SANGAMO BIOSCIENCES INC
Form 10-K
March 03, 2009
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

þ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2008

or

¨ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the transition period from to

Commission file number: 0-30171

SANGAMO BIOSCIENCES, INC.

(Exact name of registrant as specified in its charter)

Delaware	**68-0359556**
(State or other jurisdiction of incorporation or organization)	***(I.R.S. Employer Identification No.)***
501 Canal Boulevard, Suite A100 Richmond, California	**94804**
(Address of principal executive offices)	***(Zip Code)***

(510) 970-6000

(Registrant s telephone number, including area code)

None

(Former name, former address and former fiscal year, if changed since last report)

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	Name of Each Exchange on Which Registered
Common Stock, $0.01 par value per share	Nasdaq Global Market

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ¨ No þ

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. Yes ¨ No þ

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes þ No ¨

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. þ

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See definition of large accelerated filer, accelerated filer, and smaller reporting company in Rule 12b-2 of the Exchange Act.

Large accelerated filer ¨ Accelerated filer þ Non-accelerated filer ¨ Smaller reporting company ¨

(Do not check if a smaller reporting company)

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ¨ No þ

The aggregate market value of the voting stock held by non-affiliates of the registrant based upon the closing sale price of the common stock on June 30, 2008 (the last business day of the registrant s most recently completed second fiscal quarter), as reported on the Nasdaq Global Market was $365,661,037. For purposes of this calculation, directors and executive officers of the registrant have been deemed affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

Indicate the number of shares outstanding of each of the issuer s classes of common stock, as of the latest practicable date.

Class	Outstanding at February 1, 2009
Common Stock, $0.01 par value per share	41,066,389 shares

DOCUMENTS INCORPORATED BY REFERENCE

Document	Parts Into Which Incorporated
Proxy Statement for the 2009 Annual Meeting of Stockholders	Part III

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Some statements contained in this report are forward-looking with respect to our operations, research and development activities, operating results and financial condition. Statements that are forward-looking in nature should be read with caution because they involve risks and uncertainties, which are included, for example, in specific and general discussions about:

- our strategy;
- product development and commercialization of our products;
- clinical trials;
- revenues from existing and new collaborations;
- our research and development and other expenses;
- sufficiency of our cash resources;
- our operational and legal risks; and
- our plans, objectives, expectations and intentions and any other statements that are not historical facts.

Various terms and expressions similar to them are intended to identify these cautionary statements. These terms include: anticipates, believes, continues, could, estimates, expects, intends, may, plans, seeks, should and will. Actual results may differ materially from tho implied in those statements. Factors that could cause these differences include, but are not limited to, those discussed under Risk Factors and Management s Discussion and Analysis of Financial Condition and Results of Operations. Sangamo undertakes no obligation to publicly release any revisions to forward-looking statements to reflect events or circumstances arising after the date of this report. Readers are cautioned not to place undue reliance on the forward-looking statements, which speak only as of the date of this Annual Report on Form 10-K.

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PART I

ITEM 1 BUSINESS

Overview

We are the leader in the research, development and commercialization of zinc finger DNA-binding proteins (ZFPs), a naturally occurring class of proteins, and have used our knowledge and expertise to develop a proprietary technology platform. ZFPs can be engineered (see Fig. 1) to make ZFP transcription factors (ZFP TFs™), proteins that can be used to turn genes on or off, and ZFP nucleases (ZFNs™), proteins that enable us to modify DNA sequences in a variety of ways. As ZFPs act at the DNA level, they have broad potential applications in several areas including human therapeutics, plant agriculture, research reagents and cell-line engineering.

The main focus for our company is the development of novel human therapeutics and we are building a pipeline of ZFP Therapeutics™. Our lead ZFP Therapeutic, SB-509, a plasmid formulation of a ZFP TF activator of the vascular endothelial growth factor-A (VEGF-A) gene, is under evaluation in three Phase 2 clinical trials for the treatment of diabetic neuropathy (DN) and one Phase 2 trial for amyotrophic lateral sclerosis (ALS). We expect to have additional data from our Phase 2 trials in DN in 2009 and to complete enrollment and treatment in our Phase 2 study for ALS in 2009.

In 2008 we filed an Investigational New Drug (IND) application with the Food and Drug Administration (FDA) and have initiated a Phase 1 clinical trial to evaluate SB-728-T for the treatment of HIV/AIDS. SB-728-T represents the first therapeutic application of our ZFN technology. In 2009 we also expect to file an IND application for a Phase 1 trial to evaluate a ZFN-based therapeutic for the treatment of glioblastoma multiforme, a type of brain cancer.

We have preclinical development programs of ZFP Therapeutics in spinal cord injury, stroke, traumatic brain injury, neuropathic pain, and Parkinson s disease. We have additional research-stage programs in X-linked severe combined immunodeficiency (X-linked SCID), hemophilia and hemoglobinopathies.

We believe the potential commercial applications of ZFPs are broad-based and we have capitalized on our ZFP platform by facilitating the sale or licensing of ZFP TFs or ZFNs to companies working in fields outside human therapeutics.

We have a license agreement with Dow AgroSciences, LLC (DAS), a wholly owned indirect subsidiary of Dow Chemical Corporation. Under the agreement, Sangamo is providing DAS with access to Sangamo s ZFP technology and the exclusive right to use it to modify the genomes or alter the nucleic acid or protein expression of plant cells, plants, or plant cell cultures. DAS plans to market ZFP-derived plant products under the trademark EXZACT™ Precision Technology. We have retained rights to use plants or plant-derived products to deliver ZFP TFs or ZFNs into human or animals for diagnostic, therapeutic, or prophylactic purposes.

We have a license agreement with the research reagent company Sigma-Aldrich Corporation (Sigma). Sigma has the exclusive right to develop and market high value laboratory research reagents based upon Sangamo s ZFP technology. Sigma is marketing ZFN-derived gene editing tools under the trademark CompoZr™.

We also have license agreements with life sciences companies including Pfizer Inc, (Pfizer), Genentech Inc. (Genentech), Medarex, Inc., and research agreements with Amgen Inc., Novo Nordisk Inc., Novartis A/G, and Kirin Brewery Company. Under these agreements, we are providing access to Sangamo s proprietary ZFP technology to generate cell lines with novel characteristics for protein pharmaceutical production.

We have a substantial intellectual property position in the design, selection, composition, and use of engineered ZFPs to support all of these commercial activities. As of February 6, 2009, we either own outright or

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have exclusively licensed the commercial rights to approximately 243 patents issued in the United States and foreign national jurisdictions, and we have 244 patent applications owned and licensed pending worldwide. We continue to license and file new patent applications that strengthen our core and accessory patent portfolio. We believe that our proprietary position will protect our ability to research, develop, and commercialize products and services based on ZFP technology across our chosen applications.

DNA, Genes, and Transcription Factors

DNA is present in all cells except mature red blood cells, and encodes the inherited characteristics of all living organisms. A cell s DNA is organized in chromosomes as thousands of individual units called genes. Genes encode proteins, which are assembled through the process of transcription whereby DNA is transcribed into ribonucleic acid (RNA) and, subsequently, translation whereby RNA is translated into protein. DNA, RNA, and proteins comprise many of the targets for pharmaceutical drug discovery and therapeutic intervention at the molecular level.

The human body is composed of specialized cells that perform different functions and are thus organized into tissues and organs. All somatic cells in an individual s body contain the same set of genes. However, only a fraction of these genes are turned on, or expressed, in an individual human cell at any given time. Genes are regulated, i.e. turned on or turned off, in response to a wide variety of stimuli and developmental signals. Distinct sets of genes are expressed in different cell types. It is this pattern of gene expression that determines the structure, biological function, and health of all cells, tissues, and organisms. The aberrant expression of certain genes can lead to disease.

Transcription factors are proteins that bind to DNA and regulate gene expression. A transcription factor recognizes and binds to a specific DNA sequence within or near a particular gene and causes expression of that gene to be turned on (activated) or turned off (repressed). In higher organisms, transcription factors typically comprise two principal domains: the first is a DNA-binding domain, which recognizes a target DNA sequence and thereby directs the transcription factor to the proper chromosomal location; the second is a functional domain that causes the target gene to be activated or repressed (see Figure 1).

Figure 1

The Two Domain Structure of a ZFP Therapeutic

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Engineered Zinc Finger Protein Transcription Factors (ZFP TFs) for Gene Regulation and Engineered ZFP Nucleases (ZFNs) for Gene Modification

Zinc finger DNA-binding proteins or ZFPs are the largest class of naturally occurring transcription factors in organisms from yeast to man. Consistent with the two-domain structure of natural ZFP transcription factors, we take a modular approach to the design of the proteins that we engineer. The ZFP portion, the DNA-recognition domain, is typically composed of three or more zinc fingers. Each individual finger recognizes and binds to a three base pair sequence of DNA and multiple fingers can be linked together to recognize longer stretches of DNA, thereby improving specificity. By modifying the amino acids of a ZFP that directly interact with DNA, we can engineer novel ZFPs capable of recognizing pre-selected DNA sequences within, or near, virtually any gene.

We use the engineered ZFP DNA-binding domain linked to a functional domain. The ZFP DNA-binding domain brings the functional domain into the proximity of the gene of interest. Thus, Sangamo s scientists can create a ZFP TF which is capable of controlling or regulating a target gene in the desired manner. For instance, attaching an activation domain to a ZFP will cause a target gene to be turned on. Alternatively, a repression domain causes the gene to be turned off. Our lead ZFP Therapeutic SB-509 is designed to turn a gene on. SB-509 is a ZFP TF activator of the VEGF-A gene. VEGF-A has been shown to have angiogenic properties, i.e. to promote the growth of blood vessels, and to have a protective and regenerative effect on nerve tissue. We are testing this ZFP TF in Phase 2 clinical trials in subjects with DN and ALS, and we have preclinical programs in stroke, spinal cord injury and traumatic brain injury. We are also developing ZFP TFs that turn gene expression off. We have programs in neuropathic pain focused on the repression of pain receptors, Trk-A and PN3, and these ZFP TFs are in preclinical testing.

Our engineered ZFPs can also be attached to the cleavage domain of a restriction endonuclease, an enzyme that cuts DNA, creating a zinc finger nuclease or ZFN. The ZFN is able to recognize its intended gene target through its engineered ZFP DNA-binding domain (Figure 1). When a pair of ZFNs is bound to the DNA in the correct orientation and spacing, the DNA sequence is cut between the ZFP binding sites. DNA binding by both ZFNs is necessary for cleavage. This break in the DNA triggers a natural process of DNA repair in the cell. The repair process can be harnessed to achieve one of several outcomes that may be therapeutically useful. If cells are simply treated with ZFNs alone the repair process frequently results in joining together of the two ends of the broken DNA and the consequent loss of a small amount of genetic material that results in disruption of the original DNA sequence. This can result in the generation of a shortened or non-functional protein, i.e. gene disruption. We believe that ZFN-mediated gene modification may be used to disrupt a gene that is involved in disease pathology such as disruption of the CCR5 gene to treat HIV infection or the disruption of the glucocorticoid receptor gene to make engineered killer T-cells resistant to glucocorticoids as in our glioblastoma program. In contrast, if cells are treated with ZFNs in the presence of an additional donor DNA sequence that encodes the correct gene sequence, the cell can use the donor as a template to correct the cell s gene as it repairs the break resulting in ZFN-mediated gene correction. ZFN-mediated gene correction enables a corrected gene to be expressed in its natural chromosomal context and may provide a novel approach for the precise repair of DNA sequence mutations responsible for monogenic diseases such as sickle cell anemia and X-linked severe combined immunodeficiency (X-linked SCID). In addition, by making the donor sequence a gene-sized segment of DNA, a new copy of a gene can also be added into the genome at a specific location. The ability to place a gene-sized segment of DNA specifically into a pre-determined location in the genome eliminates the insertional mutagenesis concerns associated with traditional gene replacement approaches.

To date, we have designed, engineered, and assembled several thousand ZFPs and have tested many of these proteins for their affinity, or tightness of binding to their DNA target as well as their specificity, or preference for their intended DNA target. We have developed methods for the design, selection, and assembly of ZFPs capable of binding to a wide spectrum of DNA sequences and genes. We have linked ZFPs to numerous functional domains to create gene-specific ZFP TFs and have demonstrated the ability of these ZFP TFs to regulate hundreds of genes in dozens of different cell types and directly in whole organisms, including mice, rats, rabbits,

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pigs, fruit flies, worms, zebrafish and yeast, and in plant species including canola and maize. Sangamo scientists and collaborators have published data in peer-reviewed scientific journals on the transcriptional function of ZFP TFs, successful gene modification using ZFNs and the resulting changes in the behavior of the target cell, tissue, or organism. We have also administered plasmid encoding our VEGF-A activating transcription factor to humans as part of our clinical trials. We are currently evaluating the efficacy of both ZFP TFs and ZFNs in man.

ZFP Therapeutics Provide the Opportunity to Develop a New Class of Human Therapeutics

With our ability to deliver gene-specific ZFP TFs for the activation or repression of genes and ZFNs for the correction, disruption or addition of target genes and DNA sequences, we are focused on developing a new class of highly differentiated human therapeutics and believe that as more genes are validated as high-value therapeutic targets, the clinical breadth and scope of our ZFP Therapeutic applications may be substantial.

We believe that ZFP Therapeutics provide a unique and proprietary approach to drug design and may have competitive advantages over small-molecule drugs, protein pharmaceuticals and RNA-based approaches.

For example, ZFP Therapeutics can:

Potentially be used to treat a broad range of diseases. ZFP Therapeutics act at the DNA level to regulate or modify gene expression. We believe that we can generate ZFPs to recognize virtually any gene target allowing direct modulation of the gene and enabling a potentially broad applicability.

Target non-druggable targets. ZFP TFs and ZFNs act through a mechanism that is unique among biological drugs: direct regulation or modification of the disease-related or therapeutic gene as opposed to the RNA or protein target encoded by that gene. Following the genomics revolution of the 1990s, the sequencing and publication of the human genome, and the industrialization of genomics-based drug discovery, pharmaceutical and biotechnology companies have validated and characterized many new drug targets. Many of these targets have a clear role in disease processes but cannot be bound or modulated for therapeutic purposes by small molecules. Alternative therapeutic approaches may be required to modulate the biological activity of these so-called non-druggable targets. This may create a significant clinical and commercial opportunity for the therapeutic regulation or modification of disease-associated genes using engineered ZFP TFs or ZFNs. Thus, a target which may be intractable to treatment using a small molecule or monoclonal antibody can be turned on, turned off or modified at the DNA level using ZFP technology.

Provide novel activities such as activation of gene expression and gene modification to address drug targets. Engineered ZFP TFs enable not just the repression of a therapeutically relevant gene but its activation, and ZFNs enable the disruption, correction or targeted addition of a gene sequence. This gives the technology a degree of flexibility not seen in other drug platforms. Activation of gene expression and direct modification of genes are not functions that can be achieved using antisense RNA, or siRNA, which act by interfering with the expression of cellular RNA, or conventional small molecules, antibodies, or other protein pharmaceuticals that primarily act to block or antagonize the action of a protein.

Provide high specificity and selectivity for targets. ZFP Therapeutics can be designed to act with high specificity and we have published such data (*Proc. Natl. Acad. Sci (2003) vol:100, p11997-12002*). In addition, there are generally only two targets per cell for a ZFP Therapeutic which means that ZFP TFs and ZFNs need to be available in the cell in very low concentrations. In contrast, drugs that act on protein and RNA targets that are naturally present in higher cellular concentrations need to be administered in higher concentrations. Many small molecule and RNA-based approaches either affect multiple targets demonstrating so-called off-target effects or are toxic in the concentrations required to be therapeutically effective.

Be used transiently to obtain a permanent therapeutic effect. Permanent gene disruption, correction or addition requires only brief cellular expression of ZFNs.

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THERAPEUTIC PRODUCT DEVELOPMENT

ZFP Therapeutic Product Development Programs

Our lead therapeutic development programs are based on the development of a ZFP TF that has been engineered to activate a patient s own vascular endothelial growth factor-A (VEGF-A) gene. VEGF-A has been demonstrated to have both angiogenic and direct neuroproliferative, neuroregenerative and neuroprotective properties. The VEGF-A gene encodes multiple forms (isoforms) of the VEGF-A protein which exhibit slightly different properties and bind to different VEGF-A receptors. It is believed that all of these isoforms are required to be present in specific ratios to achieve a full biological effect. We believe that this differentiates Sangamo s approach. We are developing formulations of this VEGF-activating ZFP TF, also called SB-509, for the following conditions: diabetic neuropathy and ALS (see Table 1) and are evaluating the ZFP Therapeutic in several ongoing clinical trials. We are also evaluating the VEGF ZFP TF in preclinical animal studies in spinal cord injury, traumatic brain injury and stroke.

Product Candidate	Targeted Indication	Stage of Development	Protocol	Milestones
SB-509	Diabetic Neuropathy: mild to moderate	Phase 1	SB-509-401	Completed.
	Diabetic Neuropathy: mild to moderate	Phase 2	SB-509-601	Subject enrollment complete. No differences between SB-509 and placebo treated subjects were observed in the top line data. Further analysis ongoing, data in 2009.
	Diabetic Neuropathy: moderate to severe	Phase 2	SB-509-701A and B	Enrollment of first treatment group completed (Part A). Trial expanded to include second treatment group (Part B). Expect to present data from Part A and complete enrollment of Part B in 2009.
	Stem cell mobilization: mild to moderate DN	Phase 2	SB-509-703	Enrollment completed. Expect to present data in 2009.
	Amyotrophic Lateral Sclerosis	Phase 2	SB-509-801	Study initiated in 2008. Expect to complete enrollment and treatment in 2009.

Table 1: Summary of current clinical programs evaluating Sangamo s ZFP TF activator of VEGF-A, SB-509.

Diabetic Neuropathy (DN)

Market Opportunity

Diabetic peripheral sensory and motor neuropathy is one of the most frequent complications of diabetes. Symptoms include numbness, tingling sensations and pain particularly in the toes or feet which may evolve into loss of sensation and motor function as nerve damage progresses. Ulcers and sores may appear on numb areas of the foot or leg because pressure or injury goes unnoticed. Despite adequate treatment, these areas of trauma frequently become infected and this infection may spread to the bone, necessitating amputation of the leg or foot. The rate of amputation for people with diabetes is ten times higher than that for non-diabetics and more than 60%

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of non-traumatic lower-limb amputations in the United States occur among people with diabetes. In 2004, this translated to approximately 71,000 non-traumatic lower limb 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 of those about 60 percent to 70 percent have mild to severe forms of neuropathy.

Current Treatments

Apart from rigorous control of blood glucose, the only therapies approved by the FDA for the treatment of DN are analgesics and antidepressants such as Lyrica® (pregabalin) and Cymbalta® (duloxetine hydrochloride) that address the symptoms of pain but do not retard or reverse the progression of the disease.

Sangamo s Therapeutic Approach

Sangamo is developing SB-509, an injectable formulation of plasmid DNA that encodes a ZFP TF, designed to up-regulate the patient s own VEGF-A gene in an effort to address the underlying nerve damage caused by DN. Human clinical studies have demonstrated that VEGF expression is reduced in diabetic patients with neuropathy and that the more severe the symptoms the greater the reduction in VEGF-A expression (*Diabetes Care (2008) Vol: 31 p140-145*). We have completed preclinical studies of VEGF-A activation using our ZFP Therapeutic, SB-509, in animal models of DN and demonstrated that single and repeat intramuscular injections of SB-509 in rats with diabetes resulted in protection of nerve function in the treated limb as measured by sensory and motor nerve conduction velocities (*Diabetes (2006) Vol:55 p1847-1854*).

In January 2005, we filed an IND application with the FDA for SB-509 for the treatment of mild to moderate diabetic neuropathy. We completed enrollment and treatment of a Phase 1a, single blind, dose-escalation trial to measure the laboratory and clinical safety of SB-509 in human subjects and extended this study to a larger Phase 1b study (SB-509-401). Data from our Phase 1 trial demonstrated that a single treatment of SB-509 was well-tolerated and that no drug-related severe adverse events (SAEs) were observed. Moreover, data from the Phase 1b clinical trial presented at the American Diabetes Association Meeting in June 2008 demonstrate improvements in measures of nerve health. We observed a statistically significant improvement in quantitative sensory testing and nerve examination (NIS-LL) and clinically relevant trends toward improvement in nerve conduction velocity measurements in subjects with mild to moderate diabetic neuropathy over a six month period after a single administration of SB-509.

We initiated a double-blind, placebo-controlled, repeat-dosing multi-center Phase 2 clinical trial of SB-509 (SB-509-601) in November 2006 having entered into an agreement with Juvenile Diabetes Research Foundation International (JDRF) in October 2006 to provide up to $3.0 million in funding to support this trial. We completed enrollment of subjects into this trial in December 2007 and in November 2008 presented top-line data from this study. The data demonstrate that repeat administration of the drug is well tolerated in subjects with mild to moderate DN. However, no significant differences were observed between the SB-509 and placebo treated subjects in a number of measures of nerve function and health at the primary analysis point, day 180 post-treatment. We are continuing to analyze these data and expect to present a more complete data set at a suitable medical or scientific meeting in 2009.

In April 2007, we initiated a second repeat-dosing placebo-controlled Phase 2 clinical study (SB-509-701) to evaluate SB-509 in subjects with moderate to severe DN. In June 2008 we expanded this trial to include an additional cohort of subjects (group B) treated with a different dosing schedule. We presented an interim analysis of data from the first group (A) in October 2008. The data demonstrated that the drug was well tolerated in a repeat dosing setting in this population and among subjects who entered the trial with blocked sural nerves, we observed preferential recovery of NCV in SB-509-treated subjects compared with the placebo-treated group during 180 days post treatment in subjects who entered the trial with blocked sural nerves. We expect to have further data from this single-blind trial in 2009.

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In preclinical and clinical studies we have observed a mobilization of so-called Aldehyde dehydrogenase (ALDH)-bright cells into the bloodstream after treatment with SB-509. ALDH-bright cells can be identified by their ability to be stained with a substrate of aldehyde dehydrogenase, an enzyme that is highly expressed in stem cells. ALDH-bright cell populations of human bone marrow have been shown to be highly enriched in cell types thought to mediate tissue repair, including endothelial, mesenchymal, neural and hematopoietic progenitor cells. Stem cells are of interest as potential therapeutic agents as they can be induced to become cells with a special function in the body such as nerves and blood vessels and can potentially migrate from the blood circulation into areas of injury or degeneration to participate in the body s repair response. This observation may also serve as a pharmacodynamic surrogate biomarker enabling a physician to easily monitor progress of our therapy for DN after SB-509 administration. In January 2008, we initiated a single-blind, placebo-controlled, Phase 2 clinical trial (SB-509-703) in subjects with mild to moderate DN designed to evaluate the pharmacokinetics of stem cell mobilization into the bloodstream after treatment with varying doses of SB-509 as well as the clinical safety and clinical effects of SB-509 administration. We have completed enrollment of this trial and expect to have data in 2009.

Amyotrophic Lateral Sclerosis (ALS)

Market Opportunity

ALS, commonly referred to as Lou Gehrig s disease, is a progressive neurodegenerative disease that affects nerve cells in the brain and the spinal cord and is generally fatal. The progressive degeneration of the motor neurons in ALS is the primary reason that the disease is fatal. When the motor neurons die, the ability of the brain to initiate and control muscle movement is lost. Muscle weakness is a hallmark initial sign in ALS, occurring in approximately 60% of patients. The hands and feet may be affected first, causing difficulty in lifting, walking or using the hands. As the weakening and paralysis continue to spread to the muscles of the trunk, the disease eventually affects speech, swallowing, chewing and breathing. When the breathing muscles become affected, ultimately, patients need permanent ventilatory support in order to survive. More than 5,600 Americans are diagnosed with ALS each year. Approximately 35,000 people at any given time are living with ALS in the United States.

Current Treatments

There are no drugs available to cure ALS. The FDA has approved a single medication, Rilutek© (Riluzole) which modestly increases lifespan in ALS patients.

Sangamo s Therapeutic Approach

There are both animal and clinical data suggesting that a defect or deficiency in VEGF expression plays a role in ALS. We plan to evaluate whether a regional muscle or systemic effect of SB-509 delivery will result in a therapeutic effect in ALS. In September 2008 we initiated a Phase 2 clinical trial (SB-509-801) to evaluate SB-509 in subjects with ALS. We expect to complete enrollment of this study in 2009.

Human Immunodeficiency Virus (HIV) and Acquired Immunodeficiency Syndrome (AIDS)

Market Opportunity

HIV infection results in the death of immune system cells and thus leads to AIDS, a condition in which the body s immune system is depleted to such a degree that the patient is unable to fight off common infections. Ultimately, these patients succumb to opportunistic infections or cancers. According to UNAIDS/WHO, over 2.7 million people were newly infected with HIV in 2007. An estimated 2.0 million people died of AIDS in the same year. There are now over 33 million people living with HIV and AIDS worldwide. The CDC estimates that, in the United States alone, there were 1.2 million people living with HIV/AIDS, approximately 54,000 new infections and 23,000 deaths in 2007.

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Current Treatments

Currently, there are 30 antiretroviral drugs approved by the FDA to treat people infected with HIV. These drugs fall into four major classes: reverse transcriptase (RT) inhibitors, protease inhibitors, integrase inhibitors and entry and fusion inhibitors. This latter class also includes a small molecule antagonist of the CCR5 receptor, Selzentry® (maraviroc). This drug is being used in combination with other antiretroviral agents for treatment-experienced adult patients infected with CCR5-tropic HIV-1 strains that are resistant to multiple antiretroviral agents. There are no study results demonstrating the effect of Selzentry on clinical progression of HIV-1 and the drug carries a black box warning of liver toxicity.

As HIV reproduces itself, variants of the virus emerge, including some that are resistant to antiretroviral drugs. Therefore, doctors recommend that people infected with HIV take a combination of antiretroviral drugs known as highly active antiretroviral therapy, or HAART. This strategy typically combines drugs from at least two different classes of antiretroviral drugs. Currently available drugs do not cure HIV infection or AIDS. They can suppress the virus, even to undetectable levels, but they cannot eliminate HIV from the body. Hence, people with HIV need to continuously take antiretroviral drugs which can have significant side effects over time.

Sangamo s Therapeutic Approach

CCR5 is a co-receptor for HIV entry into T-cells and, if CCR5 is not expressed on their surface, HIV is less efficient at infecting these cells. A population of individuals that is immune to HIV infection, despite multiple exposures to the virus, has been identified and extensively studied. The majority of these individuals have a natural mutation, CCR5delta32, resulting in the expression of a shortened, or truncated, and non-functional CCR5 protein. This mutation appears to have no observable deleterious effect. We are using our ZFN-mediated gene disruption technology to disrupt the CCR5 gene in cells of a patient s immune system to make these cells permanently resistant to HIV infection. The aim is to provide a population of HIV-resistant cells that can fight HIV and opportunistic infections mimicking the situation in individuals that carry the natural mutation. In December 2008, in collaboration with scientists at the University of Pennsylvania, we filed an IND application for a Phase 1 trial of our CCR5 ZFP Therapeutic, SB-728-T. This trial began enrolling subjects in February 2009, at the University of Pennsylvania. We also have a research stage program to investigate this approach in hematopoietic stem cells and as an *in-vivo* application.

ZFP Therapeutic Pre-clinical Stage Programs

In addition to our ongoing Phase 2 clinical trials in DN and stem cell mobilization, ALS and our Phase 1 study in HIV/AIDS, we currently have a pre-IND program and multiple preclinical-stage programs (i.e., lead ZFP TF molecules in animal efficacy studies).

Glioblastoma Multiforme

Gliomas are the most common type of primary brain cancers; 20,000 cases are diagnosed and 14,000 glioma-related deaths occur annually in the United States. Glioblastoma multiforme (GM), the most common type of glioma, is rapidly progressive and nearly universally lethal. Currently, malignant glioma is managed through surgery and radiation which often exacerbates the already severe symptoms caused by the location of the tumor. With modern surgical and radiotherapeutic techniques the mean duration of survival has increased to 82 weeks, although 5-year survival rates have only increased from 3 to 6%. Resections of 90% of bulky tumors are usually attempted provided that vital functional anatomy is spared. Chemotherapy, resection and radiation provide only marginal survival advantage to patients. Approximately 80% of recurrent tumors arise from remnants of the original incompletely resected tumor. The median survival of recurrent glioblastoma multiforme patients treated with a second resection is 36 weeks.

In collaboration with clinicians at City of Hope (COH) we are developing a ZFP Therapeutic that uses our ZFN technology to disrupt the expression of the gene encoding the glucocorticoid receptor. Our collaborators

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have developed an engineered protein known as an IL-13 zetakine that, when expressed in cytotoxic or killer T-cells, enables them to seek out and destroy glioblastoma cells in the brain. In an investigator-sponsored IND, patients have been treated with zetakine-modified T-cells which have shown significant anti-tumor activity. In the current clinical protocol, T-cells are removed from a patient with GM and modified to express the zetakine. These modified cells are infused into the brain following surgery for the targeted elimination of residual tumor cells. Frequently, however, a glucocorticoid such as Decadron® must be administered to patients post-surgery to control brain swelling. Glucocorticoids inactivate or kill the therapeutic T-cells through a protein known as the glucocorticoid receptor (GR). Cells without a functional GR are drug-resistant and are therefore available to destroy tumor cells. Our goal is to generate zetakine positive, GR-negative T-cells thus enabling the full treatment effect to occur even in the presence of Decadron. In December 2006, we entered into a broad, exclusive license agreement with the COH for use of the zetakine with our technology. Sangamo retains commercialization rights and COH receives success-based milestone and downstream payments. We anticipate filing an IND application for a Phase 1 clinical trial of this therapeutic in 2009.

Neuropathic Pain (Cancer Pain)

Neuropathic pain comprises a set of chronic pain disorders that cannot be connected to a physical trauma, as is the case with acute pain. There are several million patients with neuropathic pain in the United States including late-stage cancer patients. Studies have shown that 90% of patients with advanced cancer experience severe pain, and that pain occurs in 30% of all cancer patients regardless of the stage of the disease. Pain usually increases in intensity as cancer progresses. The most common cancer pain is from tumors that metastasize to the bone. 60-80% of cancer patients with bone metastases experience severe pain. The second most common cancer pain is caused by tumors infiltrating nerves. Tumors near neural structures may cause the most severe pain. The few drugs currently being used to treat pain in these patients show marginal efficacy and can have very significant side effects. Chronic pain is a major and underserved market opportunity and is now an area of intense focus by pharmaceutical researchers owing to the discovery of several new pain-related pathways and drug targets. Recent studies have shown that in chronic pain, certain proteins in nerve cell membranes are up-regulated or over-expressed. Our scientists have identified ZFP TF candidates that repress the expression of two of these pain targets, Trk-A and PN3, in cell-based models. Trk-A and PN3 fall into the class of non-druggable targets. We have incorporated these ZFP TFs into gene transfer vectors and have demonstrated a statistically significant reduction of pain in an animal model of bone cancer pain after treatment with Sangamo s ZFP TF repressor of Trk-A. Further animal studies are ongoing.

Nerve Regeneration Spinal Cord Injury (SCI) and Traumatic Brain Injury (TBI)

Nerves are fragile and can be damaged by disease, pressure, stretching, or cutting. While recent advances in emergency care and rehabilitation allow many patients suffering from a nerve injury or neurodegenerative disease to survive for longer periods and live with their condition, there are currently no therapeutic options for restoring nerve function. The spectrum of direct nerve injuries ranges from pinched nerves, e.g. sciatica, to outright spinal cord severance. Spinal Cord Injury (SCI) encompasses damage to the spinal cord that results in a loss of function such as mobility or feeling. The National Spinal Cord Injury Statistical Center (NSCISC) estimates that there are approximately 11,000 new cases each year primarily in young adults. The spinal cord does not have to be severed in order for a loss of function to occur. In fact, in most people with SCI, the spinal cord is intact, but the damage to it results in loss of function. Evidence from preclinical and clinical studies using VEGF-A suggests that the targeted up-regulation of VEGF-A may be a viable approach to the treatment of degenerative nerve disease, crush injuries, SCI and traumatic brain injury. In collaboration with several academic labs, we are evaluating our ZFP TF activator of the VEGF-A gene in pre-clinical animal efficacy models of SCI. We have presented data that demonstrates a statistically significant effect on both recovery of hind-limb function and spinal cord tissue preservation following treatment at the time of injury with our ZFP TF activator of VEGF-A in a severe model of SCI. Further studies in SCI to investigate dosing and timing of dose as well as animal studies in traumatic brain injury are ongoing.

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Parkinson s Disease (PD)

Parkinson s disease is a chronic, progressive disorder of the central nervous system and results from the loss of cells in a section of the brain called the substantia nigra. These cells produce dopamine, a chemical messenger responsible for transmitting signals within the brain. Loss of dopamine causes critical nerve cells in the brain, or neurons, to fire out of control, leaving patients unable to direct or control their movement in a normal manner. The symptoms of Parkinson s may include tremors, difficulty maintaining balance and gait; rigidity or stiffness of the limbs and trunk; and general slowness of movement (also called bradykinesia). Patients may also eventually have difficulty walking, talking, or completing other simple tasks. Symptoms often appear gradually yet with increasing severity and the progression of the disease may vary widely from patient to patient. There is no cure for Parkinson s disease. Drugs have been developed that can help patients manage many of the symptoms; however they do not prevent disease progression. In January 2007, we were awarded a grant of $950,000 by The Michael J. Fox Foundation for Parkinson s Research (MJFF) to support the development of a ZFP TF activator of glial cell line-derived neurotrophic factor (GDNF) to treat PD. In collaboration with scientists at the University of California, San Francisco (UCSF), we are evaluating ZFP TFs that activate the glial cell line-derived neurotrophic factor (GDNF*)* gene in pre-clinical animal efficacy models of Parkinson s Disease.

Stroke

A stroke occurs when a blood clot blocks an artery, or a blood vessel breaks, interrupting blood flow to an area of the brain. When either of these events occurs, brain cells begin to die, frequently resulting in brain damage. When brain cells die during a stroke, abilities controlled by that area of the brain are lost. These abilities can include speech, movement and memory. How a stroke patient is affected depends on where the stroke occurs in the brain and how much the brain is damaged. According to the Centers for Disease Control, stroke killed approximately 144,000 people in 2005 and is the third largest cause of death in the United States. Data from Greater Cincinnati/Northern Kentucky Stroke Study/National Institute of Neurological Diseases and Stroke (GCNKSS/NINDS) studies show that about 780,000 people suffer a new or recurrent stroke each year. About 600,000 of these are first attacks and 180,000 are recurrent attacks. As a consequence stroke is a leading cause of serious, long-term disability in the US. About 5.8 million stroke survivors are alive today. We are evaluating our ZFP TF activator of the VEGF-*A* gene in pre-clinical animal efficacy models of stroke.

ZFP Therapeutic Research Programs

We also have several research stage ZFN-mediated gene modification programs in progress. These initiatives include programs in hemophilia and the hemoglobinopathies and in immune system disorders such as X-linked severe combined immunodeficiency (X-linked SCID).

CORPORATE RELATIONSHIPS

We are applying our ZFP technology platform to several commercial applications in which our products provide Sangamo and our strategic partners and collaborators with potential technical, competitive, and economic advantages. Where and when appropriate, we have established and will continue to pursue ZFP Therapeutic strategic partnerships, corporate partnerships in non-therapeutic areas and Enabling Technology collaborations with selected pharmaceutical, biotechnology and chemical companies to fund internal research and development activities and to assist in product development and commercialization.

Agreement with Dow AgroSciences in Plant Agriculture

Sangamo scientists and collaborators have shown that ZFP TFs and ZFNs can be used to regulate and modify genes in plants. The ability to regulate gene expression with engineered ZFP TFs may lead to the creation of new plants that increase crop yields, lower production costs and are more resistant to herbicides, pesticides, and plant pathogens, which could permit the development of branded agricultural products with unique nutritional and processing characteristics. In addition, ZFNs may be used to facilitate the efficient and reproducible generation of transgenic plants.

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We have an exclusive commercial license agreement with Dow AgroSciences LLC (DAS), a wholly owned indirect subsidiary of Dow Chemical Corporation. Under this agreement, we are providing DAS with access to our proprietary zinc finger DNA-binding protein (ZFP) technology and the exclusive right to use our ZFP technology to modify the genomes or alter the nucleic acid or protein expression of plant cells, plants, or plant cell cultures. We have retained rights to use plants or plant-derived products to deliver ZFP transcription factors (ZFP TFs) or zinc-finger nuclease (ZFN) into human or animals for diagnostic, therapeutic, or prophylactic purposes.

Pursuant to the Research License and Commercial Option Agreement which we entered into in October 2005, DAS made an initial cash payment to us of $7.5 million. In November 2005, the Company sold approximately 1.0 million shares of common stock to DAS at a price of $3.85 per share, resulting in proceeds of $3.9 million. Our agreement with DAS provided for an initial three-year research term during which DAS agreed to pay Sangamo $6.0 million in research funding over the three-year period and make additional payments of up to $4.0 million in research milestone payments during this same period, depending on the success of the research program. We agreed to supply DAS and its sublicensees with ZFP TFs and/or ZFNs for both research and commercial use over the initial three year period of the agreement.

In June 2008, DAS exercised its option under the agreement to obtain a commercial license to sell products incorporating or derived from plant cells generated using our ZFP technology, including agricultural crops, industrial products and plant-derived biopharmaceuticals. The exercise of the option triggered a one-time commercial license fee of $6.0 million, payment of the remaining $2.3 million of the previously agreed $4.0 million in research milestones, minimum sublicensing payments totaling up to $25.3 million over 11 years, development and commercialization milestone payments for each product, and royalties on sales of products. Furthermore, DAS has the right to sublicense our ZFP technology to third parties for use in plant cells, plants, or plant cell cultures, and we will be entitled to 25% of any cash consideration received by DAS under such sublicenses. The research program has been extended beyond the initial three-year research term and DAS is providing additional research funding.

DAS may terminate the agreement at any time. In addition, each party may terminate the agreement upon an uncured material breach of the other party. In the event of any termination of the agreement, all rights to use our ZFP technology will revert to us, and DAS will no longer be permitted to practice our ZFP technology or to develop or, except in limited circumstances, commercialize any products derived from our ZFP technology.

The commercial license fee of $6.0 million, the remaining research milestones of $2.3 million, and the unrecognized portion of the initial cash payment are recognized ratably over the period from option exercise through December 31, 2009, which reflects the estimated timing over which the ZFP manufacturing technology transfer will occur, as well as the period over which Sangamo will be performing additional research services for DAS.

Revenues under the agreement were $7.4 million, $5.3 million, and $5.2 million during 2008, 2007, and 2006, respectively. Related costs and expenses incurred under the agreement were $391,000, $467,000 and $568,000 during 2008, 2007 and 2006, respectively.

Agreement with Sigma-Aldrich Corporation in Laboratory Research Reagents

In July 2007, we entered into a license agreement with Sigma-Aldrich Corporation (Sigma). Under the license agreement, we are providing Sigma with access to our proprietary ZFP technology and the exclusive right to use the technology to develop and commercialize research reagents products and services in the research field, excluding certain agricultural research uses that Sangamo previously licensed to Dow AgroSciences LLC. Under the agreement, Sangamo and Sigma have agreed to conduct a three-year research program to develop laboratory research reagents using our ZFP technology. In addition, for three years we will assist Sigma in connection with Sigma s efforts to market and sell services employing our technology in the research field. We will transfer the

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ZFP manufacturing technology to Sigma or to a mutually agreed-upon contract manufacturer upon Sigma s request. Prior to the completion of this transfer, we will be responsible for supplying ZFPs for use by Sigma in performing services in the research field.

Under the terms of the agreement, Sigma made an initial payment comprising an upfront license fee and the purchase of one million (1,000,000) shares of Sangamo s common stock under a separate stock purchase agreement, resulting in a total upfront payment to Sangamo of $13.5 million, which consists of an equity investment by Sigma in Sangamo common stock valued at $8.55 million, a $3.95 million license fee, and $1.0 million of research funding. Under the license agreement, we may receive additional research funding of up to $2.0 million, development milestone payments of up to $5.0 million, and commercial milestone payments based on net sales of up to $17.0 million, subject to the continuation of the agreement. During the term of the license agreement, Sigma is obligated to pay to Sangamo minimum annual payments, a share of certain revenues received by Sigma from sublicensees, and royalty payments on the sale of licensed products and services. Sigma also has the right to sublicense the ZFP technology for research applications and we will receive 50% of any sublicensing revenues in the first two years and 25% of any sublicensing revenues thereafter. We retain the sole right to use and license our ZFP technology for GMP production purposes, for the production of materials used in or administered to humans, and for any other industrial commercial use.

The agreement may be terminated by Sigma at any time with a 90-day notice or by either party upon an uncured material breach of the other party. In the event of any termination, all rights to use our ZFP technology will revert to us, and Sigma will no longer be permitted to practice our ZFP technology or to develop or, except in limited circumstances, commercialize any products derived from our ZFP technology.

In December 2008, we achieved a major production throughput milestone as part of our agreement which triggered a payment of $1.0 million from Sigma, and was fully recognized as revenue in 2008.

Revenues related to the research license under the Sigma agreement are being recognized ratably over the three-year research term of the agreement and were $1.3 million and $603,000 during 2008 and 2007, respectively. Revenues attributable to collaborative research and development performed under the Sigma agreement were $2.0 million and $458,000 during 2008 and 2007, respectively. Royalty revenues under the Sigma agreement were $388,000 and $0 during 2008 and 2007, respectively. Related costs and expenses incurred under the Sigma agreement were $2.2 million and $316,000 during 2008 and 2007, respectively.

Enabling Technology Programs and Partners

We began marketing our Enabling Technologies to the pharmaceutical and biotechnology industry in 1998. Our Enabling Technology collaborations have been based upon applying our ZFP TF and ZFN technology and intellectual property in products and areas outside ZFP Therapeutics.

Pharmaceutical Protein Production

The production of pharmaceutical proteins, such as therapeutic antibodies, is an important area of commercial growth. According to a report by the independent business information provider Visiongain, ten years ago, there were only two monoclonal antibody drugs on the world market. Currently there are 21 FDA approved therapies. In 2007, the therapeutic antibody market was worth $21.9 billion. Sangamo scientists and their collaborators have demonstrated that ZFP-engineered mammalian cells may be used to increase the yield of systems used for pharmaceutical protein production.

We have established several research collaborations in this area. Commencing in December 2004, we had a research collaboration agreement with Pfizer to use our ZFP technology to develop enhanced cell lines for protein pharmaceutical production. Under the terms of the agreement, Pfizer funded research at Sangamo and we provided our proprietary ZFP technology for Pfizer to assess its feasibility for use in mammalian cell-based

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protein production. We generated novel cell lines and vector systems for enhanced protein production as well as novel technology for rapid creation of new production cell lines. In December 2008, we entered into a license agreement with Pfizer to provide Pfizer with a worldwide, non-exclusive license for the use of certain ZFP Nuclease (ZFNs) reagents to permanently eliminate the Glutamine Synthetase (GS) gene in Chinese Hamster Ovary (CHO) cell lines and for the use of these ZFN-modified cells for clinical and commercial production of therapeutic proteins. Under the terms of this agreement we received a one time payment of $3.0 million from Pfizer for a fully paid commercial license.

Revenues under the Pfizer agreements were $3.0 million, $96,000 and $747,000 in 2008, 2007, and 2006, respectively. Related costs and expenses incurred under the Pfizer agreements were $66,000, $358,000 and $342,000 in 2008, 2007 and 2006, respectively.

In April 2007, we established a research and license agreement with Genentech, Inc. Under our agreement with Genentech, we are developing ZFNs capable of making targeted modifications to the genome of Genentech cell lines to generate cell lines with novel characteristics for protein pharmaceutical production purposes. Genentech paid an upfront fee, will pay an ongoing technology access fee, and certain payments upon achievement of specified milestones relating to the research of ZFNs and the development and commercialization of products manufactured using a modified cell line created by our ZFN technology. The agreement was expanded to include further ZFNs in February 2008. Under the expanded agreement, we may directly offer the ZFN-related services to Genentech and Sigma will in return receive a share of certain payments made to us by Genentech. Revenues recognized under the expanded agreement are included in royalty revenues from Sigma, as described above.

Revenues attributable to collaborative research and development performed under the Genentech agreement were $389,000 during 2008 and $283,000 during 2007. Costs and expenses performed under the Genentech agreement were $147,000 during 2008 and $82,000 during 2007.

We are also providing our ZFP technology to several companies including Amgen, Inc., Novartis A/G Novo Nordisk Inc. and Kirin Brewery Company for evaluation of its use in developing enhanced cell lines for protein production.

Transgenic Animals

In April, 2008, we entered into a license agreement with Open Monoclonal Technology, Inc. (OMT). Under the agreement we have granted OMT a royalty-bearing, non-exclusive, sublicensable worldwide license for the commercial use of a transgenic animal generated using our ZFP technology. We have received an upfront license fee, and will receive payments upon the achievement of certain clinical development milestones, a share of payments received by OMT from sublicensees, and royalties on sales of any products developed using Sangamo s ZFP technology. For any given OMT product, OMT has the right to buy out its future royalty payment obligations under the agreement by paying a lump sum fee to Sangamo.

In July 2008, we entered into a research and license agreement with F. Hoffmann La Roche Ltd and Hoffmann-La Roche Inc. (Roche). During an initial research term, we will provide Roche with access to aspects of our proprietary ZFN technology for the targeted modification of a specified gene in a specified species in order to generate ZFN-modified cell lines and animals for research purposes. In addition, Roche has an option to receive an exclusive, worldwide license to use such animals in the production of therapeutic and diagnostic products.

In consideration for the rights and licenses granted to Roche, as well as our efforts in generating the specific ZFN materials provided to Roche, Roche has paid us an initial research event fee, a payment for the delivery of ZFN materials, and will pay ongoing research maintenance fees during the research term. In the event that Roche

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exercises its option to receive a commercial license, Roche will pay us an option exercise fee, payments upon the achievement of certain clinical development milestones relating to products produced under such commercial license, and royalties on sales of such products.

We have an existing agreement with Sigma to develop and commercialize research reagents and services and Sigma has the exclusive right to offer certain services involving our ZFN technology that are covered under the research agreements with Roche and OMT. Notwithstanding this exclusive right, Sigma has agreed that we may directly offer the ZFN-related services to Roche and OMT under the research agreements and Sigma will in return receive a share of certain payments made to us. Revenues recognized under the Roche and OMT agreements, net of payments made to Sigma, are included in royalty revenues attributable to the Sigma agreement, as described above.

Funding from Research Foundations

The Juvenile Diabetes Research Foundation International

In October 2006, we announced a partnership with the Juvenile Diabetes Research Foundation International (JDRF) to provide financial support to one of our Phase 2 human clinical studies (SB-509-601) of SB-509, a ZFP Therapeutic that is in development for the treatment of diabetic neuropathy. Under the agreement with JDRF and subject to its terms and conditions, including the Company s achievement of certain milestones associated with the Company s Phase 2 clinical trial of SB-509 for the treatment of mild to moderate diabetic neuropathy, JDRF will pay the Company an aggregate amount of up to $3.0 million. Through December 31, 2008, we have received $2.5 million. After the first commercial launch of SB-509 in a major market, JDRF has the right to receive, subject to certain limitations, annual payments from Sangamo, until such time when the total amount paid to JDRF, including payments made on account of certain licensing arrangements, equals three times the amount received by us from JDRF.

Under the agreement, we are obligated to use commercially reasonable efforts to carry out the Phase 2 trial and, thereafter, to develop and commercialize a product containing SB-509 for the treatment of diabetes and complications of diabetes. We are obligated to cover all costs of the Phase 2 trial that are not covered by JDRF s grant. If we fail to satisfy these obligations, JDRF may have the right, subject to certain limitations, to obtain an exclusive, sublicensable license, to the intellectual property generated by us in the course of the Phase 2 trial, to make and commercialize products containing SB-509 for the treatment of diabetes and complications of diabetes. If JDRF obtains such a license, it is obligated to pay us a percentage of its revenues from product sales and sublicensing arrangements. If JDRF fails to satisfy its obligations to develop and commercialize a product containing SB-509 under the Agreement, then their license rights will terminate and we will receive a non-exclusive, fully paid license, for any intellectual property developed during JDRF s use of the license, to research, develop and commercialize products containing SB-509 for the treatment of diabetes and complications of diabetes.

Revenues attributable to research and development activities performed under the JDRF partnership were $1.0 million in 2008 and $1.5 million in 2007. Related costs and expenses incurred during 2008 and 2007 were $3.9 million and $4.7 million, respectively.

The Michael J. Fox Foundation

In January 2007, Sangamo announced a partnership with the Michael J. Fox Foundation for Parkinson s Research (MJFF) to provide financial support of Sangamo s ZFP TFs to activate the expression of glial cell line-derived neurotrophic factor (GDNF) that has shown promise in preclinical testing to slow or stop the progression of Parkinson s disease. Under the agreement with MJFF and subject to its terms and conditions, MJFF has paid the Company $950,000 over a period of two years and through December 31, 2008 we have received the total funds due from MJFF.

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Revenues attributable to research and development performed under the MJFF partnership were $553,000 during 2008 and $397,000 during 2007. Related costs and expenses incurred under the MJFF partnership were $903,000 during 2008 and $397,000 during 2007.

INTELLECTUAL PROPERTY AND TECHNOLOGY LICENSES

Patents and licenses are important to our business. Our strategy is to file or license patent applications to protect technology, inventions and improvements to inventions that we consider important for the development of our business. We seek patent protection and licenses that relate to our technology and candidates in our pipeline and/or may be important to our future. We have filed numerous patents and patent applications with the United States Patent and Trademark Office (USPTO) and foreign patent jurisdictions. This proprietary intellectual property includes methods relating to the design of zinc finger proteins, therapeutic applications and enabling technologies. We rely on a combination of patent, copyright, trademark, proprietary know how, continuing technological innovations, trade secret laws, as well as confidentiality agreements, materials transfer agreements and licensing agreements, to establish and protect our proprietary rights.

We have licensed intellectual property directed to the design, selection, and use of ZFPs, ZFP TFs and ZFNs for gene regulation and modification from the Massachusetts Institute of Technology (MIT), Johnson & Johnson, The Scripps Research Institute (TSRI), The Johns Hopkins University (JHU), Harvard University, the Medical Research Council, the California Institute of Technology, City of Hope, and the University of Utah. These licenses grant us rights to make, use, and sell ZFPs, ZFP TFs, and ZFNs under 16 families of patent filings. As of February 6, 2009, these patent filings have resulted in 19 issued U.S. patents and 18 granted foreign patents, with 7 currently pending U.S. patent applications and 32 pending applications in foreign patent offices. We believe these licensed patents and patent applications include several of the early and important patent filings directed to design, selection, composition, and use of ZFPs, ZFP TFs, and ZFNs.

In addition to our in-licensed patent portfolio, as of February 6, 2009, we had 71 families of Sangamo-owned or co-owned patent filings, including 49 issued U.S. patents, 157 granted foreign patents, 79 pending U.S. patent applications and 126 pending foreign patent applications. These patent filings are directed to the design, composition, and use of ZFPs, ZFP TFs, and ZFNs. The earliest patents in our portfolio are set to begin expiring in 2015, with the majority of our currently issued patents expiring between 2019 and 2021. However, these patents in our estate may be subject to Patent Term Adjustment (due to delays in patent prosecution by the USPTO), Patent Term Extension (due to review of a patented product by a regulatory agency) or terminal disclaimer. Additionally, patents that may be issued from our pending applications will extend the patent exclusivity of our patent estate. Accordingly, all dates given above for patent expirations are estimates.

In the aggregate, we believe that our licensed patents and patent applications, as well as the issued Sangamo patents and pending Sangamo patent applications, will provide us with a substantial proprietary position in our commercial development of ZFP technology. In this regard, patents issued to us, applied for by us, or exclusively and non-exclusively licensed to us, cover the following types of inventions, processes and products:

ZFP and ZFN design, engineering and compositions: includes DNA target site selection and zinc finger binding domain design, target site arrays, ZFP libraries (see application US20,030,134,318, for which we have recently received a Notice of Allowance), databases and methods of construction, as well as methods to increase zinc finger binding specificity; linker designs, and methods of making modified plant zinc finger proteins;

ZFP targeted regulation of endogenous genes: methods relating to activation and inhibition of endogenous cellular genes (see newly issued US7,407,776), modulation of ZFP-regulated gene expression by small molecules, identification of accessible regions within chromatin, regulation of tocopherol synthesis in plants (see newly issued US7,361,635), regulation of endogenous plant genes (see application US20,080,070,306 for which we have recently received a Notice of Allowance);

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ZFP Therapeutics: Treatment of virally or microbially infected cells, cancer therapeutics such as methods to alter tumor growth, activation of endogenous PEDF for treatment of head and neck cancer, glioblastoma, prostate cancer and pancreatic cancer, regulation of angiogenesis (including newly issued US7,358,085), treatments for ischemic conditions, neuropathic pain, crushed nerves, Parkinson s disease, chronic pain, diabetic neuropathy, peripheral vascular disease, ocular neovascularization including age-related macular degeneration (AMD), diabetic retinopathy (DR) and retinopathy of prematurity, modulation of cardiac contractility and methods to regulate the glucocorticoid receptor;

ZFN Therapeutics: Treatments for HIV, sickle cell anemia, and X-linked severe combined immunodeficiency (SCID);

ZFP Enabling Technologies: Methods for linking genes and phenotypes, identification of genes, analysis of gene regulation, structure and biological function, methods of agricultural biotechnology, methods of altering cellular differentiation state, and methods of introducing exogenous nucleic acids of interest into a safe harbor locus (see application US20,080,299,580);