SANGAMO BIOSCIENCES INC
Form 10-K
March 03, 2009
Table of Contents

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

Table of Contents

TABLE OF CONTENTS

Table of Contents

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.

Table of Contents

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

Table of Contents

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

Table of Contents

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,

Table of Contents

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.

Table of Contents

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%

Table of Contents

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.

Table of Contents

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.

Table of Contents

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

Table of Contents

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.

Table of Contents

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.

Table of Contents

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

Table of Contents

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

Table of Contents

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

Table of Contents

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.

Table of Contents

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);

Table of Contents

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 neovascularizton 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);

ZFN Enabling Technologies: Methods for identification of regulatory DNA sequences, prediction of patient response to drug therapeutics, and development of cell lines for improved protein production.

We have been advised that certain aspects of our technology can give us and our collaborators independence from third party patent claims to gene sequences. In general, under United States patent law, a patent may be obtained for any new and useful process, machine, manufacture, or composition of matter. An underlying theme of United States patent law, as related to biotechnology, is that the sequence of a gene, as it exists in the chromosome, is not new, even when newly discovered, unless it is isolated or modified from its normal chromosomal context. As a result, for over a decade, patent courts have held that, to be patentable, a DNA sequence must be purified, isolated or modified. Accordingly, U.S. patent claims to DNA sequences can cover only isolated, purified or modified nucleic acid sequences (e.g., a purified DNA fragment or a DNA sequence inserted into a vector). We have been advised that U.S. patent claims to DNA sequences do not, and cannot, cover gene sequences as they exist in their natural chromosomal environment and international patent law is even more stringent than U.S. patent law in this regard. Most current methods for over-expression of a gene or protein involve introduction, into a cell, of a vector containing a DNA encoding the protein to be over-expressed. Since such a vector contains isolated sequences which encode the protein, it would be covered by any patent claims to those sequences. In contrast, our methods for over-expression utilize ZFP TFs that target endogenous genes as they exist in the chromosome. As a result, our methods do not require the use of isolated DNA sequences encoding the protein to be over-expressed and, our counsel has advised us, do not infringe patent claims to such sequences. Notwithstanding this advice, we realize that others could take a contrary position that could result in litigation. While we believe that we would prevail in any such litigation, the uncertainties involved in litigation generally make it impossible to provide assurance as to the ultimate outcome of such matters. See *Risk Factors Because it is difficult and costly to protect our proprietary rights, and third parties have filed patent applications that are similar to ours, we cannot ensure the proprietary protection of our technologies and products.*

The patent positions of pharmaceutical and biotechnology firms, including our patent position, are uncertain and involve complex legal and factual questions for which important legal tenets are largely unresolved. Patent applications may not result in the issuance of patents and the coverage claimed in a patent application may be significantly reduced before a patent is issued.

Although we have filed for patents on some aspects of our technology, we cannot provide assurances that patents will be issued as a result of these pending applications or that any patent that has been or may be issued will be upheld. The laws of some foreign countries may not protect our proprietary rights to the same extent as do the laws of the United States. One of our foreign patents, which forms the basis for five European Regional Phase patents, has been revoked as a result of an opposition by a third party. Our licensor, The Johns Hopkins University, appealed the revocation but in April 2007, the European Technical Board of Appeal released its

Table of Contents

decision dismissing the appeal. As of February 6, 2009, US patent number US6,265,196, licensed to Sangamo from The Johns Hopkins University, was undergoing re-examination. In addition in 2008, US5,792,640, also licensed from Johns Hopkins University, completed a first re-examination process and a re-exam certificate was issued on September 9, 2008. However, a second re-exam proceeding was ordered on November 4, 2008. We do not know what the outcome of these two re-examination processes will be. In the future, third parties may assert patent, copyright, trademark, and other intellectual property rights to technologies that are important to our business. Any claims asserting that our products infringe or may infringe proprietary rights of third parties, if determined adversely to us, could significantly harm our business. See *Risk Factors Because it is difficult and costly to protect our proprietary rights, and third parties have filed patent applications that are similar to ours, we cannot ensure the proprietary protection of our technologies and products.*

Estimated Licensing Expenses

If we are successful in the development and commercialization of our products, we will be obligated by our license agreements to make milestone and royalty payments to some or all of the licensors mentioned above. We believe that total payments under these agreements over the next three years will not exceed $1.5 million. For risks associated with our intellectual property, see *Risk Factors Because it is difficult and costly to protect our proprietary rights, and third parties have filed patent applications that are similar to ours, we cannot ensure the proprietary protection of our technologies and products*. We plan to continue to license and to internally generate intellectual property covering the design, selection, composition, and use of ZFPs; the genes encoding these proteins; and the application of ZFPs, ZFP TFs, and ZFNs in ZFP Therapeutics, Enabling Technology and research applications, and in plant agriculture research.

COMPETITION

We are the leader in the research, development, and commercialization of DNA binding proteins for the regulation of gene expression and gene modification. We are aware of several companies focused on other methods for regulating gene expression and a limited number of commercial and academic groups pursuing the development of ZFP gene regulation and gene modification technology. The field of applied gene regulation and gene modification is highly competitive and we expect competition to persist and intensify in the future from a number of different sources, including pharmaceutical, agricultural, and biotechnology companies; academic and research institutions; and government agencies that will seek to develop ZFPs as well as technologies that will compete with our ZFP technology platform.

In July 2001, we strengthened our competitive position by completing our acquisition of Gendaq Ltd. Gendaq scientists had also focused their research efforts on regulating genes through the engineering of ZFPs and they brought significant additional know-how and intellectual property into Sangamo. Despite our strong presence in the field of ZFP technology and intellectual property, any products that we develop with our ZFP TF and ZFN technology may participate in highly competitive markets.

Accordingly, our competitors may succeed in obtaining patent protection, receiving FDA approval, or commercializing ZFP Therapeutics or other competitive products before us. If we commence commercial product sales, we may be competing against companies with greater marketing and manufacturing capabilities, areas in which we have limited or no experience. In addition, any product candidate that we successfully develop may compete with existing products that have long histories of safe and effective use.

Although we are in the clinical development phase of operations and have no current therapeutic product sales, we believe the following companies, products and/or technologies may potentially be competitive with our technology or our products under development:

Small molecules in development from both in-house drug discovery programs of pharmaceutical companies such as Eli Lilly and Company, Merck & Co., Inc. and Pfizer, Inc as well as from biotechnology companies with expertise and capabilities in small molecule discovery and development such as Exelixis Inc. and Millennium Pharmaceuticals, Inc.

Table of Contents

Monoclonal antibody companies and product candidates from certain biotechnology firms such as Amgen Inc., Genentech, Inc., Medarex Inc., Medimmune, Inc. and Facet Biotech Corporation.

Protein pharmaceuticals under development at pharmaceutical and biotechnology companies such as Amgen Inc., Biogen Idec, Eli Lilly and Company, Genentech, Inc., Johnson & Johnson and numerous other pharmaceutical and biotechnology firms.

Gene therapy companies developing gene-based products in clinical trials. None of these products have yet been approved. Our competitors in this category may include Cell Genesys, Inc., GenVec Inc., Targeted Genetics Corporation and VIRxSYS Corporation.

Antisense therapeutics and RNA interference technology, including RNAi and microRNA, which are technologies that may compete with ZFP Therapeutics in the development of novel therapeutic products acting through the regulation of gene expression. These technologies are being developed by several companies including Alnylam Pharmaceuticals,Inc., Isis Pharmaceuticals, Inc., Regulus Therapeutics, LLC and Merck & Co. Inc.

Nuclease technologies: Cellectis SA and Precision BioSciences, Inc. are developing meganucleases to accomplish gene modification. We expect to face intense competition from other companies for collaborative arrangements with pharmaceutical and biotechnology, companies; for establishing relationships with academic and research institutions; and for licenses to proprietary technology. These competitors, either alone or with their collaborative partners, may succeed in developing technologies or products that are more effective or less costly than ours.

Our ability to compete successfully will depend, in part, on our ability to:

develop safe and efficacious proprietary products;

obtain access to gene transfer technology on commercially reasonable terms;

obtain required regulatory approvals;

attract and retain qualified scientific and product development personnel;

obtain and enforce patents, licenses, or other proprietary protection for our products and technologies;

formulate, manufacture, market, and sell any product that we develop; and

develop and maintain products that reach the market first and are technologically superior to or are of lower cost than other products in the market;

GOVERNMENT REGULATION

The research, testing manufacturing and marketing of human therapeutics are extensively regulated in the United States and the rest of the world.

Before marketing in the United States, any therapeutic or pharmaceutical products developed by us must undergo rigorous preclinical testing (generally conducted in animals) and clinical trials in humans and an extensive regulatory clearance process implemented by the U.S. Food and Drug Administration (FDA) under the federal Food, Drug and Cosmetic Act. The FDA regulates, among other things, the development, testing, manufacture, safety, efficacy, record keeping, labeling, storage, approval, advertising, promotion, sale, and distribution of biopharmaceutical products. The regulatory review and approval process, which includes preclinical testing and clinical trials of each product candidate, is lengthy, expensive, and uncertain. Securing FDA approval requires the submission of extensive preclinical and clinical data and supporting information including manufacturing information and stability data to the FDA for each indication to establish a product candidate s safety and efficacy. The approval process takes many years, requires the expenditure of substantial resources, involves post-marketing surveillance, and may involve ongoing requirements for post-marketing studies.

Table of Contents

Before commencing clinical investigations in humans in the U.S., we must carry out preclinical testing. In addition, our proposed clinical studies require review from the Recombinant DNA Advisory Committee (RAC), which is the advisory board to the National Institutes of Health (NIH), focusing on clinical trials involving gene transfer. We typically submit a proposed clinical protocol and other product-related information to the RAC three to six months prior to the expected IND application filing date.

Preclinical tests include laboratory and animal studies to evaluate product characteristics, potential safety and efficacy. The results of these studies must be submitted to the FDA as part of an Investigational New Drug (IND) Application, which must be reviewed by the FDA before proposed clinical testing in humans can begin. The FDA has 30 days to comment on the application and if the agency has no comments, we or our clinical partner may begin clinical trials.

Clinical trials are lengthy and are typically conducted in three sequential phases, but the phases may overlap or be combined. At each stage of testing, the proposed clinical protocol must be reviewed by the FDA and reviewed and approved by an independent ethics committee or institutional review board of each participating center before it can begin. Phase 1 usually involves the initial introduction of the investigational drug into small numbers of healthy volunteers or patients to evaluate certain factors, including its safety and dose tolerance. Phase 2 usually involves trials in a limited patient population to evaluate dosage tolerance and appropriate dosage, identify possible adverse effects and safety risks, and evaluate preliminary efficacy of the drug for specific indications. Phase 3 trials usually further evaluate clinical efficacy and test further for safety by using the drug in its final form in an expanded patient population. Phase 2 and 3 trials must be registered in a government database of clinical trials. Later clinical trials may fail to support the findings of earlier trials, which can delay, limit or prevent regulatory approvals.

We filed a Phase 1 clinical protocol for review by the RAC in the fourth quarter of 2004, an IND application in January 2005, and Phase 2 protocols for review by the FDA in 2006 and 2007 for our first product candidate, SB-509, for the potential treatment of diabetic neuropathy. In addition, in 2008 we filed an IND application for SB-509 for the treatment of ALS. We have also filed Phase 1 clinical protocols for review by the RAC for our HIV (SB-728-T) and glioblastoma programs (SB-313). Both of these program protocols received unanimous approval from this committee. In December 2008 we filed an IND application for SB-728-T for the treatment of HIV/AIDS and in February 2009, initiated a Phase 1 clinical trial of this ZFP Therapeutic in subjects infected with HIV.

We have completed enrollment of subjects in our first Phase 2 clinical trial (SB-509-601) and have two other Phase 2 clinical trials (SB-509-701 and SB-509-703) in subjects with diabetic neuropathy and a Phase 2 clinical study (SB-509-801) ongoing in subjects with ALS. Although our lead therapeutic candidate, SB-509, has shown a favorable safety profile to date through Phase 1 and Phase 2 testing, there can be no assurances that such a therapy will be tolerated after prolonged dosing or that clinical efficacy or safety of the product will be demonstrated in later stage testing.

The results of the preclinical and clinical testing of a pharmaceutical product are submitted to the FDA in the form of a New Drug Application (NDA), or a Biologic License Application (BLA), for approval to commence commercial sales. In responding to an NDA or a BLA, the FDA may grant marketing approval, grant conditional approval (such as an accelerated approval), request additional information, or deny the application if the FDA determines that the application does not provide an adequate basis for approval. Most research and development projects fail to produce data sufficiently compelling to enable progression through all of the stages of development and to obtain FDA approval for commercial sale. See also *Our potential therapeutic products are subject to a lengthy and uncertain regulatory process, and we may encounter unanticipated toxicity or adverse events or fail to demonstrate efficacy, causing us to delay, suspend or terminate the development of a ZFP Therapeutic. If these potential products are not approved, we will not be able to commercialize those products*. under Risk Factors below in Part I, Item 1A of this Form 10-K.

Table of Contents

Outside the United States, our ability to market a product is contingent upon receiving marketing authorization from the appropriate regulatory authorities. The requirements governing the conduct of clinical trials, marketing authorization, pricing, and reimbursement vary widely from country to country. At present, foreign marketing authorizations are applied for at a national level; although, within the European Union (EU), registration procedures are available to companies wishing to market a product in more than one EU member state. If the regulatory authority is presented with adequate evidence of safety, quality, and efficacy, they will grant a marketing authorization. This foreign regulatory approval process involves all of the risks associated with FDA clearance discussed above.

We have hired personnel with expertise in preclinical and clinical development of therapeutic programs and products and clinical and regulatory affairs to assist us in developing our programs and obtaining appropriate regulatory approvals as required. We also intend to work with collaborators who have experience in clinical development to assist us in obtaining regulatory approvals for collaborative products. *See Risk Factors Our potential therapeutic products are subject to a lengthy and uncertain regulatory process, and if these potential products are not approved, we will not be able to commercialize those products and Regulatory approval, if granted, may be limited to specific uses or geographic areas which could limit our ability to generate revenues.*

RESEARCH AND DEVELOPMENT EXPENSES

Research and development expenses consist primarily of salaries and personnel expenses, stock-based compensation expense, laboratory supplies, pre-clinical and clinical studies, manufacturing costs, allocated facilities costs, subcontracted research expenses and expenses for trademark registration and technology licenses. Costs to acquire technologies that are utilized in research and development and that have no alternative future use are expensed as incurred. Research and development expenses were $31.2 million, $25.6 million, and $21.5 million, for 2008, 2007, and 2006, respectively. We believe that continued investment in research and development is critical to attaining our strategic objectives. We expect these expenses will increase as we increasingly focus on development of ZFP Therapeutics. Specifically, in order to develop ZFPs as commercially relevant therapeutics, we expect to expend additional resources on manufacturing, regulatory affairs and clinical research.

EMPLOYEES

As of February 1, 2009, we had 77 full-time employees, all of whom are located in Richmond, California. None of our employees are represented by a collective bargaining organization or covered by a collective bargaining agreement, nor have we experienced work stoppages. We believe that our relations with our employees are good.

AVAILABLE INFORMATION

Sangamo can be found on the internet at http://www.sangamo.com. We make available free of charge, on or through our internet site, our annual, quarterly, and current reports and any amendments to those reports filed or furnished pursuant to Section 13(a) of the Exchange Act as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Information contained in Sangamo s internet site is not part of this report.

ITEM 1A RISK FACTORS

ZFP Therapeutics have undergone limited testing in humans and our ZFP Therapeutics may fail safety studies in clinical trials.

We have initiated and completed a Phase 1 study and initiated several Phase 2 clinical trials in our lead ZFP Therapeutic program. We have completed enrollment and treatment of the patients in several trials of SB-509 for diabetic neuropathy and thus far have not observed any serious drug-related adverse events. However if our lead

Table of Contents

ZFP Therapeutic fails one of its safety studies, it could reduce our ability to attract new investors and corporate partners. In January 2005, we filed an IND application with the FDA for SB-509, a ZFP TF activator of VEGF-A, for the treatment of mild to moderate diabetic neuropathy. We have completed enrollment and treatment of a Phase 1, single blind, single dose, dose-escalation trial to measure the laboratory and clinical safety of SB-509. We have completed enrollment of a repeat-dosing Phase 2 clinical trial (SB-509-601) and have 2 other related Phase 2 trials ongoing for this indication (SB-509-701 and SB-509-703). We also have initiated a Phase 2 clinical trial (SB 509-801) to evaluate SB-509 for the treatment of ALS. A significant number of the trial subjects have received more than one dose of SB-509 during the course of these Phase 2 studies. In addition, Phase 1 clinical trials of an identical ZFP TF have been carried out in subjects with peripheral artery disease. These early studies of a ZFP Therapeutic are a highly visible test of our ZFP Therapeutic approach. Since we have increased our focus on ZFP Therapeutic research and development, investors will increasingly assess the value of our technology based on the continued progress of ZFP Therapeutic products into and through clinical trials. If clinical trials of our lead therapeutic were halted due to safety concerns, this would negatively affect our operations and the value of our stock.

The results of early Phase 1 and Phase 2 trials are based on a small number of patients over a short period of time, and our progress may not be indicative of results in a large number of patients or of long-term efficacy in late stage clinical trials.

The results in early phases of clinical testing are based upon limited numbers of patients and a limited follow-up period. Typically, our Phase 1 clinical trials for indications of safety enroll less than 50 patients. The initial results from the Phase 1 clinical trial of our ZFP Therapeutic, SB-509 product, became available in the first half of 2006 and the complete data set was presented in June 2008. The primary end point of the trial was clinical and laboratory safety; however, we collected some preliminary efficacy data that showed trends of clinical improvement in some subjects. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late stage clinical trials even after achieving promising results in earlier stage clinical trials. If a larger population of patients does not experience positive results, or if these results are not reproducible, our products may not receive approval from the FDA. Failure to confirm favorable results from earlier trials by demonstrating the safety and effectiveness of our ZFP Therapeutic products in late stage clinical trials with larger patient populations could have a material adverse effect on our business that would cause our stock price to decline significantly.

Our first Phase 2 clinical trial (SB-509-601) for safety and efficacy has enrolled 110 patients, and top-line data from this study were presented in November 2008. While these results demonstrated that the drug was well-tolerated in a repeat-dose setting, no differences were observed in neurologic end-points between the SB-509 and placebo-treated subjects. Further analysis of such data is ongoing, and there is no assurance that clinical efficacy of SB-509 can be demonstrated at later stages of testing.

We have limited experience in conducting clinical trials.

Our ZFP Therapeutics may fail to show the desired safety and efficacy in initial clinical trials. We have completed a Phase 1 trial and have several ongoing Phase 2 clinical trials, completing enrollment on one of these studies. However, the FDA will require additional clinical testing which involves significantly greater resources, commitments and expertise that may require us to enter into a collaborative relationship with a pharmaceutical company that could assume responsibility for late-stage development and commercialization. We have limited experience in conducting clinical trials and may not possess the necessary resources and expertise to complete such trials, and there is no guarantee that we will be able to enter into collaborative relationships with third parties that can provide us with the funding and expertise for such trials.

Table of Contents

We may not be able to find acceptable patients or may experience delays in enrolling patients for our clinical trials.

We may be competing for suitable patients with other clinical trials. We or the FDA may suspend our clinical trials at any time if either believes that we are exposing the subjects participating in these trials to unacceptable health risks. The FDA or institutional review boards and/or institutional biosafety committees at the medical institutions and healthcare facilities where we sponsor clinical trials may suspend any trial indefinitely if they find deficiencies in the conduct of these trials. The FDA and institutional review boards may also require large numbers of patients, and the FDA may require that we repeat a clinical trial.

Our potential therapeutic products are subject to a lengthy and uncertain regulatory process, and we may encounter unanticipated toxicity or adverse events or fail to demonstrate efficacy, causing us to delay, suspend or terminate the development of a ZFP Therapeutic. If these potential products are not approved, we will not be able to commercialize those products.

The FDA must approve any human therapeutic product before it can be marketed in the United States. The process for receiving regulatory approval is long and uncertain, and a potential product may not withstand the rigors of testing under the regulatory approval processes.

Before commencing clinical trials in humans, we must submit an Investigational New Drug (IND) application to the FDA. The FDA has 30 days to comment on the application and if the agency has no comments, we or our commercial partner may begin clinical trials.

Clinical trials are subject to oversight by institutional review boards and the FDA. In addition, our proposed clinical studies require review from the Recombinant DNA Advisory Committee (RAC), which is the advisory board to the National Institutes of Health (NIH), focusing on clinical trials involving gene transfer. We will typically submit a proposed clinical protocol and other product-related information to the RAC three to six months prior to the expected IND application filing date.

Clinical trials:

- must be conducted in conformance with the FDA s good clinical practices, within the guidelines of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) and other applicable regulations;
- must meet requirements for Institutional Review Board (IRB) oversight;
- must follow Institutional Biosafety Committee (IBC) and NIH RAC guidelines where applicable;
- must meet requirements for informed consent;
- are subject to continuing FDA oversight;
- may require oversight by a Data Safety Monitoring Board (DSMB);
- may require large numbers of test subjects; and
- may be suspended by a commercial partner, the FDA, or us at any time if it is believed that the subjects participating in these trials are being exposed to unacceptable health risks or if the FDA finds deficiencies in the IND application or the conduct of these trials.

While we have stated our intention to file additional IND applications during the next several years, this is only a statement of intent, and we may not be able to do so because the associated product candidates may not meet the necessary preclinical requirements. In addition, there can be no assurance that, once filed, an IND application will result in the actual initiation of clinical trials.

Table of Contents

As we cannot predict whether or when we will obtain regulatory approval to commercialize our product candidates, we cannot predict the timing of any future revenue from these product candidates.

We cannot commercialize any of our ZFP Therapeutics to generate revenue until the appropriate regulatory authorities have reviewed and approved the applications for the product candidates. We cannot assure that the regulatory agencies will complete their review processes in a timely manner or that we will obtain regulatory approval for any product candidate that we or our collaborators develop. Satisfaction of regulatory requirements typically takes many years, is dependent upon the type, complexity and novelty of the product and requires the expenditure of substantial resources. Regulatory approval processes outside the United States include all of the risks associated with the FDA approval process. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action or changes in FDA policy during the period of product development, clinical trials and FDA regulatory review.

If we establish drug development collaborations, our collaborators may control aspects of our clinical trials, which could result in delays and other obstacles in the commercialization of our proposed products.

For some programs we may be dependent on third party collaborators to design and conduct our clinical trials. As a result, we may not be able to conduct these programs in the manner or on the time schedule we currently contemplate. In addition, if any of these collaborative partners withdraw support for our programs or proposed products or otherwise impair their development, our business could be negatively affected.

We have increased the focus of our research and development programs on human therapeutics, which will increase operating expenditures and the uncertainty of our business.

We have significantly increased the emphasis and focus of our research and development activities on ZFP Therapeutics. This change may increase operating expenditures due to larger financial outlays to fund preclinical studies, manufacturing, and clinical research. The focus on ZFP Therapeutics will also increase the visibility of our lead therapeutic programs and the potential impact on the stock price of news releases relating to these programs.

We are conducting proprietary research to discover ZFP Therapeutic product candidates. These programs increase our financial risk of product failure, may significantly increase our research expenditures, and may involve conflicts with future collaborators and strategic partners.

Our proprietary research programs consist of research which is funded solely by the Company and in which the Company retains exclusive rights to therapeutic products generated by such research. This is in contrast to certain of our research programs that may be funded by corporate partners and in which we may share rights to any resulting products. We have conducted proprietary research since inception. However, in the past several years, our strategy has shifted toward placing greater emphasis on proprietary research and therapeutic development and we expect this trend will continue in 2009 as we continue to prosecute our Phase 2 clinical trials and bring new ZFP Therapeutics into clinical trials. Conducting proprietary research programs may not generate corresponding revenue and may create conflicts with our collaborators or strategic partners over rights to our intellectual property with respect to our proprietary research activities. Any conflict with our collaborators or strategic partners could reduce our ability to enter into future collaborations or strategic partnering agreements and negatively impact our relationship with existing collaborators and strategic partners which could reduce our revenue and delay or terminate our product development. The implementation of this strategy will involve substantially greater business risks, the expenditure of significantly greater funds than our historic research activities and will require substantial commitments of time from our management and staff.

Table of Contents

Commercialization of our technologies will depend, in part, on strategic partnering with other companies. If we are not able to find strategic partners in the future or our strategic partners do not diligently pursue product development efforts, we may not be able to develop our technologies or products, which could slow our growth and decrease the value of our stock.

We expect to rely, to some extent, on our strategic partners to provide funding in support of our research and to perform independent research and preclinical and clinical testing. Our technology is broad based, and we do not currently possess the resources necessary to fully develop and commercialize potential products that may result from our technologies or the resources or capabilities to complete the lengthy marketing approval processes that may be required for the products. Therefore, we plan to rely on strategic partnerships to help us develop and commercialize ZFP Therapeutic products. If we are unable to find strategic partners or if the partners we find are unable or unwilling to advance our programs, or if they do not diligently pursue product approval, this may slow our progress and defer our revenues. Our partners may sublicense or abandon development programs or we may have disagreements with our partners, which would cause associated product development to slow or cease. There can be no assurance that we will be able to establish strategic collaborations for ZFP Therapeutic product development. We may require significant time to secure collaborations or strategic partners because we need to effectively market the benefits of our technology to these future collaborators and strategic partners, which use the time and efforts of research and development personnel and our management. Further, each collaboration or strategic partnering arrangement will involve the negotiation of terms that may be unique to each collaborator or strategic partner. These business development efforts may not result in a collaboration or strategic partnership.

The loss of any future strategic partnering agreements would not only delay or terminate the potential development or commercialization of products we may derive from our technologies, but it may also delay or terminate our ability to test ZFP therapeutic candidates for specific genes. If any strategic partner fails to conduct the collaborative activities successfully and in a timely manner, the preclinical or clinical development or commercialization of the affected product candidates or research programs could be delayed or terminated.

Under typical strategic partnering agreements we would expect to receive revenue for the research and development of a ZFP Therapeutic product and based on achievement of specific milestones. Achieving these milestones will depend, in part, on the efforts of our strategic partner as well as our own. If we, or any strategic partner, fail to meet specific milestones, then the strategic partnership may be terminated, which could decrease our revenues.

Our gene regulation and gene modification technology is relatively new, and if we are unable to use this technology in all our intended applications, it would limit our revenue opportunities.

Our technology involves a relatively new approach to gene regulation and gene modification. Although we have generated ZFPs for thousands of gene sequences, we have not created ZFPs for all gene sequences and may not be able do so, which could limit the usefulness of our technology. In addition, while we have demonstrated the function of engineered ZFP TFs in mammalian cell culture, yeast, insects, plants, and animals, we have not yet definitively done so in humans, and the failure to do so could restrict our ability to develop commercially viable products. If we, and our collaborators or strategic partners, are unable to extend our results to new commercially important genes, experimental animal models, and human clinical studies, we may be unable to use our technology in all its intended applications. Also, delivery of ZFP TFs and ZFNs into cells and organisms, including humans, in these and other environments is limited by a number of technical hurdles, which we may be unable to surmount. This is a particular challenge for therapeutic applications of our technology that will require the use of gene transfer systems that may not be effective for the delivery of our ZFP TFs or ZFNs in a particular therapeutic application.

The expected value and utility of our ZFP TFs and ZFNs is in part based on our belief that the targeted or specific regulation of gene expression and targeted gene modification may enable us to develop a new therapeutic approach as well as to help scientists better understand the role of genes in disease, to aid their efforts

Table of Contents

in drug discovery and development. We also believe that the regulation of gene expression and targeted gene addition will have utility in agricultural applications. There is only a limited understanding of the role of specific genes in all these fields. Life sciences companies have developed or commercialized only a few products in any of these fields based on results from genomic research or the ability to regulate gene expression. We, our collaborators, or our strategic partners, may not be able to use our technology to identify and validate drug targets or to develop commercial products in the intended markets.

We may be unable to license gene transfer technologies that we may need to commercialize our ZFP TF technology.

In order to regulate or modify a gene in a cell, the ZFP TF or ZFN must be efficiently delivered to the cell. We have licensed certain gene transfer technologies for use with our Enabling Technologies, which are ZFP TFs and ZFNs used in pharmaceutical discovery research and protein production. We are evaluating these systems and other technologies that may need to be used in the delivery of ZFP TFs or ZFNs into cells for in vitro and in vivo applications, including ZFP Therapeutics. However, we may not be able to license the gene transfer technologies required to develop and commercialize our ZFP Therapeutics. We have not developed our own gene transfer technologies, and we rely on our ability to enter into license agreements to provide us with rights to the necessary gene transfer technology. The inability to obtain a license to use gene transfer technologies with entities which own such technology on reasonable commercial terms, if at all, could delay or prevent the preclinical evaluation, clinical testing, and/or commercialization of our therapeutic product candidates.

We do not currently have the infrastructure or capability to manufacture therapeutic products on a commercial scale.

In order for us to commercialize these therapeutic products directly, we would need to develop, or obtain through outsourcing arrangements, the capability to execute all of these functions. If we are unable to develop or otherwise obtain the requisite preclinical, clinical, regulatory, manufacturing, marketing, and sales capabilities, we would be unable to directly commercialize our therapeutics products which would limit our future growth.

Even if our technology proves to be effective, it still may not lead to commercially viable products.

Even if our collaborators or strategic partners are successful in using our ZFP technology in drug discovery, protein production, therapeutic development, or plant agriculture, they may not be able to commercialize the resulting products or may decide to use other methods competitive with our technology. To date, no company has received marketing approval or has developed or commercialized any therapeutic or agricultural products based on our technology. Should our technology fail to provide safe, effective, useful, or commercially viable approaches to the discovery and development of these products, this would significantly limit our business and future growth and would adversely affect our value.

Even if our product development efforts are successful and even if the requisite regulatory approvals are obtained, our ZFP Therapeutics may not gain market acceptance among physicians, patients, healthcare payers and the medical community.

A number of additional factors may limit the market acceptance of products including the following:

- rate of adoption by healthcare practitioners;
- rate of a product s acceptance by the target population;
- timing of market entry relative to competitive products;
- availability of alternative therapies;
- price of our product relative to alternative therapies;

28

Table of Contents

availability of third-party reimbursement;

extent of marketing efforts by us and third-party distributors or agents retained by us; and

side effects or unfavorable publicity concerning our products or similar products.

Adverse events in the field of gene therapy may negatively impact regulatory approval or public perception of our potential products.

Our potential therapeutic products are delivered to patients as gene-based drugs, or gene therapy. The clinical and commercial success of our potential products will depend in part on public acceptance of the use of gene therapy for the prevention or treatment of human diseases. Public attitudes may be influenced by claims that gene therapy is unsafe, and, consequently, our products may not gain the acceptance of the public or the medical community. Negative public reaction to gene therapy in general could result in greater government regulation and stricter labeling requirements of gene therapy products, including any of our products, and could cause a decrease in the demand for any products we may develop.

Our stock price is also influenced by public perception of gene therapy and government regulation of potential products.

Reports of serious adverse events in a retroviral gene transfer trial for infants with X-linked severe combined immunodeficiency (X-linked SCID) in France and subsequent FDA actions putting related trials on hold in the United States had a significant negative impact on the public perception and stock price of certain companies involved in gene therapy. Stock prices of these companies declined whether or not the specific company was involved with retroviral gene transfer for the treatment of infants with X-linked SCID, or whether the specific company s clinical trials were placed on hold in connection with these events. Other potential adverse events in the field of gene therapy may occur in the future that could result in greater governmental regulation of our potential products and potential regulatory delays relating to the testing or approval of our potential products.

We are at the development phase of operations and may not succeed or become profitable.

We began operations in 1995 and are in the early phases of ZFP Therapeutic product development. We have incurred significant losses and our net losses for the past three fiscal years ended 2008, 2007 and 2006 were $24.3 million, $21.5 million, and $17.9 million, respectively. To date, our revenues have been generated from strategic partners, Enabling Technology collaborations, and federal government and research foundation grants. Since 2005, we have placed significant emphasis on higher-value therapeutic product development and related strategic partnerships. This shift in emphasis has the potential to increase the return on investment to our stockholders by allocating capital resources to higher value, therapeutic product development activities. At the same time, it increases our financial risk by increasing expenses associated with product development. In addition, the preclinical or clinical failure of any single product, such as our Phase 2 clinical trials of SB-509, may have a significant effect on the actual or perceived value of our shares. Our business is subject to all of the risks inherent in the development of a new technology, which included the need to:

attract and retain qualified scientific and technical staff and management, particularly scientific staff with expertise to develop our early-stage technology into therapeutic products;

obtain sufficient capital to support the expense of developing our technology platform and developing, testing, and commercializing products;

develop a market for our products;

successfully transition from a company with a research focus to a company capable of supporting commercial activities; and

attract and enter into research collaborations with research and academic institutions and scientists.

Table of Contents

If our competitors develop, acquire, or market technologies or products that are more effective than ours, this would reduce or eliminate our commercial opportunity.

Any products that we or our collaborators or strategic partners develop by using our ZFP technology platform will enter into highly competitive markets. Even if we are able to generate ZFP Therapeutics that are safe and effective for their intended use, competing technologies may prove to be more effective or less expensive, which, to the extent these competing technologies achieve market acceptance, will limit our revenue opportunities. In some cases, competing technologies have proven to be satisfactorily effective and less expensive, as has been the case with technologies competitive with our Enabling Technology applications. Competing technologies may include other methods of regulating gene expression or modifying genes. ZFP TFs and ZFNs have broad application in the life sciences industry and compete with a broad array of new technologies and approaches being applied to genetic research by many companies. Competing proprietary technologies with our product development focus include:

For ZFP Therapeutics:

- small molecule drugs;
- monoclonal antibodies;
- recombinant proteins;
- gene therapy/cDNAs;
- antisense; and
- siRNA and microRNA approaches

For our Enabling Technology Applications:

- *For protein production:* gene amplification, meganucleases, insulator technology, mini-chromosomes;
- *For target validation:* antisense, siRNA; and
- *For plant agriculture:* recombination approaches, mutagenesis approaches, meganucleases, mini-chromosomes;

In addition to possessing competing technologies, our competitors include pharmaceutical and biotechnology companies with:

- substantially greater capital resources than ours;

larger research and development staffs and facilities than ours; and

greater experience in product development and in obtaining regulatory approvals and patent protection;

These organizations also compete with us to:

attract qualified personnel;

attract parties for acquisitions, joint ventures or other collaborations; and

license the proprietary technologies of academic and research institutions that are competitive with our technology, which may preclude us from pursuing similar opportunities.

Accordingly, our competitors may succeed in obtaining patent protection or commercializing products before us. In addition, any products that we develop may compete with existing products or services that are well established in the marketplace.

Table of Contents

Our collaborators or strategic partners may decide to adopt alternative technologies or may be unable to develop commercially viable products with our technology, which would negatively impact our revenues and our strategy to develop these products.

Our collaborators or strategic partners may adopt alternative technologies, which could decrease the marketability of ZFP technology. Additionally, because many of our collaborators or strategic partners are likely to be working on more than one development project, they could choose to shift their resources to projects other than those they are working on with us. If they do so, this would delay our ability to test our technology and would delay or terminate the development of potential products based on our ZFP technology. Further, our collaborators and strategic partners may elect not to develop products arising out of our collaborative and strategic partnering arrangements or to devote sufficient resources to the development, manufacturing, marketing, or sale of these products. If any of these events occur, we may not be able to develop our technologies or commercialize our products.

We anticipate continuing to incur operating losses for the next several years. If material losses continue for a significant period, we may be unable to continue our operations.

We have generated operating losses since we began operations in 1995. The extent of our future losses and the timing of profitability are uncertain, and we expect to incur losses for the foreseeable future. We have been engaged in developing our ZFP TF technology since inception, which has and will continue to require significant research and development expenditures. In July 2007, we completed a registered direct offering to institutional investors for a total of 3,278,689 shares of common stock, at a price of $9.15 per share, resulting in net proceeds to us of $28.0 million. Also in July 2007, we entered into a license agreement and a related stock purchase agreement with Sigma-Aldrich Corporation (Sigma) under which we sold to Sigma 1.0 million shares of Sangamo s common stock valued at $8.55 million. In June 2006, in an underwritten public offering and pursuant to an effective registration statement, we sold 3,100,000 shares of common stock at a public offering price of $6.75 per share, resulting in net proceeds of approximately $20.2 million. In November 2005, we completed a registered direct offering to institutional and strategic investors for a total of 5,080,000 shares of common stock at a price of $3.85 per share to the investors, resulting in net proceeds to Sangamo of approximately $18.2 million. To date, we have generated all other funding from revenues derived from strategic partnering agreements, Enabling Technology collaborations, federal government research grants and grants awarded by research foundations. As of December 31, 2008, we had an accumulated deficit of approximately $174.1 million. We expect to incur losses for the foreseeable future. These losses will increase as we expand and extend our research and development activities into human therapeutic product development. If the time required us to generate significant product revenues and achieve profitability is longer than we currently anticipate or if we are unable to generate liquidity through equity financing or other sources of funding, we may not be able to sustain our operations.

We may be unable to raise additional capital, which would harm our ability to develop our technology and products.

We have incurred significant operating losses and negative operating cash flows since inception and have not achieved profitability. We expect capital outlays and operating expenditures to increase over the next several years as we expand our infrastructure and research and ZFP Therapeutic product development activities. While we believe our financial resources will be adequate to sustain our current operations at least through 2010, we may seek additional sources of capital through equity or debt financing. In addition, as we focus our efforts on proprietary human therapeutics, we will need to seek FDA approval of potential products, a process that could cost in excess of $100 million per product. We cannot be certain that we will be able to obtain financing on terms acceptable to us, or at all. If adequate funds are not available, our business and our ability to develop our technology and ZFP Therapeutic products would be harmed.

Table of Contents

Our stock price has been volatile and may continue to be volatile, which could result in substantial losses for investors.

During the past two years, our common stock price has fluctuated significantly, ranging from a low of $1.95 to a high of $13.65 during the year ended December 31, 2008, and a low of $6.22 to a high of $19.08 during the year ended December 31, 2007. The recent market instability caused by the turmoil in the financial industry has further contributed to the volatility of our stock price. Volatility in our common stock could cause stockholders to incur substantial losses. An active public market for our common stock may not be sustained, and the market price of our common stock may continue to be highly volatile. The market price of our common stock has fluctuated significantly in response to various factors, some of which are beyond our control, including but not limited to the following:

- announcements by us or future partners providing updates on the progress or development status of ZFP Therapeutics;
- data from clinical trials;
- changes in market valuations of similar companies;
- overall market conditions;
- deviations in our results of operations from the guidance given by us or estimates of securities analysts;
- announcements by us or our competitors of new or enhanced products, technologies or services or significant contracts, acquisitions, strategic relationships, joint ventures or capital commitments;
- regulatory developments;
- additions or departures of key personnel;
- future sales of our common stock or other securities by the Company, management or directors, liquidation of institutional funds that comprised large holdings of Sangamo stock; and
- decreases in our cash balances.

Our common stock is relatively thinly traded, which means large transactions in our common stock may be difficult to conduct in a short time frame.

We have a relatively low volume of daily trades in our common stock on the Nasdaq Global Market. For example, the average daily trading volume in our common stock on the Nasdaq Global Market over the ten-day trading period prior to February 1, 2009 was approximately 168,800 shares per day. Any large transactions in our common stock may be difficult to conduct and may cause significant fluctuations in the price of our common stock.

Because it is difficult and costly to protect our proprietary rights, and third parties have filed patent applications that are similar to ours, we cannot ensure the proprietary protection of our technologies and products.

Our commercial success will depend in part on obtaining patent protection of our technology and successfully defending any of our patents that may be challenged. The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and can involve complex legal and factual questions. No consistent policy regarding the breadth of claims allowed in biotechnology patents has emerged to date. Accordingly, we cannot predict the breadth of claims allowed in patents we own or license.

We are a party to various license agreements that give us rights under specified patents and patent applications. Our current licenses, as our future licenses frequently will, contain performance obligations. If we fail to meet those obligations, the licenses could be terminated. If we are unable to continue to license these technologies on commercially reasonable terms, or at all, we may be forced to delay or terminate our product development and research activities.

Table of Contents

With respect to our present and any future sublicenses, since our rights derive from those granted to our sublicensor, we are subject to the risk that our sublicensor may fail to perform its obligations under the master license or fail to inform us of useful improvements in, or additions to, the underlying intellectual property owned by the original licensor.

We are unable to exercise the same degree of control over intellectual property that we license from third parties as we exercise over our internally developed intellectual property. We do not control the prosecution of certain of the patent applications that we license from third parties; therefore, the patent applications may not be prosecuted exactly as we desire or in a timely manner.

The degree of future protection for our proprietary rights is uncertain, and we cannot ensure that:

- we or our licensors were the first to make the inventions covered by each of our pending patent applications;
- we or our licensors were the first to file patent applications for these inventions;
- the patents of others will not have an adverse effect on our ability to do business;
- others will not independently develop similar or alternative technologies or reverse engineer any of our products, processes or technologies;
- any of our pending patent applications will result in issued patents;
- any patents issued or licensed to us or our collaborators or strategic partners will provide a basis for commercially viable products or will provide us with any competitive advantages;
- any patents issued or licensed to us will not be challenged and invalidated by third parties; or
- we will develop additional products, processes or technologies that are patentable.

Others have filed and in the future are likely to file patent applications that are similar to ours. We are aware that there are academic groups and other companies that are attempting to develop technology that is based on the use of zinc finger and other DNA-binding proteins, and that these groups and companies have filed patent applications. Several patents have been issued, although we have no current plans to use the associated inventions. If these or other patents issue, it is possible that the holder of any patent or patents granted on these applications may bring an infringement action against our collaborators, strategic partners, or us claiming damages and seeking to enjoin commercial activities relating to the affected products and processes. The costs of litigating the claim could be substantial. Moreover, we cannot predict whether we, our collaborators, or strategic partners would prevail in any actions. In addition, if the relevant patent claims were upheld as valid and enforceable and our products or processes were found to infringe the patent or patents, we could be prevented from making, using, or selling the relevant product or process unless we could obtain a license or were able to design around the patent claims. We can give no assurance that such a license would be available on commercially reasonable terms, or at all, or that we would be able to successfully design around the relevant patent claims. There may be significant litigation in the genomics industry regarding patent and other intellectual property rights, which could subject us to litigation. If we become involved in litigation, it could consume a substantial portion of our managerial and financial resources.

We cannot guarantee that third parties will not challenge our intellectual property. One of our in-licensed foreign patents, licensed to Sangamo from Johns Hopkins University which forms the basis for five European Regional Phase patents, has been revoked as a result of an opposition by a third party. Our licensor, The Johns Hopkins University, appealed the revocation but in April 2007, the European Technical Board of Appeal released its decision dismissing the appeal. This outcome may limit our ability to exclude potential competitors in the field of targeted recombination and gene correction in Europe but does not affect our ability to practice our targeted recombination and gene correction programs

in Europe. Moreover, we also hold licenses to six US patents to the technology covered by the opposed European patent, and hold licenses to related applications

Table of Contents

pending in Canada and Japan. As of February 1, 2009, US patent number US6,265,196, licensed to Sangamo from The Johns Hopkins University, was undergoing re-examination. In addition in 2008, US5,792,640, also licensed from Johns Hopkins University, completed a first re-examination process and a re-exam certificate was issued on September 9, 2008. However, a second re-exam proceeding was ordered on November 4, 2008. We cannot predict the outcome of the reexamination, which may be unfavorable to us.

We rely on trade secrets to protect technology where we believe patent protection is not appropriate or obtainable. Trade secrets, however, are difficult to protect. While we require employees, academic collaborators, and consultants to enter into confidentiality agreements, we may not be able to adequately protect our trade secrets or other proprietary information or enforce these confidentiality agreements.

Our collaborators, strategic partners, and scientific advisors have rights to publish data and information in which we may have rights. If we cannot maintain the confidentiality of our technology and other confidential information in connection with our collaborations and strategic partnerships, then we may not be able to receive patent protection or protect our proprietary information.

Failure to attract, retain, and motivate skilled personnel and cultivate key academic collaborations will delay our product development programs and our research and development efforts.

We are a small company with 77 full-time employees as of February 1, 2009, and our success depends on our continued ability to attract, retain, and motivate highly qualified management and scientific personnel and our ability to develop and maintain important relationships with leading research and academic institutions and scientists. Competition for personnel and academic and other research collaborations is intense. The success of our technology development programs depends on our ability to attract and retain highly trained personnel. We have experienced a rate of employee turnover that we believe is typical of emerging biotechnology companies. If we lose the services of personnel with the necessary skills, it could significantly impede the achievement of our research and development objectives. We are not presently aware of any plans of specific employees to retire or otherwise leave the company. If we fail to negotiate additional acceptable collaborations with academic and other research institutions and scientists, or if our existing collaborations are unsuccessful, our ZFP Therapeutic development programs may be delayed or may not succeed.

If conflicts arise between us and our collaborators, strategic partners, scientific advisors, or directors, these parties may act in their self-interest, which may limit our ability to implement our strategies.

If conflicts arise between our corporate or academic collaborators, strategic partners, or scientific advisors or directors and us, the other party may act in its self-interest, which may limit our ability to implement our strategies. Some of our academic collaborators and strategic partners are conducting multiple product development efforts within each area that is the subject of the collaboration with us. Our collaborators or strategic partners, however, may develop, either alone or with others, products in related fields that are competitive with the products or potential products that are the subject of these collaborations. Competing products, either developed by the collaborators or strategic partners or to which the collaborators or strategic partners have rights, may result in the withdrawal of partner support for our product candidates.

Some of our collaborators or strategic partners could also become competitors in the future. Our collaborators or strategic partners could develop competing products, preclude us from entering into collaborations with their competitors, fail to obtain timely regulatory approvals, terminate their agreements with us prematurely, or fail to devote sufficient resources to the development and commercialization of products. Any of these developments could harm our product development efforts.

Table of Contents

If we do not successfully commercialize ZFP-based research reagents under our license agreement with Sigma-Aldrich Corporation or ZFP-based agricultural products with Dow AgroSciences, or if Sigma or Dow AgroSciences terminates our agreements, our ability to generate revenue under these license agreements may be limited.

In July 2007, we entered into a license agreement with Sigma to collaborate in the application and development of ZFP-based products for use in the laboratory research reagents markets, and in June 2008, following a research period, Dow AgroSciences (DAS) exercised its commercial license option under a license agreement with Sangamo relating to plant agriculture. These agreements provide Sigma with access to Sangamo s ZFP technology and the exclusive right to use Sangamo s ZFP technology to develop and commercialize products for use as research reagents and to offer services in related research fields, and provide DAS with the exclusive right to develop agricultural products using our ZFP technology in plant cells, plants, or plant cell cultures. Both companies also have the right to sublicense our technology in their respective areas. In addition to upfront payments, Sangamo may also receive additional license fees, shared sublicensing revenues, royalty payments and milestone payments depending on the success of the development and commercialization of the licensed products and services covered under both agreements. The commercial milestones and royalties are based upon net sales of licensed products.

We cannot be certain that Sigma, DAS and Sangamo will succeed in the development of commercially viable products in these fields of use, and there is no guarantee that Sigma, DAS and Sangamo will achieve the milestones set forth in the respective license agreements. To the extent Sigma, DAS and Sangamo do not succeed in developing and commercializing products or if Sigma, DAS and Sangamo fail to achieve such milestones, our revenues and benefits under the license agreements will be limited. In addition, the respective license agreements may be terminated by Sigma and DAS at any time by providing us with a 90-day notice. In the event Sigma or DAS decides to terminate the license agreements, our ability to generate revenue under such license agreements will cease.

If we do not successfully commercialize certain ZFP Therapeutic programs relating to diabetic neuropathy under our agreement with JDRF, JDRF may have the right to continue to advance the program and we may lose control of the intellectual property generated in the collaboration and development of the product and may only receive a portion of the revenue generated if commercialization by JDRF is successful.

In October 2006, we entered into a Research, Development and Commercialization Agreement with JDRF. Under the agreement and subject to its terms and conditions, including our achievement of certain milestones associated with our Phase 2 clinical trial of SB-509 (SB-509-601) for the treatment of diabetic neuropathy, JDRF has paid us a total of $2.5 million through December 31, 2008. We are obligated to cover the costs of the Phase 2 trial that are not covered by JDRF s grant.

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. 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. There is no guarantee that we will be successful in commercializing a product containing SB-509 in the future. If we fail to do so under the agreement with JDRF, we may lose control of the intellectual property generated in the development of the product and may only receive a portion of the revenue generated if commercialization by JDRF is successful.

Table of Contents

Regulatory approval, if granted, may be limited to specific uses or geographic areas, which could limit our ability to generate revenues.

Regulatory approval will be limited to the indicated use for which we can market a product. Further, once regulatory approval for a product is obtained, the product and its manufacturer are subject to continual review. Discovery of previously unknown problems with a product or manufacturer may result in restrictions on the product, manufacturer, and manufacturing facility, including withdrawal of the product from the market. In Japan and Europe, regulatory agencies also set or approve prices.

Even if regulatory clearance of a product is granted, this clearance is limited to those specific states and conditions for which the product is useful, as demonstrated through clinical trials. We cannot ensure that any ZFP Therapeutic product developed by us, alone or with others, will prove to be safe and effective in clinical trials and will meet all of the applicable regulatory requirements needed to receive marketing clearance in a given country.

Outside the United States, our ability to market a product is contingent upon receiving a marketing authorization from the appropriate regulatory authorities, so we cannot predict whether or when we would be permitted to commercialize our product. These foreign regulatory approval processes include all of the risks associated with FDA clearance described above.

Our collaborations with outside scientists may be subject to change, which could limit our access to their expertise.

We work with scientific advisors and collaborators at academic research institutions. These scientists are not our employees and may have other commitments that would limit their availability to us. Although our scientific advisors generally agree not to do competing work, if a conflict of interest between their work for us and their work for another entity arises, we may lose their services. Although our scientific advisors and academic collaborators sign agreements not to disclose our confidential information, it is possible that some of our valuable proprietary knowledge may become publicly known through them, which may cause competitive harm to our business.

Laws or public sentiment may limit the production of genetically modified agricultural products in the future, and these laws could reduce our partner s ability to sell these products.

Genetically modified products are currently subject to public debate and heightened regulatory scrutiny, either of which could prevent or delay production of agricultural products. In October 2005, we entered into a Research License and Commercial Option Agreement with DAS. In June 2008, DAS exercised its option for a commercial license to our technology. Under this agreement, we will provide DAS with access to our proprietary 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. The field-testing, production, and marketing of genetically modified plants and plant products are subject to federal, state, local, and foreign governmental regulation. Regulatory agencies administering existing or future regulations or legislation may not allow production and marketing of our genetically modified products in a timely manner or under technically or commercially feasible conditions. In addition, regulatory action or private litigation could result in expenses, delays, or other impediments to our product development programs or the commercialization of resulting products.

The FDA currently applies the same regulatory standards to foods developed through genetic engineering as those applied to foods developed through traditional plant breeding. Genetically engineered food products, however, will be subject to pre-market review if these products raise safety questions or are deemed to be food additives. Governmental authorities could also, for social or other purposes, limit the use of genetically modified products created with our gene regulation technology.

Table of Contents

Even if we are able to obtain regulatory approval for genetically modified products, our success will also depend on public acceptance of the use of genetically modified products including drugs, plants, and plant products. Claims that genetically modified products are unsafe for consumption or pose a danger to the environment may influence public attitudes. Our genetically modified products may not gain public acceptance. The subject of genetically modified organisms has received negative publicity in the United States and particularly in Europe, and such publicity has aroused public debate. The adverse publicity in Europe could lead to greater regulation and trade restrictions on imports of genetically altered products. Similar adverse public reaction or sentiment in the United States to genetic research and its resulting products could result in greater domestic regulation and could decrease the demand for our technology and products.

If we use biological and hazardous materials in a manner that causes injury or violates laws, we may be liable for damages.

Our research and development activities involve the controlled use of potentially harmful biological materials as well as hazardous materials, chemicals, and various radioactive compounds typically employed in molecular and cellular biology. We routinely use cells in culture and gene delivery vectors, and we employ small amounts of radioisotopes in trace experiments. Although we maintain up-to-date licensing and training programs, we cannot completely eliminate the risk of accidental contamination or injury from the use, storage, handling, or disposal of these materials. In the event of contamination or injury, we could be held liable for damages that result, and any liability could exceed our resources. We current