



Sangamo BioSciences Presents Positive Phase 2 ZFP Therapeutic Data From SB-509 Programs in Diabetic Neuropathy at ADA 2010

Histologic and Serologic Data Confirm Mechanism of Action of SB-509. Data Further Support Criteria for Subject Inclusion in Ongoing Phase 2b Study

RICHMOND, Calif., June 29, 2010 /PRNewswire via COMTEX News Network/ -- Sangamo BioSciences, Inc. (Nasdaq: SGMO) announced positive Phase 2 clinical data from its ZFP Therapeutic(TM) program to develop SB-509 as a treatment for diabetic neuropathy (DN) at the 70th Annual Scientific Sessions of the American Diabetes Association (ADA), held in Orlando, FL from June 25-29, 2010. Data from Sangamo's SB-509-601 and SB-509-701B Phase 2 clinical trials demonstrated that SB-509 treatment resulted in clinically beneficial improvements in subjects with moderate and severe DN as compared to placebo. The data, which were described in three oral presentations, provided direct histological evidence of SB-509's dual effect on both blood vessel and nerve growth and validated the strategy of the use of multi-endpoint disease severity criteria that have been established for enrollment into the company's ongoing Phase 2b trial in subjects with moderately severe DN.

"We have gained valuable information from our SB-509-601 and 701 Phase 2 trials whose data directly demonstrate an angiogenic role for SB-509, consistent with preclinical data, and confirm our rationale and confidence in the design of our ongoing Phase 2b trial (SB-509-901)," stated Dale Ando, M.D., Sangamo's vice president of therapeutic development and CMO. "Targeting subjects with moderately severe DN, which we believe will show the greatest benefit from the dual angiogenic and neurologic effect of SB-509 and give us the greatest response in a clinical trial, is important for the development of this disease-modifying drug. The data provided by our 701B trial demonstrate the complex character of DN and support the importance of using multiple endpoints for monitoring disease progression and for excluding subjects with mild disease severity from our Phase 2b trial."

Two presentations focused on data from Sangamo's Phase 2 trial (SB-509-601) in subjects with mild to moderate DN. The first, presented by Sangamo's collaborators at the Johns Hopkins University School of Medicine, demonstrated that treatment with SB-509 improved regrowth of epidermal nerve fibers (ENF) in subjects undergoing a standardized injury (p-value = 0.02), and increased blood vessel growth into a healing biopsy site. The timing of these effects demonstrated that the therapeutic benefit of treatment was sustained several months after the last dose was administered. The second presentation described an analysis of sVCAM-1 and sICAM-1, serum biomarkers of blood vessel damage and inflammatory diseases such as Type II diabetes, in SB-509- and placebo-treated subjects with DN. The results, which reinforce the design of Sangamo's ongoing Phase 2b trial, demonstrate that elevated sICAM-1 levels may aid in the upfront identification of a target population of SB-509-responsive subjects and serve as a stratification variable to enable balancing of severity of vascular disease in treatment and placebo groups. In addition, a statistically significant top line decrease in sVCAM-1 was seen in the SB-509 treated group (p-value = 0.03) compared to placebo (p-value = 0.33).

"These data provide histologic and serologic evidence for a positive effect of SB-509 on blood vessel growth or angiogenesis in addition to the direct neurologic effect previously described," stated Phillip Low, M.D., Professor of Neurology at the Mayo Clinic. "Diabetes causes metabolic defects that result in both blood vessel and nerve damage and lead to DN. SB-509's unique mechanism of activating the endogenous VEGF-A gene provides a dual therapeutic activity that is designed to be disease modifying."

The third presentation was of data from Sangamo's Phase 2 SB-509-701B study which focused on subjects with at least one unmeasurable nerve conduction velocity (NCV). Subjects were administered SB-509 or placebo at 0, 60 and 120 Days. Surprisingly, some subjects that met the conduction velocity criteria had relatively mild DN as measured by a Lower Extremity Neurologic Sensory Examination (LENSE). However, when subjects with clear sensory deficits were evaluated (i.e. LENSE score of greater than 10) there was a substantial benefit in the mean change in sural NCV (sNCV) from baseline at the 180 Day time point (+1.42 m/sec in the treated group; -1.14 m/sec in the placebo group, p-value = 0.07). This improvement in sNCV was strongly correlated with the sensory examination when stratified by loss of sensation to pin prick testing at various points from the toe to above the knee. The LENSE >10 group also showed a significant response to SB-509 treatment (39% response, 9/23 SB-509-treated subjects vs. 0% response, 0 out of 7 placebo-treated subjects, p-value= 0.07) as judged by recovery of an unmeasurable sNCV with a positive measurement at Day 180.

"This study is the first of its kind in subjects with this degree of nerve damage," stated Joseph Arezzo, Ph.D., Professor, Department of Neuroscience, Albert Einstein School of Medicine and Sangamo's collaborator. "Previously, subjects with an unmeasurable nerve conduction velocity would not have been entered into such trials; this is a unique data set, examining change in sNCV and in distal sensory function in subjects with objective evidence of relatively severe nerve damage. Both

measures are standard neurologic tests in DN and have been previously used as approvable end-points in Phase 3 trials. These data emphasize the importance of using multiple endpoints for assessment of DN disease severity, for both subject enrollment and evaluation of treatment. In this study, improvements in NCV were observed in those subjects treated with SB-509 who entered the study with a deficit in sensory function, not just an unmeasurable nerve."

SANGAMO PRESENTATIONS AT ADA

Summary of Oral Presentations of Data from Sangamo's SB-509-601 Study

(Abst# 346-OR): *"VEGF-A transcription Factor (SB-509) Enhances Epidermal Nerve Fiber and Blood Vessel Regeneration" presented on Monday, June 28 at 4:45pm ET.*

Epidermal Nerve Fiber Density (ENFD) and ENF Regrowth (ENFR), or regenerative sprouting, were prospectively defined endpoints in Sangamo's double-blind, repeat dosing Phase 2 clinical study (SB-509-601) in which subjects were treated at 0, 60 and 120 Days. ENFD derived from 3mm skin punch biopsies taken from the thigh at baseline (Day 0), 30 days after the final treatment (Day 150) and through Day 360 were obtained from both SB-509 and placebo treated subjects. ENFR was determined by applying a capsaicin patch to the skin of the thigh to produce a standardized nerve injury on Days 150 and 151 and using serial skin biopsies over time, post capsaicin treatment, up to Day 360, to determine nerve regrowth in both SB-509 and placebo-treated subjects. In addition a second injury model, an excision model, was used in which collateral sprouting of ENF and blood vessel growth were measured in a concentric 4mm biopsy taken over a healed 3mm biopsy site 30 days after the first biopsy.

SB-509-treated subjects had a higher ENFD at both 60 days (6.7 fibers/mm vs. 3.2 fibers/mm) and 210 days (11.1 fibers /mm vs. 8.7 fibers/mm, p-value = 0.02) following denervation using capsaicin. Similar trends of a treatment effect were observed for blood vessel growth as well as the rate of ENFR. No correlation was observed between blood vessel growth and ENFR.

This work was carried out in collaboration with Michael Polydefkis, M.D., Associate Professor of Neurology, the Johns Hopkins University School of Medicine, and was funded in part by the Juvenile Diabetes Research Foundation (JDRF).

(Abst# 351-OR): *"Serum sICAM Levels in Patients with Mild to Moderate Diabetic Peripheral Neuropathy Can Help Identify Response to SB-509 Treatment" presented on Monday, June 28 at 6:00 pm ET.*

Increased serum levels of sICAM-1 and sVCAM-1 have been shown to correlate with progression of endothelial damage and inflammatory diseases including Type II diabetes. The serum concentrations of sICAM-1 and sVCAM-1 were measured in 110 subjects with mild to moderate DN enrolled in the SB-509-601 placebo-controlled study of SB-509 treatment in patients with DN and 49 normal control subjects by ELISA (enzyme-linked immunosorbent assay). Mean baseline serum concentrations of sICAM-1 in patients with DN and control subjects were 230.6+/-87.5 and 257.7+/-100.0 ng/mL, respectively (p-value = 0.1094). In contrast, the mean baseline serum concentrations of sVCAM-1 in the 601 group and control subjects were 829.1+/-246.8 and 717.6+/-224.3 ng/mL, respectively (p-value= 0.008), indicating that sVCAM-1, but not sICAM-1, is significantly elevated in DN patients at baseline compared to normal controls. In addition, a statistically significant top line comparison decrease in vascular damage at Day 360 as measured by sVCAM-1 was seen in the SB-509 treated groups (p-value = 0.03) compared to placebo (p-value = 0.33).

A subsequent analysis showed a correlation between baseline sICAM-1 levels above 200 ng/mL and improvement in sNCV at Day 180 (2.2 m/sec, p-value = 0.04) and Day 360 (3.96 m/sec; p-value = 0.013) in subjects treated with SB-509, but not in the placebo-treated subjects. No correlation was observed between baseline sVCAM-1 levels and improvement in sNCV. These data suggest that baseline sICAM-1 levels correlated with an improvement in sNCV in DN subjects treated with SB-509, potentially identifying an SB-509 responsive population. Our data suggest that serum sICAM-1 levels may represent an easily measured biomarker to aid in identification of a target population of SB-509 responsive DN patients and as a stratification variable to ensure that we have well-balanced treatment and placebo groups. Serum sVCAM-1 levels decreased with SB-509 treatment compared to control patients and may represent a novel marker for evaluating pro-angiogenic activity of SB-509 in patients.

Summary of Oral Presentation of Data from Sangamo's SB-509-701-B Study

(Abst# 348-OR): *"Vascular Endothelial Growth Factor-A (VEGF-A) Zinc Finger Protein Activator (SB-509) reverses Loss of Nerve Potentials in Severe Diabetic Peripheral Neuropathy (DPN). Interim Phase 2 Results (SB-509-0701B Study)" presented on Monday, June 28 at 5:15 pm ET.*

A Phase 2 clinical trial (SB-509-0701-B) was undertaken in subjects with an unmeasurable NCV in at least one of six nerves assayed. Thirty subjects were treated intramuscularly in the lower extremities with 60 mgs of SB-509 and 15 with placebo at Days 0 and 60 and 120. Subjects were also tested for sensory deficit using standard neurologic testing and these measures were followed in all subjects over a period of 360 days with the primary assay point at Day 180. Surprisingly, it was determined that some subjects with unmeasurable nerves had almost normal sensory function even when assessed using the standard

clinical neurologic sensory examination LENSE (Lower Extremity Neurologic Sensory Exam) which includes assessments of pin prick, pressure and vibration at six points from the big toe to above the knee. SB-509-treated subjects with LENSE scores greater than 10 showed an improvement in change of mean NCV from baseline of 1.42 m/sec while placebo-treated subjects showed a mean reduction in NCV of 1.14 m/sec, (p-value = 0.07). In addition, data demonstrated that baseline pin prick examination was the best predictor of sural nerve conduction velocity (sNCV) improvement in SB-509 treated subjects, subjects with least sensitivity to pin prick (high LENSE scores) showing greatest improvement. A responder analysis of subjects who entered the trial with LENSE scores greater than 10 for whom an unmeasurable nerve at Day 0 had recovered at Day 180 showed that 39% (9 of 23) of SB-509 treated subjects responded compared to 0% (0 of 7) of placebo treated subjects. However, when the responder analysis was expanded to include subjects who had recovered an NCV reading and demonstrated an improvement in NCV of at least 7 m/sec at Day 180, no difference was observed between placebo and treated groups.

About SB-509

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. In preclinical animal efficacy studies in a diabetic rat model (*Diabetes*, June 1, 2006; 55(6): 1847-1854), SB-509 has proven effective in protecting motor and sural nerve function from disease-induced nerve damage. The drug has been tested in several repeat dosing Phase 2 clinical trials and has an excellent safety profile to date. Visit <http://www.clinicaltrials.gov> for further information about Sangamo's clinical trial of this drug.

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. Diabetes is a growing problem. 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 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 a Phase 2b clinical trial for evaluation of safety and clinical effect in patients with diabetic neuropathy and a Phase 2 trial in ALS. Sangamo also has two Phase 1 clinical trials to evaluate safety and clinical effect of a treatment for recurrent glioblastoma multiforme. Other therapeutic development programs are focused on 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 website 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 the clinical trials of SB-509, research and development of novel ZFP TFs and ZFNs and therapeutic applications of Sangamo's ZFP technology platform, including the treatment of diabetic neuropathy. 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 the SB-509 clinical trials, whether the SB-509 clinical trials will validate and support tolerability and efficacy of SB-509, technological challenges, 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 the its Annual Report on Form 10-K and most recent Quarterly Report on Form 10-Q. Sangamo assumes no obligation to update the forward-looking information contained in this press release.

SOURCE Sangamo BioSciences, Inc.

Copyright (C) 2010 PR Newswire. All rights reserved