology. The study is designed to assess safety and tolerability of treatment in approximately 10 subjects with recurrent or refractory malignant GBM. In addition, data will be collected on the survival of the infused, modified CTLs as well as tumor response and survival. The trial will be conducted exclusively at City of Hope.

About Diabetic Neuropathy

Diabetic neuropathy is a progressive degenerative disease that is one of the most frequent complications of diabetes, affecting between 14 and 16.5 million Americans in 2007. High blood glucose levels lead to nerve damage over time, primarily affecting peripheral nerves. Symptoms include numbness, tingling sensations and pain particularly in the toes or feet, which gradually evolve to loss of sensation and motor function as nerve damage progresses. Ulcers and sores may appear on numb areas of the foot as pressure wounds or injuries go unnoticed. Despite palliative treatment, these areas of trauma frequently become infected and this infection may spread to the bone, necessitating amputation of the leg or foot. More than 60 percent of non-traumatic lower-limb amputations in the United States occur among people with diabetes. In 2004, this translated to approximately 71,000 amputations. The Centers for Disease Control estimates that from 1980 through 2007, the number of Americans with diabetes increased from 5.6 million to 23.6 million and that of those about 60 percent to 70 percent have mild to severe forms of neuropathy.

About Glioblastoma Multiforme (GBM)

An estimated 40,000 tumors are diagnosed each year; about 22,000 of these will be malignant. Of these primary brain tumors, gliomas are the most common type, approximately 20,000 cases are diagnosed and 13,000 glioma-related deaths occur annually in the US. Glioblastoma multiforme (GBM), a type of glioma, is rapidly progressive and nearly uniformly lethal. Currently, malignant glioma is managed through a combination of chemotherapy, surgery and radiation if the location and size of tumor allow these treatments. With modern combination therapy, the mean duration of survival has increased to 82 weeks, although 5-year survival rates have only increased from 3% to 6%. Approximately 80% of recurrent tumors arise from remnants of the original incompletely resected tumor. The median survival of recurrent glioblastoma multiforme patients that are eligible to be treated with re-resection is 36 weeks. Due to the location of these tumors in the central nervous system, current treatments often exacerbate the already severe morbidities. Immunotherapeutic strategies, such as anti-VEGF and chimaeric T cell receptors, are increasingly being used since they are very tumor specific and limit side effects in the recurrent disease setting.

About Sangamo

Sangamo BioSciences, Inc. is focused on the research and development of novel DNA-binding proteins for therapeutic gene regulation and modification. The most advanced ZFP Therapeutic(TM) development program is currently in Phase 2 clinical trials for evaluation of safety and clinical effect in patients with diabetic neuropathy and ALS. Sangamo also has two Phase 1 clinical trials to evaluate safety and clinical effect of a ZFP Therapeutic for the treatment of HIV/AIDS. Other therapeutic development programs are focused on cancer, neuropathic pain, nerve regeneration, Parkinson's disease and monogenic diseases. Sangamo's core competencies enable the engineering of a class of DNA-binding proteins known as zinc finger DNA-binding proteins (ZFPs). By engineering ZFPs that recognize a specific DNA sequence Sangamo has created ZFP transcription factors (ZFP TF) that can control gene expression and, consequently, cell function. Sangamo is also developing sequence-specific ZFP Nucleases (ZFN) for gene modification. Sangamo 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 web site at http://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 to clinical trials of ZFP Therapeutics in diabetic neuropathy and glioblastoma, the research and development of novel ZFP TFs and ZFNs as ZFP Therapeutics, applications of Sangamo's ZFP technology platform to specific human disease as well as plant agriculture, high value research reagents and cell-line engineering, establishing strategic partnerships for SB-509 and other therapeutic programs. Actual results may differ materially from these forward-looking statements due to a number of factors, including technological challenges, uncertainties relating to the initiation, completion and outcome of stages of ZFP Therapeutic clinical trials, Sangamo's ability to develop commercially viable products and technological developments by our competitors. See Sangamo's SEC filings, and in particular, the risk factors described in Sangamo's Annual Report on Form 10-K and most recent Quarterly Reports on Form 10-Q. Sangamo BioSciences, Inc. assumes no obligation to update the forward-looking information contained in this press release.

SOURCE Sangamo BioSciences, Inc.

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