

SANGAMO BIOSCIENCES INC

Form 10-K

February 26, 2013

[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, 2012

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**  
*(State or other jurisdiction of  
incorporation or organization)*

**501 Canal Boulevard,**

**Richmond, California**  
*(Address of principal executive offices)*

**68-0359556**  
*(I.R.S. Employer  
Identification No.)*

**94804**  
*(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)*

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## 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
<b>Securities registered pursuant to Section 12(g) of the Act: None</b>	

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

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 ☒

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 ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ 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. ☒

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 ☒ 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 ☒

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, 2012 (the last business day of the registrant's most recently completed second fiscal quarter), as reported on the NASDAQ Global Market was \$277,748,267. 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, 2013
Common Stock, \$0.01 par value per share	53,353,402 shares
<b>DOCUMENTS INCORPORATED BY REFERENCE</b>	

Document	Parts Into Which Incorporated
Proxy Statement for the 2013 Annual Meeting of Stockholders	Part III

**Table of Contents**

**TABLE OF CONTENTS**

	<b>Page</b>
<b><u>PART I</u></b>	
Item 1. <u>Business</u>	4
Item 1A. <u>Risk Factors</u>	25
Item 1B. <u>Unresolved Staff Comments</u>	40
Item 2. <u>Properties</u>	40
Item 3. <u>Legal Proceedings</u>	40
Item 4. <u>Mine Safety Disclosures</u>	40
<b><u>PART II</u></b>	
Item 5. <u>Market for the Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities</u>	41
Item 6. <u>Selected Financial Data</u>	43
Item 7. <u>Management's Discussion and Analysis of Financial Condition and Results of Operations</u>	43
Item 7A. <u>Quantitative and Qualitative Disclosures About Market Risk</u>	51
Item 8. <u>Financial Statements and Supplementary Data</u>	52
Item 9. <u>Changes in and Disagreements with Accountants on Accounting and Financial Disclosure</u>	75
Item 9A. <u>Controls and Procedures</u>	75
Item 9B. <u>Other Information</u>	76
<b><u>PART III</u></b>	
Item 10. <u>Directors, Executive Officers and Corporate Governance</u>	77
Item 11. <u>Executive Compensation</u>	77
Item 12. <u>Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters</u>	77
Item 13. <u>Certain Relationships and Related Transactions, and Director Independence</u>	77
Item 14. <u>Principal Accounting Fees and Services</u>	77
<b><u>PART IV</u></b>	
Item 15. <u>Exhibits and Financial Statement Schedules</u>	78

**Table of Contents**

**SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS**

Some statements contained in this report are forward-looking with respect to our operations, research, development and commercialization activities, clinical trials, operating results and financial condition. These statements involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

our strategy;

development and commercialization of our products;

clinical trials;

partnering;

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.

In some cases, you can identify forward-looking statements by terms such as: anticipates, believes, continues, could, estimates, expects, may, plans, seeks, should and will. These statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties. Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. We discuss many of these risks in greater detail under the headings Risk Factors and Management's Discussion and Analysis of Financial Results of Operations in this Form 10-K. 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.

ZFP Therapeutic® is a registered trademark of Sangamo BioSciences, Inc. This report also contains trademarks and trade names that are the property of their respective owners.

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**Table of Contents**

**PART I**

**ITEM 1 BUSINESS**

**Overview**

We are a clinical stage biopharmaceutical company focused on the research, development and commercialization of engineered DNA-binding proteins for the development of novel therapeutic strategies for unmet medical needs. Our current mission is to develop ZFP Therapeutics® through early stage clinical testing, strategically partner with biopharmaceutical companies at points of value inflection and have the partner execute late-stage clinical trials and commercial development. In the long term, our goal is to integrate marketing and development operations and to capture the value of late-stage and commercial ZFP Therapeutic products for ourselves.

We, and our licensed partners, are the leaders in the research, development and commercialization of zinc finger DNA-binding proteins (ZFPs), a naturally occurring class of proteins. We have used our knowledge and expertise to develop a proprietary technology platform. ZFPs can be engineered (Figure 2) to make ZFP nucleases (ZFNs), proteins that can be used to modify DNA sequences in a variety of ways and ZFP transcription factors (ZFP TFs), proteins that can be used to turn genes on or off. As ZFPs act at the DNA level, they have broad potential applications in several areas including human therapeutics, plant agriculture and research reagents, as well as production of transgenic animals 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-728-T, a ZFN-modified autologous T-cell product for the treatment of HIV/AIDS, is the first therapeutic application of our ZFN technology and is being evaluated in ongoing clinical trials, the most advanced of which are a Phase 2 study (SB-728-902 Cohort 5) and a Phase 1/2 study (SB-728-1102) in HIV-infected subjects. We expect to present data from these programs at appropriate scientific and medical meetings in 2013.

In January 2012, we established a collaborative partnership with Shire AG (Shire) to research, develop and commercialize some of our preclinical ZFP Therapeutic development programs, including programs in hemophilia, Huntington's disease and other monogenic diseases. We also have several proprietary preclinical programs in monogenic diseases, including hemoglobinopathies such as sickle cell disease and  $\beta$ -thalassemia and several lysosomal storage disorders. In addition, we have research stage programs in other monogenic diseases, including certain immunodeficiencies.

We believe the potential commercial applications of ZFPs are broad-based and we have also licensed our ZFP platform in fields outside human therapeutics as follows to facilitate the sale or license of ZFNs and ZFP TFs:

We have a license agreement with the research reagent company Sigma-Aldrich Corporation (Sigma). Sigma has the exclusive rights to develop and market high value laboratory research reagents based upon our ZFP technology as well as ZFP-modified cell lines for commercial production of protein pharmaceuticals and ZFP-engineered transgenic animals. Sigma is marketing ZFN-derived gene editing tools under the trademark CompoZr® and is selling transgenic animals through its SAGE™ Labs business unit.

We have a license agreement with Dow AgroSciences, LLC (DAS), a wholly owned subsidiary of Dow Chemical Corporation. Under the agreement, we have provided DAS with access to our ZFP technology and the exclusive rights to use it to modify the genomes or alter protein expression of plant cells, plants, or plant cell cultures. DAS markets our ZFN technology 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.

## **Table of Contents**

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 1, 2013, we either own outright or have exclusively licensed the commercial rights to approximately 366 patents issued in the United States and foreign national jurisdictions, and we have 508 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 intellectual property position is a critical element in our ability to research, develop, and commercialize products and services based on ZFP technology across our chosen applications.

### **DNA, Genes, and Proteins**

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 (Figure 1). Proteins are involved in virtually all cell functions. DNA, RNA, and proteins comprise many of the targets for pharmaceutical drug discovery and therapeutic intervention.

**Figure 1:**

#### **Schematic of the relationship between the human genome, DNA, RNA and protein**

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. Similarly, a mistake in the DNA sequence of a gene can result in corresponding error in the protein encoded by the gene, which may have serious consequences for the cell and its function. A number

## **Table of Contents**

of disorders have been identified that are caused by the inheritance of a single defective gene. These so-called monogenic diseases include hemophilia, Huntington's disease, sickle cell anemia and lysosomal storage disorders.

### **Zinc finger DNA-binding proteins (ZFPs) are Transcription Factors**

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). ZFPs, are the largest class of naturally occurring transcription factors in organisms from yeast to humans. In higher organisms, naturally occurring transcription factors typically comprise two principal domains: the first is a DNA-binding domain, (designated in Figure 2 as the Recognition 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. Sangamo has added to these naturally occurring functional domains to include domains enabling genome modification at the site determined by the DNA-binding domain.

**Figure 2:**

### **Schematic of the Two-Domain Structure of a ZFP Therapeutic**

#### **Engineered ZFP Nucleases (ZFNs) can be designed for Gene Modification and Engineered Zinc Finger Protein Transcription Factors (ZFP TFs) for Gene Regulation**

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-four 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, 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

## **Table of Contents**

the proximity of the gene of interest. Our ability to use our highly specific ZFP technology to precisely target a DNA sequence in a gene of interest provides us with a range of gene editing and gene regulation functions that can be applied in many different cell types.

Our engineered ZFPs can be attached to a 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. When a pair of such 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, and both domains of the restriction endonuclease must be present, in the correct orientation to interact with each other, in order to mediate DNA 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 (Figure 3). If cells are simply treated with ZFNs alone the repair process joins the two ends of the broken DNA together and frequently results in the loss of a small amount of genetic material at the site of the break. This disrupts the original DNA sequence and can result in the generation of a shortened or non-functional protein, effectively knocking out the protein. We believe that ZFN-mediated gene modification may be used to disrupt a gene that is involved in disease pathology such as disruption, or knock out, of the CCR5 gene to treat HIV infection.

In contrast, if cells are treated with ZFNs in the presence of an additional DNA sequence that encodes the correct gene sequence (referred to as a donor DNA), 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 hemophilia, sickle cell anemia or 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 broadens the range of mutations of a gene that can be corrected in a single step and eliminates the insertional mutagenesis concerns associated with traditional gene replacement approaches, in which the insertion of a new corrective copy of the gene typically occurs at random locations in the genome. Our In Vivo Protein Replacement Platform, in which our ZFN technology is used to insert a gene encoding a therapeutic protein into a safe harbor site such as the Albumin gene is an approach that we are investigating for the potential long-term treatment of hemophilia and lysosomal storage disorders.

We can also create ZFP TFs which are capable of controlling or regulating the expression of a target gene in the desired manner (Figure 3). 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. We have a preclinical ZFP Therapeutic program for Huntington's disease in which we are evaluating a ZFP TF designed to differentially down regulate the mutated disease-causing Huntingtin gene, while leaving expression of the normal gene unchanged.



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**Table of Contents**

**Figure 3:**

**ZFP Therapeutics can be designed to accomplish a range of functions in gene editing and gene regulation.**

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 in whole organisms, including mice, rats, rabbits, pigs, fruit flies, worms, zebrafish and yeast, and in plant species including canola and maize. We and our collaborators have published data in peer-reviewed scientific journals on the transcriptional function of ZFP TFs, successful and highly-specific gene modification using ZFNs and the resulting changes in the behavior of the target cell, tissue, or organism. Sigma is currently using ZFNs to generate transgenic animals and cell lines that have specific genetic modifications that make them useful models of human disease. These high value biologic tools are being used by academics, and biotechnology and pharmaceutical companies for medical research and drug development. We are currently evaluating the safety and efficacy of ZFNs in human clinical trials.

We have several strategies for the application of our ZFP Therapeutics depending on the disease or indication. We can deliver these therapeutic proteins *ex-vivo* (outside the body) to isolated cells of the blood, such as T-cells, in the case of our clinical HIV program, and hematopoietic stem cells for our preclinical programs in HIV and monogenic blood diseases such as sickle cell anemia and  $\beta$ -thalassemia. We are also developing ZFP Therapeutics in which we deliver our therapeutic proteins *in-vivo*, either systemically (directly into the blood stream) as in our hemophilia and lysosomal storage disorder programs, or directly into a specific tissue such as the brain as in our Huntington's disease program.

## **Table of Contents**

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

With our ability to generate gene-specific ZFNs for the disruption or addition/correction of target genes and DNA sequences and ZFP TFs for the activation or repression of genes and with multiple strategies for administration, we are focused on developing a new class of highly differentiated human therapeutics. We believe that as more genes are linked to specific diseases, the clinical breadth and scope of our ZFP Therapeutic applications may be substantial.

We believe that our ZFP technology provides a unique and proprietary basis for a broad new class of drugs that have differential competitive advantages over small-molecule drugs, protein pharmaceuticals and RNA-based approaches, enabling the development of therapies for a broad range of unmet medical needs.

For example, ZFP Therapeutics can:

**Provide novel activities such as gene modification and regulation of gene expression to address drug targets.** Engineered ZFNs enable the disruption, correction or targeted addition of a gene sequence and ZFP TFs enable not only repression of the expression of a therapeutically relevant gene but also its activation in a cell. This gives our technology a degree of flexibility not seen in other drug platforms. Our ZFN gene editing technology, which requires only brief cellular expression of ZFNs, allows the permanent correction of a mutation in a defective gene. This provides a novel therapeutic and potentially life-long clinical benefit in the treatment of monogenic diseases, such as hemophilia and sickle cell anemia. In contrast, direct modification of genes cannot 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 therapeutic solutions for targets that cannot be effectively addressed by existing drug modalities.** ZFNs and ZFP TFs act through a mechanism that is unique among biological drugs: direct modification or regulation 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, pharmaceutical and biotechnology companies have validated and characterized many new drug targets. Many of these targets have a direct 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 modification or regulation of disease-associated genes using engineered ZFNs or ZFP TFs. Thus, a target which may be intractable to treatment using a small molecule or monoclonal antibody can be modified, turned on or turned off at the DNA level using ZFP technology.

**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, 11997-12002; *J Neurosci.* (2010) 30(49):16469-74; *Nat Biotechnol.* (2008) 26(7):808-16 and *Nature* (2011)478(7369):391-4). In addition, as there are only two copies of each gene, there are generally only two targets per cell for a ZFP Therapeutic, which means that ZFNs and ZFP TFs 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.

**Table of Contents****THERAPEUTIC PRODUCT DEVELOPMENT****ZFP Therapeutic Product Development Programs****Figure 4:****Sangamo's ZFP Therapeutic pipeline.****Clinical Stage Programs****Product**

<b>Candidate</b>	<b>Targeted Indication</b>	<b>Stage of Development</b>	<b>Protocol</b>	<b>Milestones</b>
SB-728-T	HIV/AIDS	Phase 2	SB-728-902 Cohort 5	Trial initiated in January 2012. Expect to present data in 2013.
		Phase 1/2	SB-728-1101	Trial initiated in January 2012 Expect to present data in 2013.
		Phase 1/2	SB-728-1002	Trial initiated in October 2010.
		Phase 1	SB-728-902	Enrollment completed, in long term follow-up.
		Phase 1	SB-728-T*	Enrollment completed, in long-term follow-up.
SB-313xTZ	Glioblastoma	Phase 1	GRm13Z40-2*	Trial ongoing at City of Hope.

Table 1: Summary of ongoing clinical trials evaluating our ZFP Therapeutics.

(\*Investigator sponsored trial)

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

HIV infection results in the death of immune system cells, particularly CD4<sup>+</sup> T-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 2.5 million people were newly infected with HIV in 2011. An estimated 1.7 million people died of AIDS in the same year. There are now over 34 million people living with HIV and AIDS worldwide. The United States Centers for Disease Control and Prevention (CDC) estimates that, in 2009 in the United States alone, there were 1.2 million people living with HIV/AIDS. Approximately 50,000 new infections occurred each year between 2006 and 2009, and more than 21,000 people with AIDS died in 2009.

## **Table of Contents**

### *Current Treatments and Unmet Medical Need*

Currently, there are over 30 antiretroviral drugs approved by the U.S. Food and Drug Administration (FDA) to treat people infected with HIV. These drugs fall into four major classes: reverse transcriptase 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. The drug carries a black box warning of liver toxicity.

As HIV reproduces, 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 three 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 take antiretroviral drugs continuously. The drugs are expensive and can have significant side effects over time. There is no therapeutic approach available which protects CD4+ T-cells, reduces viral load and does not require daily dosing.

### *Sangamo's Therapeutic Approach*

Our therapeutic approach aims to use our ZFN-mediated gene editing technology to replicate a naturally occurring human mutation which renders individuals largely resistant to infection with the most common strain of HIV. CCR5 is a co-receptor for HIV entry into T-cells and if CCR5 is not expressed on their surface HIV infects them with lower efficiency. 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, CCR5 delta-32, resulting in the expression of a shortened, or truncated, and non-functional CCR5 protein. This mutation appears to have no observable deleterious effect. Individuals who carry the CCR5 delta-32 mutation on only one of their two CCR5 gene copies (heterozygotes), tend to take longer to develop AIDS and are classified as so-called long term non-progressors. In addition, a study published in *Blood* in December 2010 reported an effective cure when an AIDS patient with leukemia received a bone marrow transplant from a matched donor with this CCR5 delta-32 mutation. This approach transferred the hematopoietic stem cells (HSCs) residing in the bone marrow from the delta-32 donor, and provided a self-renewable and potentially lifelong source of HIV-resistant immune cells. After transplantation, the AIDS patient was able to discontinue all anti-HIV drug treatments, CD4 counts increased, and viral load dropped to an undetectable level, demonstrating effective transplantation of protection from HIV infection.

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, an Investigative New Drug application (IND) was filed for a Phase 1 trial of our CCR5 ZFP Therapeutic, SB-728-T. This single-dose, investigator-sponsored trial began enrolling subjects in February 2009, at the University of Pennsylvania. In September 2009, we filed an IND application and initiated a dose-escalation Phase 1 clinical trial (SB-728-902) of SB-728-T. Both Phase 1 studies were in HIV-infected individuals who were on HAART. The studies were designed primarily to evaluate the safety and tolerability of this ZFP Therapeutic approach; however, subjects' CD4 T-cell counts, levels of CCR5-modified T-cells and viral burden were also monitored. Preliminary data from both trials were presented in the first quarter of 2011 and demonstrated that the approach was well-tolerated in these subjects. In addition, we observed durable engraftment and persistence of SB-728-T, the ability of these cells to traffic to the gut mucosa and improvements the overall CD4 T-cell count and the CD4:CD8 ratio in multiple subjects.

In October 2010, we also initiated a new Phase 1/2 study (SB-728-1002) to evaluate SB-728-T in HIV-infected individuals who are not yet on HAART. We have completed accrual of this trial. In January 2012, we

## **Table of Contents**

announced the initiation of two new studies (SB-728-1101 and SB-728-902, Cohort 5), based on data from our Phase 1 trials that demonstrated a correlation between the estimated numbers of engrafted cells in which both copies of the CCR5 gene were modified (biallelic modification) and the reduction in viral load in treated subjects that underwent a HAART treatment interruption (TI). Using different approaches, both studies aim to increase the numbers of biallelically modified engrafted cells in SB-728-T-treated subjects and to evaluate the effect of increasing the numbers of these cells on the immune system and on viral load during a TI. These trials are ongoing and we expect to present data from them in 2013.

We also have a preclinical stage program to investigate this approach to treating HIV in hematopoietic stem cells. Together with our collaborators at City of Hope Medical Center and the University of Southern California, we have funding for this program from a \$14.5 million Disease Team Research Award granted by the California Institute for Regenerative Medicine (CIRM) in October 2009, of which we expect to receive a total of \$5.2 million during the term of our four-year collaboration. In 2014, we expect to file an IND application for AIDS-based lymphoma based on this work.

### ***Other Clinical Development Programs***

Clinicians at City of Hope (COH) are evaluating a ZFP Therapeutic that uses our ZFN technology to disrupt the expression of the gene encoding the glucocorticoid receptor in T-cells expressing an engineered protein known as an IL-13 zetakine. The engineered T-cells would thus be able to seek out and destroy glioblastoma cells in the brain even in the presence of glucocorticoids which have a neutralizing effect on T-cells but are frequently used to treat patients after surgery to remove the tumor.

In 2009, our collaborators at COH filed an investigator-sponsored IND application for a Phase 1 clinical trial of this therapeutic and have an ongoing Phase 1 trial in subjects with recurrent/refractory GBM. However, due to changes in the standard of care for glioblastoma patients namely the introduction of Avastin subjects with recurrent GBM are not presenting with the same pattern of recurrent tumor as when the trial protocol was conceived. Thus, subjects whose clinical profiles fit the original trial design have been difficult to recruit. We expect that our collaborators will report data if, and when, they have treated an appropriate number of subjects.

In October 2011, we discontinued development of our product candidate SB-509 which was previously being evaluated for the treatment of diabetic neuropathy, Amyotrophic Lateral Sclerosis (ALS), stroke, spinal cord injury and traumatic brain injury.

### **ZFP Therapeutic Pre-Clinical Stage Programs**

#### **Programs Partnered with Shire**

##### ***Hemophilia***

Hemophilia, a rare bleeding disorder in which the blood does not clot normally, is an example of a monogenic disease (a disease that is caused by a genetic defect in a single gene). There are several types of hemophilia caused by mutations in genes that encode factors which help the blood clot and stop bleeding when blood vessels are injured. Individuals with hemophilia experience bleeding episodes after injuries and spontaneous bleeding episodes that often leads to joint disease such as arthritis. The most prevalent form of the disease, hemophilia A, is caused by a defect in clotting Factor VIII while defects in clotting Factor IX lead to hemophilia B. The most severe forms of hemophilia affect males. According to the National Hemophilia Foundation, hemophilia A occurs in about one in every 5,000 male births in the US with approximately 25,000 males currently affected in the US, and hemophilia B in about 1 in every 25,000 male births with approximately 5,000 males currently affected. The standard treatment for individuals with hemophilia is replacement of the defective clotting factor with regular infusion of recombinant clotting factors or plasma concentrates. These therapies are expensive, carry the risk of transmission of blood-borne diseases such as hepatitis and other viral infections and sometimes stimulate the body to produce antibodies against the factors that inhibit the benefits of treatment. In these situations, other clotting factors such as Factor VII and X may be used to treat patients.

## **Table of Contents**

In collaboration with Shire we are working on four gene targets, clotting factors VII, VIII, IX and X to develop ZFP Therapeutics to treat hemophilia. Using our ZFN technology we are pursuing two approaches in the development of these therapeutics: correction of the disease-causing mutation in the endogenous copy of the Factor VIII or IX gene and addition of a new correct copy of the Factor VIII or XI gene into a safe-harbor site, the Albumin gene or locus, using our In Vivo Protein Replacement Platform. We have published data demonstrating functional correction of the human factor IX gene in the liver by direct intravenous delivery of ZFNs in a mouse model of the disease. We have ongoing preclinical studies to develop therapies for hemophilia A and B which will provide a permanent correction that would reduce or eliminate the need for infusions of clotting factor products. Our goal is to submit IND applications for these ZFP Therapeutics in 2014.

### ***Huntington s disease***

Huntington s disease (HD) is an inherited, progressive neurologic disease for which there is no treatment or cure. The disease is caused by a particular type of mutation in a single gene, the Huntingtin (HTT) gene. Most patients inherit one normal and one defective or mutant copy of the HTT gene, which is enough to cause HD. The mutation is characterized by expansion of a repeated stretch of DNA sequence within the gene called a CAG repeat. A normal copy of the HTT gene usually has 10 to 29 of these CAG repeats but a defective copy has many more generally greater than 39 repeats. While the protein produced by the normal copy of the gene appears to be essential for development (mice lacking the gene do not survive to birth), the product of the mutated gene is damaging to nerve cells. Symptoms, which include deterioration of muscle control, cognition and memory, usually develop between 35 and 44 years of age. It is known that the greater the number of CAG repeats, the earlier the onset. HD is usually fatal within 10 to 20 years after the onset of symptoms. The disease has a high prevalence for an inherited disorder, affecting approximately 30,000 people (one in 10,000) in the US. An additional 150,000 people in the U.S. carry a 50% risk of developing the disease.

Research in animal models of the disease has shown that lowering the levels of the defective HTT protein can prevent, or even reverse, disease progression. However, to date most HTT-lowering methods decrease levels of both the normal and mutant forms of HTT, raising potential safety concerns given the importance of normal HTT protein. In collaboration with Shire, we are developing ZFP TFs that can selectively repress the expression of the mutant disease-causing form of HTT while leaving expression levels of the normal gene unchanged. Preclinical studies in animal models of the disease are ongoing and our goal is to file an IND application for a ZFP Therapeutic for HD in 2015.

### **Proprietary Programs**

#### ***Hemoglobinopathies***

Mutations in the genes encoding globin, the oxygen carrying protein of red blood cells, lead to the hemoglobinopathies, sickle cell disease (SCD) and  $\beta$ -thalassemia. The mutation that gives rise to SCD causes the red blood cells to form an abnormal sickle or crescent shape. The cells are fragile and deliver less oxygen to the body s tissues. They can also get stuck more easily in small blood vessels and break into pieces that can interrupt healthy blood flow. These problems further decrease the amount of oxygen flowing to body tissues. Almost all patients with SCD have painful episodes (called crises), which can last from hours to days. Current standard of care is to manage and control symptoms, and to limit the number of crises. Treatments include blood transfusions, iron-chelation therapy and administration of hydroxyurea, pain medications and antibiotics. The CDC estimates that there are 90,000 to 100,000 Americans living with SCD which occurs in approximately 1 out of every 500 African-American births and 1 out of every 36,000 Hispanic-American births.

There are several forms of  $\beta$ -thalassemia. Broadly, the disorder results in excessive destruction of red blood cells leading to life-threatening anemia, enlarged spleen, liver and heart, and bone abnormalities. Cooley s anemia (beta thalassemia major) is a severe form of thalassemia that requires regular, often monthly, blood

## **Table of Contents**

transfusions and subsequent iron-chelation therapy to treat iron overload. The CDC estimates that 1,000 people have Cooley's anemia in the United States, and an unknown number carry the genetic trait and can pass it on to their children. Thalassemia is most common among people of Mediterranean descent and is also found among people from the Arabian Peninsula, Iran, Africa, Southeast Asia, and Southern China.

Bone marrow or stem cell transplants can be curative for both of these indications; however they are currently not an option for most patients as they are often unable to find well-matched cell donors. We are developing ZFP Therapeutics for both SCD and  $\beta$ -thalassemia based on the use of our ZFN gene editing technology in a patient's own (autologous) bone marrow stem cells. We are currently in preclinical development and our goal is to file an IND application for a product in 2014.

### ***Lysosomal Storage Disorders***

Lysosomal storage disorders (LSDs) are a heterogeneous group of inherited disorders including Fabry disease, Gaucher disease, Pompe disease and Hurler syndrome. They are caused by defects in genes that encode proteins known as enzymes, which break down and eliminate unwanted substances in the cells of the body. These enzymes are found in structures called lysosomes which act as recycling sites in cells, breaking down unwanted material into simple products for the cell to use to build new materials. A defect in a lysosomal enzyme leads to the accumulation of toxic levels of the substance that the enzyme would normally eliminate and resulting cell damage which can lead to serious health problems. There are nearly 50 of these disorders altogether and they may affect different parts of the body, including the skeleton, brain, skin, heart and central nervous system. While their individual incidence tends to be rare, this group as a whole has a prevalence of more than 1:5,000 live births according to the National Institute of Neurological Disorders and Stroke.

There is no cure for LSDs, and treatments have not yet been developed for many of these diseases. For certain disorders, including Gaucher and Fabry, enzyme replacement therapies (ERTs) are available. However, these require frequent administration, are costly and there is a risk of immunogenicity.

We are developing a genetic approach to enzyme replacement for several LSDs based on systemic delivery of our ZFN gene editing technology to the liver to enable production of the corrective enzyme by the body. We are in preclinical development with several product candidates and our goal is to file two IND applications for such product candidates in 2015.

### ***ZFP Therapeutic Research Programs***

We have research stage programs in other monogenic diseases, including certain immunodeficiency disorders.

## **CORPORATE RELATIONSHIPS**

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

### **Therapeutic Collaborations**

#### ***Collaboration and License Agreement with Shire AG in Human Therapeutics and Diagnostics***

On January 31, 2012, we entered into a collaboration and license agreement with Shire, pursuant to which we are collaborating to research, develop and commercialize human therapeutics and diagnostics based on our

## **Table of Contents**

ZFP technology. Under the agreement, the two companies may develop potential human therapeutic or diagnostic products for seven gene targets. The initial four gene targets are blood clotting Factors VII, VIII, IX and X, and products developed for such initial gene targets would be used for treating or diagnosing hemophilia. In June 2012, Shire selected a fifth gene target for the development of a ZFP therapeutic for Huntington's disease. Shire has the right, subject to certain limitations, to designate two additional gene targets. Pursuant to the agreement, we have granted Shire an exclusive, world-wide, royalty-bearing license, with the right to grant sublicenses, to use our ZFP technology for the purpose of developing and commercializing human therapeutic and diagnostic products for the gene targets.

The initial research term of the agreement is six years and is subject to extensions upon mutual agreement and under other specified circumstances. We are responsible for all research activities through the submission of an IND or European Clinical Trial Application (CTA), while Shire is responsible for clinical development and commercialization of products generated from the research program from and after the acceptance of an IND or CTA for the product. Shire will reimburse us for our internal and external research program-related costs.

Under the agreement, we received an upfront license fee of \$13.0 million. In addition, for each gene target, we are eligible to receive \$33.5 million in payments upon the achievement of specified research, regulatory, clinical development milestones, as well as \$180 million in payments upon the achievement of specified commercialization and sales milestones. The total amount of potential milestone payments for each of the seven gene targets, assuming the achievement of all specified milestones in the Agreement, is \$213.5 million. The milestone payments for each gene target through the acceptance of an IND or CTA submission total \$8.5 million. We will also receive royalty payments that are a tiered double-digit percentage of net sales of products developed under the collaboration. To date, we have not received any payments from Shire related to milestone or royalty payments.

The agreement may be terminated by (i) us or Shire, in whole or in part, for the uncured material breach of the other party, (ii) us or Shire for the bankruptcy or other insolvency proceeding of the other party and (iii) Shire, in its entirety, beginning 24 months after the effective date of the agreement upon 90 days advance written notice. In addition, Shire may terminate the agreement with respect to an individual gene target at any time, and under certain circumstances may designate a replacement gene target for a terminated gene target. As a result, actual future milestone payments could be lower than the amounts stated above.

### **Strategic Partnerships in Non Therapeutic Applications of the Technology**

#### ***Agreement with Sigma-Aldrich Corporation in Laboratory Research Reagents, Transgenic Animal and Commercial Protein Production Cell-line Engineering***

In July 2007, we entered into a license agreement with Sigma. Under the license agreement, we agreed to provide Sigma with access to its 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 we previously licensed to Dow AgroSciences LLC. Under the agreement, we and Sigma agreed to conduct a three-year research program to develop laboratory research reagents using our ZFP technology during which time we assisted Sigma in connection with its efforts to market and sell services employing our technology in the research field. We transferred the ZFP manufacturing technology to Sigma.

In October 2009, we expanded the license agreement with Sigma. In addition to the original terms of the license agreement, Sigma received exclusive rights to develop and distribute ZFP-modified cell lines for commercial production of protein pharmaceuticals and certain ZFP-engineered transgenic animals for commercial applications. Under the terms of the agreement, Sigma made an upfront cash payment of \$20.0 million, consisting of a \$4.9 million purchase of 636,133 shares of our common stock, valued at \$4.9 million, and a \$15.1 million upfront license fee. The upfront license fee was recognized on a straight-line basis from the effective date of the expanded license through July 2010, which represents the period over which we were obligated to perform research services for Sigma. Under the terms of the agreement, we are eligible to



## **Table of Contents**

receive commercial license fees of \$5.0 million based on a percentage of net sales and sublicensing revenue and thereafter a reduced royalty rate of 10.5% of net sales and sublicensing revenue. During the term of the license agreement, Sigma is obligated to pay us 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. In addition, upon the achievement of certain cumulative commercial milestones Sigma will make milestone payments to us up to an aggregate of \$25.0 million. The agreements 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. As a result, actual future milestone payments could be lower than the amounts stated above. 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.

### ***Other Programs and Partners in Transgenic Animal and Commercial Protein Production Cell-line Engineering***

Prior to our agreement with Sigma we marketed our ZFP TF and ZFN technology and intellectual property in products and areas outside ZFP Therapeutics directly to the pharmaceutical and biotechnology industry and established agreements in cell line engineering for pharmaceutical protein production and the development of transgenic animals.

### ***Pharmaceutical Protein Production***

In April 2007, we entered into a research and license agreement with Genentech, Inc. pursuant to which we provided Genentech with access to our proprietary ZFN technology for use in mammalian cell-based protein pharmaceutical production. Under this agreement, we developed and delivered to Genentech ZFNs capable of making certain targeted modifications to the genome of an identified Genentech cell line to generate cell lines with novel characteristics for protein pharmaceuticals. We also granted Genentech a non-exclusive, worldwide, sublicensable right to use our ZFNs to generate cell lines with novel characteristics for protein pharmaceutical production purposes and to generate the same targeted modifications in the Genentech cell lines using our ZFN technology. Genentech has continuing obligations to pay us an annual technology access fee and, for each product developed by Genentech containing a protein expressed by the modified cell line created using our ZFN technology, aggregate milestone payments of up to \$5.4 million upon achievement of specified milestones relating to the development and commercialization of such products. The research and license agreement continues until the later of ten years or expiration of specified patents relating to our ZFN technology covered under the agreement.

In February 2008, our relationship with Genentech was expanded under similar terms to the original agreement increasing the number of potential targets in the genome of the identified Genentech cell line against which Genentech may use or apply our ZFN technology in mammalian cell-based protein pharmaceutical production. The expanded agreement continues until the later of ten years or expiration of specified patents relating to our ZFN technology covered under the agreement.

### ***Transgenic Animals***

In April 2008, we entered into a license agreement with Open Monoclonal Technology, Inc. (OMT), pursuant to which we granted a royalty-bearing, non-exclusive, sublicensable worldwide license to OMT for the commercial use of a transgenic animal generated using our ZFN technology. For any given OMT product, OMT has the right to buy out its future royalty payment obligations under the license agreement by paying a lump sum fee to us. OMT may terminate the license agreement at any time. Either party may terminate the agreement upon a material breach by the other party.

## **Table of Contents**

In July 2008, we entered into a research and license agreement with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. (collectively, Roche), pursuant to which we provided Roche with access to aspects of our proprietary ZFN technology to generate ZFN-modified cell lines and animals having targeted modifications in a specified gene in a specified species, solely for research purposes. In December 2009, pursuant to the research and license agreement, Roche exercised an option to receive an exclusive, worldwide license to use such animals in the production of therapeutic and diagnostic products. This exclusive commercial license shall continue, on a country-by-country and product-by-product basis, until the later of 10 years after the first commercial sale in such country or the expiration of the last valid patent claim covering such product. Roche paid us an additional research fee upon the delivery of the ZFN specified in the research and license agreement, a quarterly ongoing research maintenance fee during the research term and will pay milestone payments upon the achievement of certain clinical development milestones relating to products produced under such commercial license, and low-single digit royalties on sales of such products. The aggregate milestone payments for therapeutic products will not exceed \$5.75 million, but the diagnostics milestone payments are not similarly capped. Under the research and license agreement, on a product-by-product basis, Roche has the right to buy out its future royalty payment obligations by paying specified fixed amounts

### ***Agreement with Dow AgroSciences in Plant Agriculture***

We and our collaborators have shown that ZFNs and ZFP TFs 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.

In October 2005, we entered into an exclusive commercial license with DAS. Under this agreement, we provided DAS with access to our proprietary ZFP technology and the exclusive right to use the 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 ZFNs and ZFP TFs into humans or animals for diagnostic, therapeutic, or prophylactic purposes. Our agreement with DAS provided for an initial three-year research term. 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.

We agreed to supply DAS and its sublicensees with ZFNs and ZFP TFs for both research and commercial use over the initial three year period of the agreement and have amended and extended this provision. The agreement also provides for minimum sublicense fees each year due to us every October, provided the agreement is not terminated by DAS. Annual fees range from \$250,000 to \$3.0 million and total \$25.3 million over 11 years. 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. We do not have any performance obligations with respect to the sublicensing activities to be conducted by DAS. DAS has the right to terminate the agreement at any time; accordingly, our actual sublicense fees over the term of the agreement could be lower than \$25.3 million. In addition, each party may terminate the agreement upon an uncured material breach of the agreement by 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. We amended the agreement with DAS to extend the period of reagent manufacturing and research services through December 31, 2012.

## **Table of Contents**

### **Funding from Research Foundations**

#### ***California Institute for Regenerative Medicine***

In October 2009, the California Institute for Regenerative Medicine (CIRM), a State of California entity, granted a \$14.5 million Disease Team Research Award to develop an AIDS-related lymphoma therapy based on the application of ZFN gene editing technology in stem cells. The four year grant supports an innovative research project conducted by a multidisciplinary team of investigators, including investigators from the University of Southern California, City of Hope National Medical Center and Sangamo BioSciences. We expect to receive total funding up to \$5.2 million from the total amount awarded based on expenses incurred for research and development efforts by us as prescribed in the agreement. The award is intended to substantially fund our research and development efforts related to the agreement. The State of California has the right to receive, subject to the terms and conditions of the agreement, payments from us resulting from sales of a commercial product resulting from research and development efforts supported by the grant, not to exceed two times the amount we receive in funding under the agreement with CIRM. Through December 31, 2012, we have received \$2.4 million in funding from CIRM under this agreement.

#### ***CHDI Foundation, Inc.***

In April 2011, Sangamo entered into an agreement with the CHDI Foundation (CHDI) to develop a novel therapeutic for Huntington's disease based on Sangamo's proprietary ZFP technology. The ZFP therapeutic approach targets the gene that causes Huntington's disease. Under the agreement, CHDI paid the Company \$1.3 million, the total funds due over a period of one year which substantially funded the Company's research efforts related to the agreement. During 2012, the agreement was amended to extend the project through August 2012 and to increase total potential funding from \$1.3 million to \$2.1 million, plus reimbursement for certain direct expenses related to the project. The agreement with CHDI terminated on August 31, 2012. Through December 31, 2012, we have received \$2.2 million in funding from CHDI and we do not expect receive any further funding under this agreement.

#### ***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 of SB-509, a ZFP Therapeutic that was in development for the treatment of diabetic neuropathy. Under the agreement JDRF was obligated to pay us an aggregate amount of up to \$3.0 million which was received in full by the end of 2009.

In January 2010, we amended the agreement and subject to its terms and conditions, JDRF agreed to provide additional funding of up to \$3.0 million for our Phase 2b trial in diabetic neuropathy which partially funded expenses related to the trial. In October 2011, we announced that the Phase 2b trial had failed to meet both its primary and secondary end-points and further development of SB-509 was discontinued. We received \$2.8 million of the total \$3.0 million available under the amended agreement with JDRF and we do not expect receive any further funding under this agreement.

#### ***The Michael J. Fox Foundation***

In January 2007, we entered into a partnership with the Michael J. Fox Foundation for Parkinson's Research (MJFF) to provide financial support of our program to develop ZFP TFs to activate the expression of glial cell line-derived neurotrophic factor (GDNF). Under the agreement with MJFF and subject to its terms and conditions, MJFF paid us \$1.0 million, the total funds due under the agreement, over a period of two years. In June 2010, we received a commitment for additional funding of \$0.9 million from MJFF to support further studies of ZFP TF activators of GDNF and intended to substantially fund our research efforts related to the agreement. Through December 31, 2012, we have received the entire \$1.9 million in funding available under the agreements with MJFF and we do not expect to receive any further funding under this agreement.

## **Table of Contents**

### **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 technology. 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 jurisdictions. This proprietary intellectual property includes methods relating to the design of zinc finger and TALE (Transcription activator-like effector) 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, research agreements and licensing agreements, to establish and protect our proprietary rights.

#### **Technology Licenses**

We have licensed intellectual property directed to the design, selection, and use of ZFPs, ZFNs and ZFP TFs for gene modification and regulation from the Massachusetts Institute of Technology, Johnson & Johnson, The Scripps Research Institute, The Johns Hopkins University, 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, ZFNs, and ZFP TFs under 15 families of patent filings. As of February 1, 2013, these patent filings have resulted in 21 issued U.S. patents and 40 granted foreign patents, with 6 currently pending U.S. patent applications and 30 pending applications in foreign patent offices.

We believe that these in-licensed patents and patent applications include several of the early and important patent filings directed at the design, selection, composition and use of ZFPs, ZFNs and ZFP TFs, particularly the agreements with Johns Hopkins University, the Massachusetts Institute of Technology, Johnson & Johnson and The Scripps Research Institute.

#### ***Johns Hopkins University***

We entered into a license agreement with the Johns Hopkins University on June 29, 1995, as subsequently amended, whereby Johns Hopkins University granted us a worldwide exclusive license to technology and patents relating to nuclease and gene targeting technology for all fields of use, including the right to sublicense. Under the license agreement, we are obligated to pay low single-digit royalties on licensed product sales, a low single-digit percentage of license fees received from sublicensees and a high single-digit or low teens percentage of sublicense royalties received from sublicensees for sales of products. We are subject to an annual minimum royalty, which we currently pay. The license agreement expires upon the expiration of the last patent covered by the license agreement. Although many of the JHU in-licensed patents have now expired, based on currently issued patents, the license agreement will terminate on or about February 10, 2014. Johns Hopkins University may terminate the license agreement upon a material default by us that remains uncured following written notice. We may terminate the license agreement at any time upon six months written notice.

#### ***Massachusetts Institute of Technology***

We entered into a patent license agreement with the Massachusetts Institute of Technology, or MIT, on May 9, 1996, as subsequently amended, whereby MIT granted us a worldwide exclusive license to technology and patents relating to the design, selection and use of ZFPs for all fields of use, including the right to sublicense. Under the patent license agreement, we are obligated to pay an annual license fee, low single-digit royalties of product sales, an up-front sublicense and annual sublicense fees, a percentage of its sublicense revenues, and milestone payments upon achievement of certain commercial development milestones. The aggregate milestone payments under the patent license agreement are \$450,000, of which \$150,000 has been paid. The patent license agreement expires upon the expiration of the last patent covered by the patent license agreement. Based on currently issued patents and

## **Table of Contents**

currently filed patent applications, the patent license agreement will terminate on or about September 13, 2022. MIT may terminate the license agreement upon a material default by us that remains uncured following written notice. We may terminate the license agreement at any time upon six months' written notice.

### ***Johnson & Johnson***

We entered into a sublicense agreement with Johnson & Johnson on May 9, 1996, whereby Johnson & Johnson granted us a worldwide exclusive sublicense to technology and patents for the research, development and commercialization of human and animal therapeutic and diagnostic products using engineered ZFPs, including the right to sublicense. These patents were originally exclusively licensed by Johnson & Johnson from The Scripps Research Institute. Under the sublicense agreement, we will pay low single-digit royalty payments based upon sales of license products by us or our sublicensees and a milestone payment upon the achievement of a commercial development milestone. The sublicense agreement expires upon the expiration of the last patent covered by the sublicense agreement. Based on currently issued patents and currently filed patent applications, the sublicense agreement will terminate on or about October 3, 2025. Johnson & Johnson has the right to terminate the sublicense agreement upon a breach or default by us that remains uncured following written notice of such default. We may terminate the sublicense agreement at any time upon sixty days' written notice.

### ***The Scripps Research Institute***

We entered into a license agreement with The Scripps Research Institute on March 14, 2000, as subsequently amended, whereby The Scripps Research Institute granted us a worldwide exclusive license to technology and patents for the research, development and commercialization of products and services using engineered ZFPs, excluding the use of these engineered ZFPs in plant agriculture, therapeutics and diagnostics. Under the license agreement, we are required to pay a low-single digit royalty on sales of licensed products by us and our sublicensees, subject to an annual minimum. The license agreement expires upon the expiration of the last patent covered by the license agreement. Based on currently issued patents and currently filed patent applications, the license agreement will terminate on or about June 5, 2018. Each party may terminate the license agreement upon a material default by the other party that remains uncured following written notice.

### **Sangamo Intellectual Property**

In addition to our in-licensed patent portfolio, as of February 1, 2013, we had 107 families of Sangamo-owned or co-owned patent filings, including 84 issued U.S. patents, 221 granted foreign patents, 111 pending U.S. patent applications and 361 pending foreign patent applications. These patent filings are directed to the design, composition and use of ZFPs, ZFNs, and ZFP TFs and TALE proteins. 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 and the actual dates of expirations may differ.

We believe that our licensed patents and patent applications, as well as the issued Sangamo patents and pending Sangamo patent applications, in the aggregate, will provide us with a substantial intellectual property 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 and nuclease domain design, target site arrays, ZFP libraries 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;

## **Table of Contents**

*ZFP targeted regulation of endogenous genes:* methods relating to activation and inhibition of endogenous cellular genes, modulation of ZFP-regulated gene expression by small molecules, identification of accessible regions within chromatin, regulation of tocopherol synthesis in plants, and regulation of endogenous plant genes;

*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 ocular neovascularization including age-related macular degeneration (AMD), diabetic retinopathy (DR) and retinopathy of prematurity, modulation of cardiac contractility and methods to regulate the glucocorticoid receptor, treatments for HIV (see newly issued US8268618 and US patent publication US20120294838);

*ZFN Therapeutics:* Treatments for HIV (see (see patent publication US20120309091, US20120308528 and US20120093787), SCD, beta-thalassemia, and X-linked severe combined immunodeficiency (SCID), donor integration into a safe harbor locus (see newly issued US8110379), models for Parkinson's Disease (see US patent publication US20120192301);

*Non-Therapeutic Applications of ZFPs:* 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, methods of chromatin modification, and methods of introducing exogenous nucleic acids of interest into a safe harbor locus, and methods of genome editing;

*Non-Therapeutic Applications of ZFNs:* Methods for identification of regulatory DNA sequences, prediction of patient response to drug therapeutics, and development of cell lines for improved protein production, inactivation of DHFR in a Chinese hamster ovary cell (see newly issued US8313925) or glutamine synthetase (see newly issued US8153399);

*TALE protein methods of design and use;* and

*Methods of use with stem cells* (see published US patent application US20120252122).

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, patent courts have held that a DNA sequence must be purified, isolated or modified to be patentable. 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 the 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 gene regulation 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.*

## **Table of Contents**

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. Our issued US patent US8153399 is currently the subject of a re-examination procedure. We do not know what the outcome of this procedure will be. The claims of this patent may be amended such that claim scope is reduced or the patent may be revoked as a result of this procedure.

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 plan to continue to license and generate intellectual property internally covering the design, selection, composition, and use of ZFPs; the genes encoding these proteins; and the application of ZFPs, ZFNs, and ZFP TFs in ZFP Therapeutics, and non-therapeutic applications of the technology including applications in research and plant agriculture, and intellectual property relating to TALE design and use.

## **COMPETITION**

We, and our licensed partners, are the leaders in the research, development, and commercialization of DNA binding proteins for gene modification and regulation of gene expression. We are aware of several companies focused on other methods for and modifying genes and 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, such as TALE proteins and the CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats)/Cas9 system.

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 Pfizer, Inc., GlaxoSmithKline (GSK), Novartis, Merck & Co., Inc., as well as from biotechnology companies with expertise and capabilities in small molecule discovery and development such as Gilead and Genzyme.

## **Table of Contents**

Monoclonal antibody companies and product candidates from certain biotechnology firms such as Genentech, Inc. and Amgen.

Protein pharmaceuticals under development at pharmaceutical and biotechnology companies such as Pfizer, Baxter, Bayer, Novo Nordisk, Genzyme, Shire, BioMarin, Biogen Idec and numerous other pharmaceutical and biotechnology firms.

Gene therapy companies developing gene-based products in clinical trials. uniQure's product for lipoprotein lipase deficiency (LPLD) was recently approved in Europe but no other products have yet been approved. Our competitors in this category may include but not be limited to uniQure, Bluebird bio, RegenX, Asklepios and Lentigen Corporation.

Cell therapy companies developing cell-based products. Our competitors in this category may include Dendreon and Adaptimmune.

Nuclease technologies, Life Technologies, Inc. and Cellectis SA are developing TALE nucleases and Cellectis SA and Precision BioSciences, Inc. are developing meganucleases to accomplish gene modification.

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. and Regulus Therapeutics, LLC.

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, efficacious and commercially attractive 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;

enter into collaborative and strategic partnerships with others, including our competitors, to develop our technology and product candidates;

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



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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 we develop 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

## **Table of Contents**

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.

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 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, 2007 and 2009 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 and August 2009, we filed IND applications for SB-728-T for the treatment of HIV/AIDS leading to the initiation of Phase 1 studies in February and October 2009. In October 2010 and January 2012 we initiated Phase 1/2 clinical trials and a Phase 2 trial of this ZFP Therapeutic in subjects infected with HIV.

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.

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## **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), a centralized registration procedure is available to companies wishing to market an Advanced Therapies 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, clinical manufacturing 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.

## **EMPLOYEES**

As of February 1, 2013, we had 84 full-time employees, all of whom are located at our headquarters 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**

We were incorporated in June 1995 in the state of Delaware.

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 our internet site is not part of, nor incorporated by reference into, this report.

## **ITEM 1A RISK FACTORS**

This Form 10-K contains forward-looking information based on our current expectations. Because our actual results may differ materially from any forward-looking statements made by or on our behalf, this section includes a discussion of important factors that could affect our actual future results, including, but not limited to, our revenues, expenses, net loss and loss per share.

### **Risks Relating to Development, Commercialization and Regulatory Approval of our Products and Technology**

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

In December 2008, in collaboration with scientists at the University of Pennsylvania, we filed an Investigational New Drug (IND) application for a Phase 1 trial of our CCR5 ZFN-based therapeutic, SB-728-T, for treatment of HIV/AIDS. In September 2009, we announced the FDA's review and acceptance of our IND application to initiate an open-label, repeat-dosing Phase 1 clinical trial of SB-728-T (SB-728-902). Preliminary data from these studies demonstrated that, to date, treatment of aviremic HIV-infected subjects with SB-728-T

## **Table of Contents**

has been well-tolerated. We also have an on-going Phase 2 (SB-728-902, Cohort 5) and two Phase 1/2 trials (SB-728-1101 and 1002) for this indication. In addition, we have previously completed enrollment and the treatment phase of a Phase 1 and several Phase 2 clinical trials of our ZFP Therapeutic, SB-509, for diabetic neuropathy and ALS and the drug was well tolerated in these studies. However, if one of our ZFP Therapeutic fails one of its safety studies, it could reduce our ability to attract new investors and corporate partners.

All of these studies are designed primarily to evaluate the safety and tolerability of this ZFP Therapeutic approach. Our clinical studies are a highly visible test of our ZFP Therapeutics. Since we have increased our focus on therapeutic research and development, investors 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 ZFP Therapeutic products were halted due to safety concerns, this would negatively affect our operations and the value of our stock.

### ***Our progress in early Phase 1 and Phase 2 trials may not be indicative 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 25 patients. Our Phase 2 and late-stage clinical trials generally enroll a larger number of patients. Accordingly, any positive data obtained in early Phase 1 and Phase 2 trials may not be indicative of long-term efficacy in late-stage clinical trials. In September 2011, we announced preliminary data from our Phase 1 clinical program to develop SB-728-T for the treatment of HIV/AIDS. The data demonstrated a statistically significant relationship between SB-728-T and the reduction of HIV viral load. In January 2012, we initiated a Phase 2 clinical study (SB-728-902, Cohort 5) and a Phase 1/2 clinical study (SB-728-1101) for the treatment of HIV/AIDS and we expect to present data from these trials in 2013. However, there is no guarantee that these and other future studies of SB-728-T in later stage trials involving larger patient groups may produce positive results.

In addition, the initial results from the Phase 1 clinical trial of our ZFP Therapeutic product, SB-509, 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. Notwithstanding this preliminary efficacy data, the top-line data from our Phase 2b clinical study for SB-509-901 did not meet the key primary or secondary endpoints for the study and as a result we have discontinued development of our SB-509 program in October 2011.

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 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.

## **Table of Contents**

Before commencing clinical trials in humans, we must submit an 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. 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. 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.

***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 an ongoing Phase 2 trial and two Phase 1/2 studies of a ZFP Therapeutic for HIV/AIDS. However, the FDA will require additional clinical testing which involves significantly greater resources, commitments and expertise and so it is likely that we would 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. In our collaborative agreement to develop ZFP Therapeutics with Shire, we are responsible for all activities through submission of IND Applications and European Clinical Trial Applications (CTA) and Shire is responsible for clinical development and commercialization of products arising from the alliance.

***While we have stated that we intend to file IND applications for several ZFP Therapeutic programs over the next three years, we may encounter difficulties that may delay, suspend or scale back our efforts.***

We have previously announced a strategy for our ZFP Therapeutic programs that enables the potential filing of seven IND applications by the end of 2015. The preparation and submission of IND applications requires us to conduct rigorous and time-consuming pre-clinical testing,

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studies, and documentation relating to, among other things, the toxicity, safety, manufacturing, chemistry and clinical protocol of new ZFP Therapeutic products. We may experience unforeseen difficulties that could delay or otherwise prevent us from executing this strategy

## **Table of Contents**

successfully. For example, we may encounter problems in the manufacturing of our ZFP Therapeutic products and fail to demonstrate consistency in the formulation of the drug. Our pre-clinical tests may produce negative or inconclusive results, which may lead us to decide, or regulators may require us, to conduct additional pre-clinical testing. If we cannot obtain positive results in pre-clinical testing, we may decide to abandon the projects altogether. Furthermore, the filing of several IND applications involves significant cost and labor, and we may not have sufficient resources and personnel to complete the filing of all intended IND applications, which may force us to scale back the number of IND applications or forego potential IND applications that we believe are promising. Any delay, suspension or reduction of our efforts to pursue our pre-clinical and IND strategy could have a material adverse effect on our business and cause our stock price to decline.

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

We may experience difficulties or delays in recruiting and enrolling a sufficient number of patients to participate in our clinical trials due to a variety of reasons, including competition from other clinical trial programs for the same indication, failure of patients to meet our enrollment criteria and premature withdraws of patients prior to the completion of clinical 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. Any delay resulting from our failure to enroll a sufficient number of patients on a timely basis may have a material adverse affect on our business.

***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 ensure 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.

***Regulatory approval, if granted, will 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 appropriate regulatory authorities; therefore 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.

## **Table of Contents**

***Commercialization of our technologies will depend, in part, on strategic partnering with other companies. If we are not able to find partners in the future or our 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 partners or if the partners we find, such as Shire, 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 further strategic collaborations for ZFP Therapeutic product development. We may require significant time to secure collaborations or partners because we need to effectively market the benefits of our technology to these future collaborators and partners, which may direct the attention and resources of our research and development personnel and management away from our primary business operations. Further, each collaboration or partnering arrangement will involve the negotiation of terms that may be unique to each collaborator or partner. These business development efforts may not result in a collaboration or partnership.

The loss of 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 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 partnering agreements we would expect to receive revenue for the research and development of a ZFP Therapeutic product based on achievement of specific milestones, as well as royalties based on a percentage of sales of the commercialized products. Achieving these milestones will depend, in part, on the efforts of our partner as well as our own. If we, or any partner, fail to meet specific milestones, then the partnership may be terminated, which could reduce our revenues. For more information on risks relating to our third party collaborative agreements, see Risks Relating to our Collaborative Relationships.

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

In order to regulate or modify a gene in a cell, the ZFP must be efficiently delivered to the cell. We have licensed certain gene transfer technologies for our ZFP in research. We are evaluating these systems and other technologies that may need to be used in the delivery of ZFP 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. Our approach has been to license appropriate technology as required. 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, drug development collaborations, clinical testing, and/or commercialization of our therapeutic product candidates.



## **Table of Contents**

***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 to do so, which could limit the usefulness of our technology. In addition, while we have demonstrated the function of engineered ZFNs and ZFP TFs in mammalian cells, yeast, insects, plants, and animals, we have not yet demonstrated clinical benefit of this technology 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.

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

Effective delivery of ZFNs and ZFP TFs into the appropriate target cells and tissues is critical to the success of the therapeutic applications of our ZFP technology. In order to have a meaningful therapeutic effect, the ZFP Therapeutic must be delivered to sufficient numbers of cells in the targeted tissue. The ZFN or ZFP TF must be present in that tissue for sufficient time to effect either modification of a therapeutically relevant gene or regulation of its expression. In our current clinical and preclinical programs, we administer our ZFP Therapeutics as a nucleic acid that encodes the ZFN or ZFP TF. We use different formulations to deliver the ZFP Therapeutic depending on the required duration of expression, the targeted tissue and the indication that we intend to treat. However, there can be no assurances that we will be able to effectively deliver our ZFNs and ZFP TFs to produce a beneficial therapeutic effect.

***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 us or by grant funding and in which we retain 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. 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 partnering agreements and negatively impact our relationship with existing collaborators and partners which could reduce our revenue and delay or terminate our product development. As we continue to focus our strategy on proprietary research and therapeutic development, we expect to experience greater business risks, expend significantly greater funds and require substantial commitments of time from our management and staff.

## **Table of Contents**

*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 our ZFP Therapeutic 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;

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.

Therefore, even after we have obtained the required regulatory approval for our ZFP Therapeutic products, we may not be able to commercialize these products successfully if we cannot achieve an adequate level of market acceptance.

*We do not currently have the infrastructure or capability to manufacture, market and sell therapeutic products on a commercial scale.*

In order for us to commercialize our therapeutic products directly, we would need to develop, or obtain through outsourcing arrangements, the capability to manufacture, market and sell our products on a commercial scale. Currently we do not have the ability nor the financial resources to establish the infrastructure and organizations needed to execute these functions, including such infrastructure needed for the commercialization of any product from our HIV/AIDS programs, which can be complex and costly. If we are unable to establish adequate manufacturing, sales, marketing and distribution capabilities, we will not be able to directly commercialize our therapeutics products, which would limit our future growth.

## **Risks Relating to our Industry**

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

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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 effective and less expensive. Competing technologies may include other methods of regulating gene expression or modifying genes. ZFNs and ZFP TFs

## **Table of Contents**

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 but are not limited to:

For ZFP Therapeutics:

small molecule drugs;

monoclonal antibodies;

recombinant proteins;

gene therapy/cDNAs;

antisense;

siRNA and microRNA approaches, exon skipping;

TALE proteins; and

Meganucleases.

For our Non-Therapeutic Applications:

*For protein production:* gene amplification, meganucleases, TALE technology, insulator technology, mini-chromosomes and CRISPR/Cas9 technology;

*For target validation:* antisense, siRNA, TALE technology and CRISPR/Cas9 technology;

*For plant agriculture:* recombination approaches, mutagenesis approaches, meganucleases, TALE technology, CRISPR/Cas9 technology, mini-chromosomes; and

*For transgenic animals:* somatic nuclear transfer, embryonic stem cell, TALE, CRISPR/Cas9 technology and transposase technologies.

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.

***Adverse public perception in the field of gene therapy may negatively impact regulatory approval of, or demand for, 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

## **Table of Contents**

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.

***Laws or public sentiment may limit the production of genetically modified agricultural products, and these laws could reduce our partner's ability to sell such 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. We have a research license and commercial option agreement with DAS through which we 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.

Even if the regulatory approval for genetically modified products developed under our agreement with DAS was obtained, 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.

## **Risks Relating to our Finances**

***We have incurred significant operating losses since inception and anticipate that we will incur continued losses for the foreseeable future.***

We have generated operating losses since we began operations in 1995. Our net losses for the three years ended December 31, 2012, 2011 and 2010 were \$22.3 million, \$35.8 million and \$24.9 million, respectively. 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 technology since inception, which has and will continue to require significant research and development expenditures. To date, we have generated our funding from issuance of equity securities, revenues derived from strategic partnering agreements, other collaborations in non-therapeutic applications of our technology, federal government research grants and grants awarded by research foundations. As of December 31, 2012, we had an accumulated deficit of \$275.5 million. From 2005 to date, we have generated an aggregate of approximately \$157.2 million in net proceeds from the sale of our equity securities. We expect to continue to incur additional operating losses for the next several years as we continue to expand and extend our research and development activities into human therapeutic product development. If the time required 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 be forced to curtail or suspend our operations.

## **Table of Contents**

*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 2013, we may need to seek additional sources of capital through equity or debt financing. Since the financial crisis in 2008, the credit markets have experienced significant upheaval, while the equity market has exhibited a high degree of volatility. These external factors have contributed to the difficulty of emerging biotechnology companies in raising capital through equity or debt financing. While we have observed improvements in the capital market recently, we cannot be certain that this trend will continue or that we will not experience similar difficulties in accessing the capital market in the future. 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 hundreds of millions of dollars per product. We cannot be certain that we will be able to obtain financing on terms acceptable to us, or at all. Our failure to obtain adequate and timely funding will materially adversely affect our business and our ability to develop our technology and ZFP Therapeutic products. Furthermore, any sales of additional equity securities may result in dilutions to our stockholders and any debt financing may include business and financial covenants that restricts our operations.

*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, and we have incurred significant losses since inception. To date, our revenues have been generated from strategic partners, other collaborations in non-therapeutic applications of our technology, and federal government and research foundation grants. Our focus on higher-value therapeutic product development and related strategic partnerships requires us to incur substantial expenses associated with product development. In addition, the preclinical or clinical failure of any single product may have a significant effect on the actual or perceived value of our stock. Our business is subject to all of the risks inherent in the development of a new technology, which includes 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; and

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

### **Risks Relating to our Relationships with Collaborators and Strategic Partners**

*If conflicts arise between us and our collaborators or strategic partners, 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 or strategic partners 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.

## **Table of Contents**

Some of our collaborators or strategic partners could also become our 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.

***Our collaborators and strategic partners 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 and strategic partners 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, which may negatively impact our business operations. In addition, if any of these collaborators or strategic partners withdraws support for our programs or proposed products or otherwise impair their development; our business could be negatively affected.

On January 31, 2012, we entered into a research and collaborative agreement with Shire AG (Shire), pursuant to which we are engaging in a joint program with Shire to research, develop and commercialize human therapeutics and diagnostics for hemophilia and other monogenic diseases based on our ZFP technology. Under this agreement, we are responsible for all research activities through the submission of an IND or European Clinical Trial Application (CTA), while Shire is responsible for clinical development and commercialization of products generated from the research program from and after the acceptance of an IND or CTA for the product. Under the agreement, we may be eligible to receive milestone payments upon the achievement of specified clinical development, commercialization and post-commercialization milestones. The total amount of potential milestone payments for each gene target, assuming the achievements of all specified milestones in the agreement, is \$213.5 million. We will also receive royalty payments based on specified percentages of net sales of products. Once an IND or CTA is submitted, Shire will have control and broad discretion over all aspects of the clinical development and commercialization of any product developed under the program, and we will have little, if any, influence on how such programs will be conducted. Our lack of control over the clinical development of gene targets in our agreement with Shire could cause delays or other difficulties in the development and commercialization of our product candidates, which may prevent us from receiving any milestone, royalty payments and other benefits under the agreement.

***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.

***If we do not successfully commercialize ZFP-based research reagents, ZFP-modified cell lines for commercial protein production, or ZFP-engineered transgenic animals 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. The agreement provides



## **Table of Contents**

Sigma with access to our ZFP technology and the exclusive right to use our ZFP technology to develop and commercialize products for use as research reagents and to offer services in related research fields. This relationship was expanded in October 2009 when we amended our license agreement with Sigma to provide Sigma with the exclusive rights to develop and distribute ZFP-modified cell lines for commercial production of protein pharmaceuticals and, certain ZFP-engineered transgenic animals for commercial applications. In June 2008, following a research period, Dow AgroSciences (DAS) exercised its commercial license option under a license agreement with us relating to plant agriculture. This agreement provides 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, we 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 typically based upon net sales of licensed products.

We cannot be certain that we or our collaboration partners will succeed in the development of commercially viable products in these fields of use, and there is no guarantee that we or our collaboration partners will achieve the milestones set forth in the respective license agreements. To the extent we or our collaboration partners do not succeed in developing and commercializing products or if we or our collaboration partners 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.

***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.

## **Risks Relating to our Intellectual Property and Business Operation**

***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.

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

## **Table of Contents**

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 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, TALE 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 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.



## **Table of Contents**

*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 currently carry insurance covering certain claims arising from our use of these materials. However, if we are unable to maintain our insurance coverage at a reasonable cost and with adequate coverage, our insurance may not cover any liability that may arise. We are subject to federal, state, and local laws and regulations governing the use, storage, handling, and disposal of these materials and specified waste products. To date, we have not experienced significant costs in complying with regulations regarding the use of these materials.

*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 84 full-time employees as of February 1, 2013, 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. 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. 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.

## **Risks Relating to our Common Stock and Corporate Organization**

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

During the quarter ended December 31, 2012, the closing price our common stock price, as reported by the NASDAQ Global Market, ranged from a low of \$5.05 to high of \$6.35. During the past two fiscal years our common stock price has fluctuated, ranging from a low of \$2.95 to a high of \$6.49 during the year ended December 31, 2012, and a low of \$2.36 to a high of \$8.66 during the year ended December 31, 2011. The market instability caused by the financial crisis of 2008 has 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 collaborators providing updates on the progress or development status of ZFP Therapeutics;

data from clinical trials;

initiation or termination of clinical trials;

changes in market valuations of similar companies;

overall market and economic conditions;

deviations in our results of operations from the guidance given by us or estimates of securities analysts;



## **Table of Contents**

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 us, management or directors, liquidation of institutional funds that comprised large holdings of our stock; and

decreases in our cash balances.

***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. These external events may have a negative impact on public perception of our business, which could cause our stock price to decline.

***Anti-takeover provisions in our certificate of incorporation and Delaware law could make an acquisition of the Company more difficult and could prevent attempts by our stockholders to remove or replace current management.***

Anti-takeover provisions of Delaware law and in our certificate of incorporation and our bylaws may discourage, delay or prevent a change in control of our company, even if a change in control would be beneficial to our stockholders. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. In particular, under our certificate of incorporation our board of directors may issue up to 5,000,000 shares of preferred stock with rights and privileges that might be senior to our common stock, without the consent of the holders of the common stock. Moreover, without any further vote or action on the part of the stockholders, the board of directors would have the authority to determine the price, rights, preferences, privileges, and restrictions of the preferred stock. This preferred stock, if it is ever issued, may have preference over, and harm the rights of, the holders of common stock. Although the issuance of this preferred stock would provide us with flexibility in connection with possible acquisitions and other corporate purposes, this issuance may make it more difficult for a third party to acquire a majority of our outstanding voting stock.

Similarly, our authorized but unissued common stock is available for future issuance without stockholder approval.

In addition, our bylaws:

state that stockholders may not act by written consent but only at a stockholders' meeting;

establish advance notice requirements for nominations for election to the board of directors or proposing matters that can be acted upon at stockholders' meetings; and

prohibit stockholders from calling a special meeting of stockholders.



**Table of Contents**

We are also subject to Section 203 of the Delaware General Corporation Law, which provides, subject to certain exceptions, that if a person acquires 15% of our voting stock, the person is an interested stockholder and may not engage in business combinations with us for a period of three years from the time the person acquired 15% or more of our voting stock.

**ITEM 1B UNRESOLVED STAFF COMMENTS**

None.

**ITEM 2 PROPERTIES**

We currently lease approximately 27,000 square feet of research and office space located at 501 Canal Boulevard in Richmond, California. The lease expires in August of 2014. We believe such facilities are sufficient for the foreseeable future.

**ITEM 3 LEGAL PROCEEDINGS**

We are not a party to any material pending legal proceeding. From time to time, we may be involved in legal proceeding arising in the ordinary course of business.

**ITEM 4 MINE SAFETY DISCLOSURES**

Not Applicable.



**Table of Contents****PART II****ITEM 5 MARKET FOR THE REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES**

Our common stock has traded on the NASDAQ Global Market under the symbol **SGMO** since our initial public offering on April 6, 2000.

The high and low closing prices of our common stock for each quarterly period during the last two fiscal years as reported by the NASDAQ Global Market were as follows:

**Common Stock**

	Price	
	High	Low
Year ended December 31, 2012		
First Quarter	\$ 5.67	\$ 2.95
Second Quarter	\$ 5.58	\$ 4.13
Third Quarter	\$ 6.49	\$ 4.90
Fourth Quarter	\$ 6.35	\$ 5.05
Year ended December 31, 2011		
First Quarter	\$ 8.66	\$ 6.77
Second Quarter	\$ 8.36	\$ 5.59
Third Quarter	\$ 6.52	\$ 4.18
Fourth Quarter	\$ 3.45	\$ 2.36

**Holders**

As of February 1, 2013, there were 73 holders of record of Sangamo's common stock. This number does not include street name or beneficial holders, whose shares are held of record by banks, brokers, financial institutions and other nominees.

**Dividends**

Sangamo has not paid dividends on its common stock, and currently does not plan to pay any cash dividends in the foreseeable future.

**Stock Trading Plans**

Our directors, executive officers and other insiders, including Edward O. Lanphier II, President and CEO, have adopted stock trading plans pursuant to Rule 10b5-1 of the Securities Exchange Act of 1934, as amended, and have made sales, from time to time, pursuant to such plans.

**Table of Contents**

**Stock Performance Graph**

*The above Stock Performance Graph and related information shall not be deemed soliciting material or to be filed with the Securities and Exchange Commission, nor shall such information be incorporated by reference into any future filing under the Securities Act of 1933 or Securities Exchange Act of 1934, each as amended, except to the extent that the Company specifically incorporates it by reference into such filing.*

**Table of Contents****ITEM 6 SELECTED FINANCIAL DATA**

The following Selected Financial Data should be read in conjunction with Item 7 Management's Discussion and Analysis of Financial Condition and Results of Operations and Item 8 Financial Statements and Supplementary Data included elsewhere in this Annual Report on Form 10-K.

**Selected Financial Data**

	2012	Year Ended December 31,			2008
		2011	2010	2009	
(In thousands, except per share data)					
<b>Statement of Operations Data:</b>					
Total revenues	\$ 21,655	\$ 10,319	\$ 20,805	\$ 22,187	\$ 16,186
Operating expenses:					
Research and development	31,709	32,098	33,154	28,984	31,229
General and administrative	12,144	14,042	12,586	12,605	10,332
Total operating expenses	43,853	46,140	45,740	41,589	41,561
Loss from operations	(22,198)	(35,821)	(24,935)	(19,402)	(25,375)
Other income/(expense)	(66)	71	81	815	1,073
Net loss	\$ (22,264)	\$ (35,750)	\$ (24,854)	\$ (18,587)	\$ (24,302)
Basic and diluted net loss per common share	\$ (0.42)	\$ (0.71)	\$ (0.55)	\$ (0.44)	\$ (0.60)
Shares used in computing basic and diluted net loss per common share	52,741	50,512	45,167	42,048	40,825

	2012	2011	As of December 31,		2008
			2010	2009	
(In thousands)					
<b>Balance Sheet Data:</b>					
Cash, cash equivalents, marketable securities, and interest receivable	\$ 76,321	\$ 84,463	\$ 60,622	\$ 85,281	\$ 65,025
Working capital	59,575	78,488	54,222	70,116	54,221
Total assets	82,533	87,336	62,999	87,439	67,850
Accumulated deficit	(275,509)	(253,245)	(217,495)	(192,641)	(174,054)
Total stockholders' equity	64,896	80,132	55,907	71,782	55,396

**ITEM 7 MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS**

The discussion in Management's Discussion and Analysis of Financial Condition and Results of Operations contains trend analysis, estimates and other forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. These forward-looking statements include, without limitation, statements containing the words "believes," "anticipates," "expects," "continue," and other words of similar import or the negative of those terms or expressions. Such forward-looking statements are subject to known and unknown risks, uncertainties, estimates and other factors that may cause the actual results, performance or achievements of the Company, or industry results, to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements. Actual results could differ materially from those set forth in such forward-looking statements as a result of, but not limited to, the Risk Factors described in Part I, Item 1A. You should read the following discussion and analysis along with the Selected Financial Data and the financial statements and notes attached to those statements included elsewhere in this report.



## **Table of Contents**

### **Overview**

We are a clinical stage biopharmaceutical company focused on the research, development and commercialization of engineered DNA-binding proteins for the development of novel therapeutic strategies for unmet medical needs. Our scientific and business development endeavors currently focus on the engineering of novel zinc finger DNA-binding proteins (ZFPs) for the regulation and modification of genes. Our strategy is to develop highly specific ZFP nucleases (ZFNs) and ZFP transcription factors (ZFP TFs) through early stage clinical testing and strategically partner with biopharmaceutical companies at points of value inflection to execute late-stage clinical trials and commercial development. In the long term, our goal is to forward integrate to capture the value of late-stage and commercial ZFP Therapeutic products for ourselves.

We have incurred net losses since inception and expect to incur losses in the future as we continue our research and development activities. To date, we have funded our operations primarily through the issuance of equity securities, borrowings, payments from corporate collaborations and research grants.

Our revenues have consisted primarily of revenues from our corporate partners for ZFNs and ZFP TFs, contractual payments from strategic partners for research programs and research milestones, and research grant funding. We expect revenues will continue to fluctuate from period to period and there can be no assurance that new collaborations or partner funding will continue beyond their initial terms or that we are able to meet the milestones specified in these agreements.

In the development of our ZFP technology platform, we are focusing our resources on higher-value ZFP Therapeutic product development. We are conducting a Phase 2 and two Phase 1/2 clinical trials to evaluate a ZFP Therapeutic for the treatment of HIV/AIDS. Development of novel therapeutic products is costly and is subject to a lengthy and uncertain regulatory process by the FDA. Our future products will be gene-based therapeutics. Adverse events in both our own clinical program and other programs may have a negative impact on regulatory approval, the willingness of potential commercial partners to enter into agreements and the perception of the public.

In January 2012, we established a collaborative partnership with Shire AG (Shire) to research, develop and commercialize some of our preclinical ZFP Therapeutic development programs, including programs in hemophilia, Huntington's disease and other monogenic diseases. We also have several proprietary preclinical programs in monogenic diseases, including hemoglobinopathies such as sickle cell disease (SCD) and  $\beta$ -thalassemia and several lysosomal storage disorders. In addition, we have research stage programs in other monogenic diseases, including certain immunodeficiencies.

For the year ended December 31, 2012, we incurred a consolidated net loss of \$22.3 million, or \$0.42 per share, compared to a net loss of \$35.8 million, or \$0.71 per share, for the same period in 2011. As of December 31, 2012, we had cash, cash equivalents, marketable securities and interest receivable totaling \$76.3 million compared to \$84.5 million as of December 31, 2011. As of December 31, 2012, we had an accumulated deficit of \$275.5 million.

The accompanying discussion and analysis of our financial condition and results of operations are based upon our consolidated financial statements and the related disclosures, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates, assumptions and judgments that affect the reported amounts in our consolidated financial statements and accompanying notes. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. We believe the following policies to be the most critical to an understanding of our financial condition and results of operations because they require us to make estimates, assumptions and judgments about matters that are inherently uncertain.

## **Table of Contents**

### ***Revenue Recognition***

Revenues from research activities made under strategic partnering agreements and collaborations are recognized as the services are provided when there is persuasive evidence that an arrangement exists, delivery has occurred, the price is fixed or determinable, and collectability is reasonably assured. Revenue generated from research and licensing agreements typically includes upfront signing or license fees, cost reimbursements, research services, minimum sublicense fees, milestone payments and royalties on future licensee's product sales.

*Multiple Element Arrangements prior to the adoption of ASU No. 2009-13, Revenue Recognition – Multiple Deliverable Revenue Arrangements (ASU 2009-13).* For revenue arrangements entered into before January 1, 2011, that include multiple deliverables, the elements of such agreement were divided into separate units of accounting if the deliverables met certain criteria, including whether the fair value of the delivered items could be determined and whether there was evidence of fair value of the undelivered items. In addition, the consideration was allocated among the separate units of accounting based on their fair values, and the applicable revenue recognition criteria are considered separately for each of the separate units of accounting. Prior to the adoption of ASU 2009-13, we recognized nonrefundable signing, license or non-exclusive option fees as revenue when rights to use the intellectual property related to the license were delivered and over the period of performance obligations if we had continuing performance obligations. We estimated the performance period at the inception of the arrangement and reevaluated it each reporting period. Changes to these estimates were recorded on a prospective basis.

*Multiple Element Arrangements after the adoption of ASU 2009-13.* ASU 2009-13 amended the accounting standards for certain multiple element revenue arrangements to:

provide updated guidance on whether multiple elements exist, how the elements in an arrangement should be separated, and how the arrangement consideration should be allocated to the separate elements;

require an entity to allocate arrangement consideration to each element based on a selling price hierarchy, also called the relative selling price method, where the selling price for an element is based on vendor-specific objective evidence ( VSOE ), if available; third-party evidence ( TPE ), if available and VSOE is not available; or the best estimate of selling price ( ESP ), if neither VSOE nor TPE is available; and

eliminate the use of the residual method and require an entity to allocate arrangement consideration using the selling price hierarchy. For revenue agreements with multiple element arrangements, such as license and development agreements, entered into on or after January 1, 2011, the Company will allocate revenue to each non-contingent element based on the relative selling price of each element. When applying the relative selling price method, the Company determines the selling price for each deliverable using VSOE of selling price or TPE of selling price. If neither exists the Company uses ESP for that deliverable. Revenue allocated is then recognized when the basic four revenue recognition criteria are met for each element. The collaboration and license agreement entered into with Shire in January 2012 was evaluated under these updated accounting standards.

Additionally, the Company recognizes milestone payments, which are subject to substantive contingencies, upon completion of specified milestones, which represents the culmination of an earnings process, according to contract terms. Fees from licensees upon sublicensing Sangamo technologies by them to third parties (sublicense fees) are recognized as revenue in the period such fees are due. Minimum annual sublicense fees are also recognized as revenue in the period in which such fees are due. Royalty revenues are generally recognized when earned and collectability of the related royalty payment is reasonably assured. The Company recognizes cost reimbursement revenue under collaborative agreements as the related research and development costs for services are rendered. Deferred revenue represents the portion of research or license payments received which have not been earned.

**Table of Contents**

Sangamo's research grants are typically multi-year agreements and provide for the reimbursement of qualified expenses for research and development as defined under the terms of the grant agreement. Revenue under grant agreements is recognized when the related qualified research expenses are incurred.

**Research and Development Expenses**

We expense research and development expenses as incurred. Research and development expenses consist of direct and research-related allocated overhead costs such as facilities costs, salaries and related personnel costs, and material and supply costs. In addition, research and development expenses include costs related to clinical trials, validation of our testing processes and procedures and related overhead expenses. Research and development costs incurred in connection with collaborator-funded activities are expensed as incurred. Costs to acquire technologies that are utilized in research and development that have no alternative future use are expensed as incurred. Expenses resulting from clinical trials are recorded when incurred based in part on factors such as estimates of work performed, patient enrollment, progress of patient studies and other events. We make good faith estimates that we believe to be accurate, but the actual costs and timing of clinical trials are highly uncertain, subject to risks and may change depending upon a number of factors, including our clinical development plan.

**Stock-Based Compensation**

We measure and recognize compensation expense for all stock-based payment awards made to our employees and directors, including employee stock options, employee stock purchases related to the Employee Share Purchase Plan (ESPP) and restricted stock units (RSUs), on estimated fair values. The fair value of stock-based awards is amortized over the vesting period of the award using a straight-line method over the requisite service period.

To estimate the value of a stock option award and purchases related to ESPP, we use the Black-Scholes option pricing model. This model requires inputs such as expected life, expected volatility and risk-free interest rate. These inputs are subjective and generally require significant analysis and judgment to develop. While estimates of expected life and volatility are derived primarily from our historical data, the risk-free rate is based on the U.S. Treasury yield curve in effect at the time of grant commensurate with the expected life assumption. To estimate the value of RSUs, we use the closing market value of our common stock on the date the award is issued. Further, we are required to estimate forfeitures at the time of grant and revise those estimates in subsequent periods if actual forfeitures differ from those estimates. If factors change and different assumptions are employed in determining the fair value of stock-based awards, the stock-based compensation expense recorded in future periods may differ significantly from what was recorded in the current period.

**Results of Operations****Years Ended December 31, 2012, 2011 and 2010****Revenues**

	Year Ended December 31,							
	2012	2011	Change	% Change	2011	2010	Change	% Change
	(In thousands, except percentage values)							
Revenues:								
Collaboration agreements	\$ 18,186	\$ 6,110	\$ 12,076	198%	\$ 6,110	\$ 16,819	\$ (10,709)	(64%)
Research grants	3,469	4,209	\$ (740)	(18%)	4,209	3,986	223	6%
Total revenues	\$ 21,655	\$ 10,319	\$ 11,336	110%	\$ 10,319	\$ 20,805	\$ (10,486)	(50%)

## Table of Contents

Total revenues consisted of revenues from collaboration agreements and research grants. We anticipate revenues over the next several years will primarily be derived from our collaboration agreements with Shire, Sigma-Aldrich Corporation (Sigma) and Dow AgroSciences LLC (DAS), a wholly owned subsidiary of Dow Chemical Corporation.

Revenues from our corporate collaboration agreements were \$18.2 million in 2012, \$6.1 million in 2011, and \$16.8 million in 2010. The increase in 2012 from 2011 was primarily due to revenues of \$11.0 million in connection with our license agreement with Shire, which was entered into in January 2012. These revenues included amortization of a \$13.0 million upfront license payment and revenues for research services provided to Shire. The decrease in 2011 from 2010 was primarily due to the completion in July 2010 of the amortization period of revenues related to the commercial license fee received from Sigma under our expanded agreement of October 2009.

Research grant revenues were \$3.5 million in 2012, \$4.2 million in 2011 and \$4.0 million in 2010. The decrease of \$0.7 million in 2012 from 2011 was primarily due to decreased revenues of \$0.5 million from the California Institute for Regenerative Medicine (CIRM) as well as \$0.4 million from the Michael J. Fox Foundation for Parkinson's Research (MJFF), partially offset by higher revenues of \$0.2 million from the Juvenile Diabetes Research Foundation International (JDRF) from a final study payment in support of development of our SB-509 program for the treatment of diabetic neuropathy (DN) which was terminated in October 2011. The increase in 2011 compared to 2010 relates to \$1.1 million of increased revenues from our agreement with the CHDI Foundation, Inc. (CHDI) to develop a novel therapeutic for Huntington's disease, increased revenues of \$0.7 million from CIRM and increased revenues of \$0.4 million for other research grants, partially offset by decreased revenues of \$1.0 million related to funding from JDRF. Additionally, in 2010, we received \$1.0 million in funds awarded and recognized as revenue for four qualifying therapeutic discovery projects under the Patient Protection and Affordable Care Act.

During 2012, revenues related to Shire, Sigma and DAS represented 51%, 11% and 22%, respectively, of total revenues. During 2011, revenues related to Sigma, DAS, CIRM and CHDI represented 15%, 43%, 18% and 11% of total revenues, respectively. During 2010, revenues related to Sigma and DAS represented 59% and 21%, respectively, of total revenues.

## Operating Expenses

	Year Ended December 31,							
	2012	2011	Change	% Change	2011	2010	Change	% Change
	(In thousands, except percentage values)							
Operating expenses:								
Research and development	\$ 31,709	\$ 32,098	\$ (389)	(1%)	\$ 32,098	\$ 33,154	\$ (1,056)	(3%)
General and administrative	12,144	14,042	\$ (1,898)	(14%)	14,042	12,586	1,456	12%
Total operating expenses	\$ 43,853	\$ 46,140	\$ (2,287)	(5%)	\$ 46,140	\$ 45,740	\$ 400	1%

## Research and Development Expenses

We expect to continue to devote substantial resources to research and development in the future and expect research and development expenses to increase in the next several years if we are successful in advancing our HIV/AIDS program in the clinic and if we are able to progress our earlier stage ZFP therapeutic product candidates into clinical trials as well as our programs under collaboration with Shire. Pursuant to the terms of the agreement with Shire, future expenses related to research activities related to the collaboration will be reimbursed by Shire, including employee and external research costs. The reimbursement funds received from Shire will be recognized as revenue as the costs are incurred and collection is reasonably assured.



## Table of Contents

Research and development expenses were \$31.7 million in 2012 compared to \$32.1 million in 2011 and \$33.2 million in 2010. The decrease of \$0.4 million in 2012 compared to 2011 was primarily due to decreased clinical and manufacturing expenses related to our HIV/AIDS program as well as our terminated SB-509 program of \$4.5 million and lower stock-based compensation of \$0.8 million, partially offset by higher expenses related to our pre-clinical ZFP Therapeutic programs of \$3.5 million, including our programs under collaboration with Shire, as well as higher personnel related expenses of \$0.8 million. The decrease of \$1.1 million in 2011 from 2010 was primarily due to decreased clinical expenses related to our terminated SB-509 program of \$5.0 million, specifically our Phase 2b study in diabetic neuropathy, partially offset by increased spending on our HIV/AIDS program of \$2.4 million.

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-728-T, a ZFN-modified autologous T-cell product for the treatment of HIV/AIDS, is the first therapeutic application of our ZFN technology and is being evaluated in ongoing clinical trials, the most advanced of which are a Phase 2 study (SB-728-902 Cohort 5) and a Phase 1/2 study (SB-728-1102) in HIV-infected subjects. We expect to present data from these programs at appropriate scientific and medical meetings in 2013.

We have established a collaborative partnership for some of our preclinical ZFP Therapeutic development programs in certain monogenic diseases, genetic conditions that result from a defect in a single gene. In January 2012, we entered into a collaboration and license agreement with Shire, to research, develop and commercialize ZFP Therapeutics for hemophilia, Huntington's disease and other monogenic diseases based on our ZFP technology. We also have several proprietary preclinical programs in monogenic diseases, including hemoglobinopathies such as SCD and  $\beta$ -thalassemia and several lysosomal storage disorders. In addition, we have research stage programs in other monogenic diseases, including certain immunodeficiencies.

We also continue to fulfill our obligations under the terms of our non-therapeutic collaborations with Sigma and DAS. We provided manufacturing and research assistance to DAS for our ZFP technology through 2012. In addition, to the extent we continue to receive royalties from Sigma, we will incur fees related to certain technologies that we have in-licensed.

Drug development is inherently uncertain and the successful completion of our development programs is subject to numerous technological challenges and risks and we cannot presently estimate anticipated completion dates for any of our programs. Material cash inflows associated with the sale of products, if any, which result from our research efforts are not expected for at least five years. 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 these products and 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.*

The table below shows research and development expenses for our primary clinical development program, SB-728-T, expenses associated with other clinical stage programs as well as expenses related to our pre-clinical and research stage programs, including our therapeutic programs under collaboration with Shire and non-therapeutic collaborations.

Programs	Year Ended December 31, (In thousands)		
	2012	2011	2010
SB-728-T clinical programs	\$ 9,115	\$ 11,297	\$ 6,980
Other clinical programs	510	5,645	13,058
Pre-clinical and research programs	22,083	15,156	13,116
Total research and development expenses	\$ 31,708	\$ 32,098	\$ 33,154

## **Table of Contents**

### **General and Administrative Expenses**

General and administrative expenses consist primarily of salaries and personnel related expenses for executive, finance and administrative personnel, stock-based compensation expenses, professional fees, allocated facilities expenses, patent prosecution expenses and other general corporate expenses. As we pursue commercial development of our therapeutic leads we expect the business aspects of the Company to become more complex. We may be required in the future to add personnel and incur additional costs related to the maturity of our business.

General and administrative expenses were \$12.1 million in 2012, \$14.0 million in 2011 and \$12.6 million in 2010. The decrease of \$1.9 million in 2012 from 2011 was primarily due to lower stock-based compensation of \$1.9 million as well as lower professional services of \$0.8 million, partially offset by higher personnel related expenses of \$0.6 million due to higher headcount, salaries and incentive compensation, and other allocated facility expenses of \$0.2 million. The increase of \$1.4 million in 2011 from 2010 was primarily due to increased professional services of \$0.9 million, including legal fees, and higher salaries and personnel related expenses of \$0.5 million due to higher headcount.

### ***Other income (expense), net***

Other expense was \$0.1 million in 2012, compared to other income of \$0.1 million in 2011 and 2010. The expense in 2012 was primarily related to disposal of fixed assets, partially offset by interest income of \$0.1 million. Other income in 2011 and 2010 was comprised of interest income.

### **Liquidity and Capital Resources**

#### ***Liquidity***

Since inception, we have incurred significant net losses and we have funded our operations primarily through the issuance of equity securities, payments from corporate collaborators and strategic partners and research grants.

As of December 31, 2012, we had cash, cash equivalents, marketable securities and interest receivable totaling \$76.3 million compared to \$84.5 million as of December 31, 2011. The decrease was primarily attributable to the use of capital required to fund our continuing operations, including the advancement of our ZFP Therapeutic programs. The decrease was also attributable to the completion of an underwritten public offering of our common stock in April 2011, in which 6,700,000 shares of our common stock were sold at a public offering price of \$7.70 per share. The net proceeds to us from the offering, after deducting underwriting discounts and commissions and other offering expenses, were approximately \$50.2 million.

Our most significant use of capital pertains to salaries and benefits for our employees and external development expenses, such as manufacturing and clinical trial activity, related to our ZFP Therapeutic programs. Our cash and investment balances are held in a variety of interest bearing instruments, including obligations of U.S. government agencies, U.S. treasury debt securities, corporate debt securities and money market funds. Cash in excess of immediate requirements is invested in accordance with our investment policy with a view toward capital preservation and liquidity.

In January 2012, we entered into a collaboration and license agreement with Shire, pursuant to which we are collaborating with Shire to research, develop and commercialize certain gene targets in human therapeutics and diagnostics for hemophilia, Huntington's disease and other monogenic diseases based on our ZFP technology. Under the Agreement, we received an upfront license fee of \$13.0 million. We are also eligible to receive milestone payments, however, our eligibility is based on our achievement of specified research, regulatory, clinical development, commercialization and sales milestones and depends upon ours and Shire's ability to continue to progress our programs under collaboration. We will also be eligible to receive royalty payments that are a tiered double-digit percentage of net sales of products developed under the collaboration, if any.

## **Table of Contents**

### *Cash Flow*

Net cash used in operating activities was \$8.1 million in 2012, \$25.9 million in 2011 and \$23.9 million in 2010. For all periods, net cash used in operating activities primarily reflects our net operating losses. The decrease in net cash used in operating activities in 2012 compared to 2011 was primarily the result of a \$13.0 million upfront payment related to our collaboration and license agreement entered into with Shire in January 2012, as well as lower operating expenses in 2012 compared to 2011. The increase in net cash used in operating activities in 2011 compared to 2010 was primarily the result of decreased cash received related to our revenues in 2011 as well as increased operating expenses.

Net cash provided by investing activities was \$11.3 million in 2012. Net cash used in investing activities was \$20.0 million in 2011. Net cash provided by investing activities was \$12.4 million in 2010. Cash flows from investing activities for all periods primarily related to purchases, sales and maturities of marketable securities.

Net cash provided by financing activities was \$1.7 million in 2012, \$51.9 million in 2011 and \$1.2 million in 2010. Cash provided by financing activities in 2012 and 2010 primarily related to proceeds from the issuance of common stock upon exercise of stock options. Net cash provided by financing activities in 2011 was primarily attributable to the completion of an underwritten public offering of the our common stock in April 2011, in which 6,700,000 shares of our common stock were sold at a public offering price of \$7.70 per share. The net proceeds to us from the sale of shares in this offering, after deducting underwriting discounts and commissions and other offering expenses, were approximately \$50.2 million.

### *Operating Capital and Capital Expenditure Requirements*

We anticipate continuing to incur operating losses for at least the next several years. While we expect our rate of cash usage to increase in the future, in particular to support our product development endeavors, we believe that the available cash resources as well as funds received from corporate collaborators, strategic partners and research grants will enable us to maintain our currently planned operations through 2014. Future capital requirements will be substantial and if our capital resources are insufficient to meet future capital requirements, we will need to raise additional capital to fund our operations, including ZFP Therapeutic development activities, through equity or debt financing. We regularly consider fund raising opportunities and may decide, from time to time, to raise capital based on various factors, including market conditions and our plans of operation. Additional capital may not be available on terms acceptable to us, or at all. If adequate funds are not available, or if the terms of potential funding sources are unfavorable, our business and our ability to develop our technology and our ZFP Therapeutic products would be harmed. Furthermore, any sales of additional equity securities may result in dilutions to our stockholders, and any debt financing may include covenants that restrict our business.

Our future capital requirements will depend on many forward looking factors, including the following:

the initiation, progress, timing and completion of clinical trials for our product candidates and potential product candidates;

the outcome, timing and cost of regulatory approvals;

the success of our collaboration agreement with Shire;

delays that may be caused by changing regulatory requirements;

the number of product candidates that we pursue;

the costs involved in filing and prosecuting patent applications and enforcing and defending patent claims;

the timing and terms of future in-licensing and out-licensing transactions;

the cost and timing of establishing sales, marketing, manufacturing and distribution capabilities;

the cost of procuring clinical and commercial supplies of our product candidates;

**Table of Contents**

the extent to which we acquire or invest in businesses, products or technologies; and

the possible costs of litigation.

There is no provision for income taxes because we have only incurred losses since our inception. As of December 31, 2012, we had net operating loss carryforwards for federal and state income tax purposes of approximately \$187.1 million and \$163.1 million, respectively. If not utilized, the net federal and state operating loss carryforwards will begin to expire in 2013. We also have federal and state research tax credit carryforwards of \$5.1 million and \$5.9 million, respectively. The federal research credits will begin to expire in 2018 while the state research credits have no expiration date. Utilization of our net operating loss carryforwards and research tax credit carryforwards may be subject to substantial annual limitations due to the ownership change limitations provided by the Internal Revenue Code and similar state provisions. The annual limitation could result in the expiration of the net operating loss carryforwards and research tax credit carryforwards before use.

**Contractual Obligations and Commercial Commitments**

As of December 31, 2012, we had contractual obligations and commercial commitments as follows (in thousands):

Contractual Obligations	Total	Payments Due by Period			
		Less Than 1 Year	1-3 Years	3-5 Years	More Than 5 Years
Operating leases	\$ 1,033	\$ 616	\$ 417	\$	\$
License obligations	3,413	568	755	998	1,093
Total contractual obligations	\$ 4,446	\$ 1,184	\$ 1,172	\$ 998	\$ 1,093

Operating leases consist of base rents for facilities we occupy in Richmond, California. License obligations consist of ongoing license maintenance fees associated with cancelable in-licensed patent agreements.

**Recent Accounting Pronouncement**

In June 2011, Accounting Standards Codification Topic 220, *Comprehensive Income* was amended to increase the prominence of items reported in other comprehensive income. Accordingly, a company can present all non-owner changes in stockholders' equity either in a single continuous statement of comprehensive income or in two separate but consecutive statements. We adopted this guidance as of January 1, 2012 on a retrospective basis and the adoption did not have a material effect on our consolidated financial statements.

**ITEM 7A QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK**

Our exposure to market risk relates to our cash, cash equivalents and investments. The goals of our investment policy are preservation of capital, fulfillment of liquidity needs and capturing a market rate of return based on our investment policy parameters and market conditions. We select investments that maximize interest income to the extent possible within these guidelines. To achieve our goals, we maintain a portfolio of cash equivalents and investments in securities of high credit quality and with varying maturities to match projected cash needs.

The securities in our investment portfolio are not leveraged, are classified as available for sale and are, due to their short-term nature, subject to minimal interest rate risk. Our investments currently consist of U.S. Treasury securities, U.S. government-sponsored enterprise securities and corporate notes. Our investment policy, approved by our Board of Directors, limits the amount we may invest in any one type of investment issuer, thereby reducing credit risk concentrations. All investments have a fixed interest rate and are carried at market value, which approximates cost. We do not use derivative financial instruments in our investment portfolio. We do not believe that a decrease in interest rates would have a material negative impact on the value of our investment portfolio.

**Table of Contents**

**ITEM 8 FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA**

**SANGAMO BIOSCIENCES, INC.**

**INDEX TO CONSOLIDATED FINANCIAL STATEMENTS**

	<b>Page</b>
<u>Report of Independent Registered Public Accounting Firm</u>	53
<u>Consolidated Balance Sheets</u>	54
<u>Consolidated Statements of Operations</u>	55
<u>Consolidated Statements of Comprehensive Loss</u>	56
<u>Consolidated Statements of Stockholders' Equity</u>	57
<u>Consolidated Statements of Cash Flows</u>	58
<u>Notes to Consolidated Financial Statements</u>	59

**Table of Contents**

**REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

The Board of Directors and Stockholders

Sangamo BioSciences, Inc.

We have audited the accompanying consolidated balance sheets of Sangamo BioSciences, Inc. as of December 31, 2012 and 2011, and the related consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2012. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of Sangamo BioSciences, Inc. as of December 31, 2012 and 2011, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2012, in conformity with U.S. generally accepted accounting principles.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the effectiveness of Sangamo BioSciences Inc.'s internal control over financial reporting as of December 31, 2012, based on the criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated February 26, 2013 expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP

San Jose, California

February 26, 2013

**Table of Contents****SANGAMO BIOSCIENCES, INC.****CONSOLIDATED BALANCE SHEETS**

	December 31,	
	2012	2011
	(In thousands, except share and per share amounts)	
ASSETS		
Current assets:		
Cash and cash equivalents	\$ 21,679	\$ 16,766
Marketable securities	41,868	67,366
Interest receivable	190	331
Accounts receivable	4,129	919
Other current assets	203	
Prepaid expenses	296	310
Total current assets	68,365	85,692
Marketable securities, non-current	12,584	
Property and equipment, net	1,543	1,603
Other assets	41	41
Total assets	\$ 82,533	\$ 87,336
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable and accrued liabilities	\$ 4,013	\$ 5,515
Accrued compensation and employee benefits	2,473	1,672
Deferred revenue	2,304	17
Total current liabilities	8,790	7,204
Deferred revenue, non-current	8,847	
Total liabilities	17,637	7,204
Commitments and contingencies		
Stockholders' equity:		
Common stock, \$0.01 par value; 80,000,000 shares authorized, 53,058,525 and 52,554,795 shares issued and outstanding at December 31, 2012 and 2011, respectively	531	526
Additional paid-in capital	339,848	332,839
Accumulated deficit	(275,509)	(253,245)
Accumulated other comprehensive income	26	12
Total stockholders' equity	64,896	80,132
Total liabilities and stockholders' equity	\$ 82,533	\$ 87,336

See accompanying Notes to Consolidated Financial Statements.



**Table of Contents****SANGAMO BIOSCIENCES, INC.****CONSOLIDATED STATEMENTS OF OPERATIONS**

	<b>Year Ended December 31,</b>		
	<b>2012</b>	<b>2011</b>	<b>2010</b>
	<b>(In thousands, except per share amounts)</b>		
<b>Revenues:</b>			
Collaboration agreements	\$ 18,186	\$ 6,110	\$ 16,819
Research grants	3,469	4,209	3,986
 Total revenues	 21,655	 10,319	 20,805
<b>Operating expenses:</b>			
Research and development	31,709	32,098	33,154
General and administrative	12,144	14,042	12,586
 Total operating expenses	 43,853	 46,140	 45,740
 Loss from operations	 (22,198)	 (35,821)	 (24,935)
Other income (expense), net	(66)	71	81
 Net loss	 \$ (22,264)	 \$ (35,750)	 \$ (24,854)
 Basic and diluted net loss per share	 \$ (0.42)	 \$ (0.71)	 \$ (0.55)
 Shares used in computing basic and diluted net loss per share	 52,741	 50,512	 45,167

See accompanying Notes to Consolidated Financial Statements.

**Table of Contents**

**SANGAMO BIOSCIENCES, INC.**

**CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS**

	<b>Year Ended December 31,</b>		
	<b>2012</b>	<b>2011</b>	<b>2010</b>
	<b>(In thousands, except per share amounts)</b>		
Net loss	\$ (22,264)	\$ (35,750)	\$ (24,854)
Change in unrealized gain (loss) on available-for-sale securities	14	18	(24)
Comprehensive loss	\$ (22,250)	\$ (35,732)	\$ (24,878)

**Table of Contents****SANGAMO BIOSCIENCES, INC.****CONSOLIDATED STATEMENTS OF STOCKHOLDERS EQUITY**

	Common Stock		Additional Paid-in Capital (In thousands, except share data)	Accumulated Deficit	Accumulated Other Comprehensive Income/ (Loss)	Total Stockholders Equity
	Shares	Amount				
Balances at December 31, 2009	44,994,409	\$ 450	\$ 263,955	\$ (192,641)	\$ 18	\$ 71,782
Issuance of common stock upon exercise of stock options and in connection with restricted stock units	249,156	2	736			738
Issuance of common stock under employee stock purchase plan	134,174	2	445			447
Stock-based compensation			7,818			7,818
Comprehensive loss:						
Net unrealized loss on marketable securities					(24)	(24)
Net loss				(24,854)		(24,854)
Comprehensive loss						(24,878)
Balances at December 31, 2010	45,377,739	\$ 454	\$ 272,954	\$ (217,495)	\$ (6)	\$ 55,907
Issuance of common stock in connection with underwritten public offering	6,700,000	67	50,152			50,219
Issuance of common stock upon exercise of stock options and in connection with restricted stock units	324,416	3	1,191			1,194
Issuance of common stock under employee stock purchase plan	152,640	2	461			463
Stock-based compensation			8,081			8,081
Comprehensive loss:						
Net unrealized gain on marketable securities					18	18
Net loss				(35,750)		(35,750)
Comprehensive loss						(35,732)
Balances at December 31, 2011	52,554,795	\$ 526	\$ 332,839	\$ (253,245)	\$ 12	\$ 80,132
Issuance of common stock upon exercise of stock options and in connection with restricted stock units	328,355	3	1,216			1,219
Issuance of common stock under employee stock purchase plan	175,375	2	455			457
Stock-based compensation			5,338			5,338
Comprehensive loss:						
Net unrealized gain on marketable securities					14	14
Net loss				(22,264)		(22,264)
Comprehensive loss						(22,250)

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Balances at December 31, 2012	53,058,525	\$ 531	\$ 339,848	\$ (275,509)	\$	26	\$ 64,896
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See accompanying Notes to Consolidated Financial Statements.

**Table of Contents****SANGAMO BIOSCIENCES, INC.****CONSOLIDATED STATEMENTS OF CASH FLOWS**

	Year Ended December 31,		
	2012	2011	2010
	(In thousands)		
<b>Operating activities:</b>			
Net loss	\$ (22,264)	\$ (35,750)	\$ (24,854)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation	660	646	676
Amortization of premium / discount on marketable securities	889	1,576	1,187
Stock-based compensation	5,338	8,081	7,818
Net loss on disposal of property and equipment	123		
Net changes in operating assets and liabilities:			
Interest receivable	141	6	4
Accounts receivable	(3,414)	(553)	(297)
Prepaid expenses and other assets	14	(13)	97
Accounts payable and accrued liabilities	(1,503)	(139)	3,196
Accrued compensation and employee benefits	800	315	(28)
Deferred revenue	11,134	(64)	(11,733)
<b>Net cash used in operating activities</b>	<b>(8,082)</b>	<b>(25,895)</b>	<b>(23,934)</b>
<b>Investing activities:</b>			
Purchases of marketable securities	(91,428)	(112,974)	(100,027)
Maturities of marketable securities	103,470	83,412	113,096
Proceeds from sales of marketable securities		10,139	
Purchases of property and equipment	(723)	(576)	(695)
<b>Net cash provided by / (used in) investing activities</b>	<b>11,319</b>	<b>(19,999)</b>	<b>12,374</b>
<b>Financing activities:</b>			
Proceeds from issuance of common stock	1,676	51,876	1,185
<b>Net cash provided by financing activities</b>	<b>1,676</b>	<b>51,876</b>	<b>1,185</b>
<b>Net increase / (decrease) in cash and cash equivalents</b>	<b>4,913</b>	<b>5,982</b>	<b>(10,375)</b>
Cash and cash equivalents, beginning of period	16,766	10,784	21,159
<b>Cash and cash equivalents, end of period</b>	<b>\$ 21,679</b>	<b>\$ 16,766</b>	<b>\$ 10,784</b>

See accompanying Notes to Consolidated Financial Statements.

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**Table of Contents**

**SANGAMO BIOSCIENCES, INC.**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

**NOTE 1 ORGANIZATION AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES**

***Sangamo***

Sangamo BioSciences, Inc. (the Company or Sangamo) was incorporated in the State of Delaware on June 22, 1995 and is focused on the research, development and commercialization of novel therapeutic strategies for unmet medical needs. Sangamo's gene regulation and gene modification technology platform is enabled by the engineering of a class of transcription factors known as zinc finger DNA-binding proteins (ZFPs). Potential applications of Sangamo's technology include development of human therapeutics, plant agriculture and enhancement of pharmaceutical protein production. Sangamo will require additional financial resources to complete the development and commercialization of its products including ZFP Therapeutics.

Sangamo is currently working on a number of long-term development projects that will involve experimental technology. The projects may require several years and substantial expenditures to complete and ultimately may be unsuccessful. The Company plans to finance operations with available cash resources, collaborations and strategic partnerships funds received under research grants and from the issuance of equity or debt securities. Sangamo believes that its available cash, cash equivalents and investments as of December 31, 2012, along with expected revenues collaborations and strategic partnerships, will be adequate to fund its operations at least through 2013. Sangamo will need to raise substantial additional capital to fund subsequent operations and complete the development and commercialization of its products either through significant corporate partnerships, research grants or issuance of debt or equity securities. Additional capital may not be available on terms acceptable to us, or at all. If adequate funds are not available, or if the terms of potential funding sources are unfavorable, the Company's business and ability to develop its technology and ZFP Therapeutic products would be harmed. Furthermore, any sales of additional equity securities may result in dilutions to the Company's stockholders, and any debt financing may include covenants that restrict the Company's business.

***Basis of Presentation***

The preparation of financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions that affect the amounts reported in the financial statements and the accompanying notes. Actual results could differ from those estimates. The consolidated financial statements include the accounts of Sangamo and its wholly owned subsidiary, Gendaq Limited, after elimination of all intercompany balances and transactions.

***Cash and Cash Equivalents***

Sangamo considers all highly liquid investments purchased with original maturities of three months or less at the purchase date to be cash equivalents. Cash and cash equivalents consist of deposits in money market investment accounts, government sponsored entity debt securities, US Treasury debt securities and corporate bank accounts.

***Marketable Securities***

Sangamo classifies its marketable securities as available-for-sale and records its investments at estimated fair value based on quoted market prices or observable market inputs of almost identical assets, with the unrealized holding gains and losses included in accumulated other comprehensive income.

The Company's investments are subject to a periodic impairment review. The Company recognizes an impairment charge when a decline in the fair value of its investments below the cost basis is judged to be other-

## **Table of Contents**

than-temporary. The Company considers various factors in determining whether to recognize an impairment charge, including the length of time and extent to which the fair value has been less than the Company's cost basis, the financial condition and near-term prospects of the investee, and the Company's intent and ability to hold the investment for a period of time sufficient to allow for any anticipated recovery in the market value. Realized gains and losses on available-for-sale securities are included in other (expense)/income, which is determined using the specific identification method.

### ***Fair Value of Financial Instruments***

The carrying amounts for financial instruments consisting of cash and cash equivalents, accounts receivable, accounts payable and accrued liabilities approximate fair value due to their short maturities. Marketable securities are stated at their estimated fair values, based on quoted market prices for the same or similar instruments. The counterparties to the agreements relating to the Company's investment securities consist of the US Treasury, various major corporations, governmental agencies and financial institutions with high credit standing.

### ***Property and Equipment***

Property and equipment are stated at cost, less accumulated depreciation. Depreciation is calculated using the straight-line method based on the estimated useful lives of the related assets (generally three to five years). For leasehold improvements, depreciation is calculated using the straight-line method based on the shorter of the useful life or the lease term. The Company reviews its property, plant and equipment assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable.

### ***Revenue Recognition***

Revenues from research activities made under strategic partnering agreements and collaborations are recognized as the services are provided when there is persuasive evidence that an arrangement exists, delivery has occurred, the price is fixed or determinable, and collectability is reasonably assured. Revenue generated from research and licensing agreements typically includes upfront signing or license fees, cost reimbursements, research services, minimum sublicense fees, milestone payments and royalties on future licensee's product sales.

*Multiple Element Arrangements prior to the adoption of ASU No. 2009-13, Revenue Recognition Multiple Deliverable Revenue Arrangements (ASU 2009-13).* For revenue arrangements entered into before January 1, 2011, that include multiple deliverables, the elements of such agreement were divided into separate units of accounting if the deliverables met certain criteria, including whether the fair value of the delivered items could be determined and whether there was evidence of fair value of the undelivered items. In addition, the consideration was allocated among the separate units of accounting based on their fair values, and the applicable revenue recognition criteria are considered separately for each of the separate units of accounting. Prior to the adoption of ASU 2009-13, the Company recognized nonrefundable signing, license or non-exclusive option fees as revenue when rights to use the intellectual property related to the license were delivered and over the period of performance obligations if the Company had continuing performance obligations. The Company estimated the performance period at the inception of the arrangement and reevaluated it each reporting period. Changes to these estimates were recorded on a prospective basis.

*Multiple Element Arrangements after the adoption of ASU 2009-13.* ASU 2009-13 amended the accounting standards for certain multiple element revenue arrangements to:

provide updated guidance on whether multiple elements exist, how the elements in an arrangement should be separated, and how the arrangement consideration should be allocated to the separate elements;

## **Table of Contents**

require an entity to allocate arrangement consideration to each element based on a selling price hierarchy where the selling price for an element is based on vendor-specific objective evidence ( VSOE ), if available; third-party evidence ( TPE ), if available and VSOE is not available; or the best estimate of selling price ( ESP ), if neither VSOE nor TPE is available; and

eliminate the use of the residual method and require an entity to allocate arrangement consideration using the relative selling price method.

For revenue agreements with multiple element arrangements, such as license and development agreements, entered into on or after January 1, 2011, the Company will allocate revenue to each non-contingent element based on the relative selling price of each element. When applying the relative selling price method, the Company determines the selling price for each deliverable using VSOE of selling price or TPE of selling price. If neither exists the Company uses ESP for that deliverable. Revenue allocated is then recognized when the basic four revenue recognition criteria are met for each element. The collaboration and license agreement entered into with Shire AG (Shire) in January 2012 was evaluated under these amended accounting standards.

Additionally, the Company may be entitled to receive certain milestone payments which are contingent upon reaching specified objectives. These milestone payments are recognized as revenue in full upon achievement of the milestone if there is substantive uncertainty at the date the arrangement is entered into that objectives will be achieved and if the achievement is based on the Company's performance.

Minimum annual sublicense fees are also recognized as revenue in the period in which such fees are due. Royalty revenues are generally recognized when earned and collectability of the related royalty payment is reasonably assured. The Company recognizes cost reimbursement revenue under collaborative agreements as the related research and development costs for services are rendered. Deferred revenue represents the portion of research or license payments received which have not been earned.

Sangamo's research grants are typically multi-year agreements and provide for the reimbursement of qualified expenses for research and development as defined under the terms of the grant agreement. Revenue under grant agreements is recognized when the related qualified research expenses are incurred.

During 2012, revenues related to Shire, Sigma-Aldrich Corporation (Sigma) and Dow AgroSciences LLC (DAS) represented 51%, 11% and 22%, respectively, of total revenues. During 2011, revenues related to Sigma, DAS, California Institute for Regenerative Medicine (CIRM) and CHDI Foundation, Inc. (CHDI) represented 15%, 43%, 18% and 11% of total revenues, respectively. During 2010, revenues related to Sigma and DAS represented 59% and 21%, respectively, of total revenues.

### ***Research and Development Expenses***

Research and development costs are expensed as incurred. Research and development expenses consist of direct and research-related allocated overhead costs such as facilities costs, salaries and related personnel costs, and material and supply costs. In addition, research and development expenses include costs related to clinical trials, validation of the Company's testing processes and procedures and as well as related overhead expenses. Research and development costs incurred in connection with collaborator-funded activities are expensed as incurred. Costs to acquire technologies that are utilized in research and development that have no alternative future use are expensed as incurred.

### ***Stock-Based Compensation***

The Company measures and recognizes compensation expense for all stock-based payment awards made to Sangamo employees and directors, including employee share options, restricted stock units (RSUs) and employee share purchases related to the Employee Share Purchase Plan (ESPP), based on estimated fair values at grant date. The fair value of equity-based awards is amortized over the vesting period of the award using a straight-line method.



## **Table of Contents**

To estimate the value of an award, the Company uses the Black-Scholes option pricing model. This model requires inputs such as expected life, expected volatility and risk-free interest rate. These inputs are subjective and generally require significant analysis and judgment to develop. While estimates of expected life and volatility are derived primarily from the Company's historical data, the risk-free rate is based on the U.S. Treasury yield curve in effect at the time of grant commensurate with the expected life assumption. Further, the Company is required to estimate forfeitures at the time of grant and revise those estimates in subsequent periods if actual forfeitures differ from those estimates. The Company uses historical data to estimate pre-vesting option forfeitures and record stock-based compensation expense only for those awards that are expected to vest.

### ***Income Taxes***

Income tax expense has been provided using the liability method. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities as measured by the enacted tax rates that will be in effect when these differences reverse. The Company provides a valuation allowance against net deferred tax assets if, based upon the available evidence, it is not more likely than not that the deferred tax assets will be realized.

### ***Net Loss Per Share***

Basic net loss per share has been computed by dividing the net loss by the weighted-average number of shares of common stock outstanding during the period. Diluted net loss per share is calculated by dividing net loss by the weighted average number of shares of common stock and potential dilutive securities outstanding during the period.

Because Sangamo is in a net loss position, diluted net loss per share excludes the effects of common stock equivalents consisting of options, which are all anti-dilutive. The total stock options outstanding excluded from the calculation of diluted net loss per share at the end of 2012, 2011 and 2010 were 9,184,346, 8,346,190 and 8,109,901, respectively.

### ***Segments***

The Company operates in one segment. Management uses one measurement of profitability and does not segregate its business for internal reporting. As of December 31, 2012 and 2011, all of the Company's assets were maintained in the U.S. For the years ended December 31, 2012, 2011 and 2010, 100% of revenues and operating expenses were generated and incurred in the U.S.

**Table of Contents****NOTE 2 INVESTMENTS AND FAIR VALUE MEASUREMENT**

The table below summarizes the Company's available-for-sale securities (in thousands):

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized (Losses)	Estimated Fair Value
<b>December 31, 2012</b>				
Cash equivalents:				
U.S. government sponsored entity debt securities	\$ 2,997	\$	\$	\$ 2,997
Money market funds	15,839			15,839
<b>Total</b>	<b>18,836</b>			<b>18,836</b>
Marketable securities:				
U.S. government sponsored entity debt securities	54,426	26		54,452
<b>Total</b>	<b>54,426</b>	<b>26</b>		<b>54,452</b>
<b>Total cash equivalents and marketable securities</b>	<b>\$ 73,262</b>	<b>\$ 26</b>	<b>\$</b>	<b>\$ 73,288</b>
<b>December 31, 2011</b>				
Cash equivalents:				
Money market funds	\$ 15,258			\$ 15,258
<b>Total</b>	<b>15,258</b>			<b>15,258</b>
Marketable securities:				
U.S. government sponsored entity debt securities	27,020		(7)	27,013
U.S. treasury debt securities	751	1		752
Corporate debt securities	39,583	18		39,601
<b>Total</b>	<b>67,354</b>	<b>19</b>	<b>(7)</b>	<b>67,366</b>
<b>Total cash equivalents and marketable securities</b>	<b>\$ 82,612</b>	<b>\$ 19</b>	<b>\$ (7)</b>	<b>\$ 82,624</b>

As of December 31, 2012, all of investments had maturity dates within two years and there were no material unrealized losses during 2012. Approximately 83% of the Company's available-for-sale securities mature within the next twelve months of the date of the balance sheet date and approximately 17% of the Company's available-for-sale securities have maturities between twelve and twenty-four months from the date of the balance sheet date. The Company had no material realized losses or other-than-temporary impairments of available-for-sale securities for the years ended December 31, 2012, 2011 and 2010.

***Fair Value Measurement***

The Company measures certain financial assets at fair value on a recurring basis, including cash equivalents and available-for-sale securities. The fair value of these assets was determined based on a three-tier hierarchy under the authoritative guidance for fair value measurements and disclosures that prioritizes the inputs used in measuring fair value as follows:

Level 1: Unadjusted quoted prices in active markets that are accessible at the measurement date for identical, unrestricted assets or liabilities;

Level 2: Quoted prices in markets that are not active, or inputs which are observable, either directly or indirectly, for substantially the full term of the asset or liability;

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Level 3: Prices or valuation techniques that require inputs that are both significant to the fair value measurement and unobservable (i.e., supported by little or no market activity).

When observable market prices for identical securities that are traded in less active markets are used, the Company classifies its available-for-sale debt instruments as Level 2. When observable market prices for

**Table of Contents**

identical securities are not available, available-for-sale debt instruments are priced using benchmark curves, benchmarking of like securities, sector groupings, and matrix pricing as well as model processes. These models are proprietary valuation models of pricing providers or brokers. These valuation models incorporate a number of inputs, including, listed in approximate order of priority: benchmark yields, reported trades, broker/dealer quotes, issuer spreads, two-sided markets, benchmark securities, bids, offers and reference data including market research publications. For certain security types, additional inputs may be used, or some of the Standard Inputs may not be applicable. Evaluators may prioritize inputs differently on any given day for any security based on market conditions, and not all inputs listed are available for use in the evaluation process for each security evaluation on any given day.

The fair value measurements of cash equivalents and available-for-sale marketable securities are identified at the following levels within the fair value hierarchy (in thousands):

	December 31, 2012 Fair Value Measurements			
	Total	Level 1	Level 2	Level 3
Assets:				
Cash equivalents:				
U.S. government sponsored entity debt securities	\$ 2,997	\$	\$ 2,997	\$
Money market funds	15,839	15,839		
Total	18,836	15,839	2,997	
Marketable securities:				
U.S. government sponsored entity debt securities	54,452		54,452	
Total	54,452		54,452	
Total cash equivalents and marketable securities	\$ 73,288	\$ 15,839	\$ 57,449	\$

	December 31, 2011 Fair Value Measurements			
	Total	Level 1	Level 2	Level 3
Assets:				
Cash equivalents:				
Money market funds	\$ 15,258	\$ 15,258	\$	\$
Total	15,258	15,258		
Marketable securities:				
U.S. government sponsored entity debt securities	27,013		27,013	
U.S. treasury debt securities	752		752	
Corporate debt securities	39,601		39,601	
Total	67,366		67,366	
Total cash equivalents and marketable securities	\$ 82,624	\$ 15,258	\$ 67,366	\$

**NOTE 3 STOCK-BASED COMPENSATION**

The following table shows total stock-based compensation expense recognized in the consolidated statements of operations (in thousands):

Year Ended December 31,

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	2012	2011	2010
Research and development	\$ 2,892	\$ 3,769	\$ 3,612
General and administrative	2,446	4,312	4,206
Total stock-based compensation expense	\$ 5,338	\$ 8,081	\$ 7,818

**Table of Contents**

As of December 31, 2012, total stock-based compensation expense related to unvested stock options to be recognized in future periods was \$9.8 million, which is expected to be expensed over a weighted-average period of 2.79 years. As of December 31, 2012, total compensation expense related to unvested RSUs to be recognized in future periods was \$3.5 million, which is expected to be expensed over a weighted-average period of 2.40 years. There was no capitalized stock-based employee compensation expense as of December 31, 2012.

**Valuation Assumptions**

The employee stock-based compensation expense was determined using the Black-Scholes option valuation model. Option valuation models require the input of subjective assumptions and these assumptions can vary over time.

The Company primarily bases its determination of expected volatility through its assessment of the historical volatility of its common stock. The Company relied on its historical exercise and post-vested termination activity for estimating its expected term for use in determining the fair value of these options.

The weighted-average estimated fair value per share of options granted during 2012, 2011 and 2010 was \$3.76, \$3.20 and \$3.85, respectively, based upon the assumption in the Black-Scholes valuation model. The weighted average assumptions used for estimating the fair value of the employee stock options are as follows:

	Year Ended December 31,		
	2012	2011	2010
Risk-free interest rate	0.74-1.34%	0.93-2.11%	1.5-2.6%
Expected life of option (in years)	5.40-5.58	5.39-5.41	5.23-5.41
Expected dividend yield of stock	0%	0%	0%
Expected volatility	0.87-0.88	0.83-0.86	0.83-0.84

Employees purchased approximately 175,000, 153,000 and 134,000 shares of common stock through the 2010 Purchase Plan at an average exercise price of \$2.61, \$3.02 and \$3.34 per share during the fiscal years 2012, 2011 and 2010, respectively.

The weighted-average estimated fair value of shares purchased under the Company's ESPP during 2012, 2011 and 2010 were \$2.51, \$1.62 and \$2.76, respectively, based upon the assumptions in the Black-Scholes valuation model. The weighted average assumptions used for estimating the fair value of the ESPP purchase rights are as follows:

	Year Ended December 31,		
	2012	2011	2010
Risk-free interest rate	0.05-0.30%	0.05-0.61%	0.2-1.0%
Expected life of option (in years)	0.5-2.0	0.5-2.0	0.5-2.0
Expected dividend yield of stock	0%	0%	0%
Expected volatility	0.93-1.37	0.58-0.85	0.62-1.14

**NOTE 4 MAJOR CUSTOMERS, PARTNERSHIPS AND STRATEGIC ALLIANCES****Collaboration Agreements*****Collaboration and License Agreement with Shire AG in Human Therapeutics and Diagnostics***

On January 31, 2012, the Company entered into a collaboration and license agreement (the Agreement) with Shire AG (Shire), pursuant to which the Company and Shire collaborate to research, develop and commercialize human therapeutics and diagnostics for monogenic diseases based on Sangamo's novel ZFP technology. Under the Agreement, the Company and Shire may develop potential human therapeutic or diagnostic products for seven gene targets. The initial four gene targets selected were blood clotting Factors VII, VIII, IX and X, and

## Table of Contents

products developed for such initial gene targets will be used for treating or diagnosing hemophilia. In June 2012, Shire selected a fifth gene target for the development of a ZFP therapeutic for Huntington's disease, an inherited neurodegenerative disease for which there are currently no therapies available to slow the disease progression. Shire has the right, subject to certain limitations, to designate two additional gene targets. Pursuant to the Agreement, the Company granted Shire an exclusive, world-wide, royalty-bearing license, with the right to grant sublicenses, to use Sangamo's ZFP technology for the purpose of developing and commercializing human therapeutic and diagnostic products for the gene targets. The initial research term of the Agreement is six years and is subject to extensions upon mutual agreement and under other specified circumstances.

Under the terms of the Agreement, the Company is responsible for all research activities through the submission of an Investigative New Drug Application (IND) or European Clinical Trial Application (CTA), while Shire is responsible for clinical development and commercialization of products generated from the research program from and after the acceptance of an IND or CTA for the product. Shire reimburses Sangamo for its internal and external research program-related costs.

The Company received an upfront license fee of \$13.0 million. The Company will also be eligible to receive up to \$213.5 million of contingent payments for each gene target if specified research, regulatory, clinical development, commercialization and sales milestone events occur, including payments for each gene target through the acceptance of an IND or CTA submission totaling \$8.5 million. The Company will also be eligible to receive royalty payments that are a tiered double-digit percentage of net sales of licensed product sold by Shire or its sublicensees developed under the collaboration, if any. To date, no products have been approved and therefore no royalty fees have been earned under the Agreement with Shire.

All contingent payments under the Agreement, when earned, will be non-refundable and non-creditable. The Company has evaluated the contingent payments under the Agreement with Shire based on the authoritative guidance for research and development milestones and determined that certain of these payments meet the definition of a milestone and that all such milestones are substantive milestones because they are related to events (i) that can be achieved based in whole or in part on either the Company's performance or on the occurrence of a specific outcome resulting from the Company's performance, (ii) for which there was substantive uncertainty at the date the agreement was entered into that the event would be achieved and (iii) that would result in additional payments being due to the Company. Accordingly, revenue for these achievements will be recognized in its entirety in the period when the milestone is achieved and collectability is reasonably assured.

The Company has identified the deliverables within the arrangement as a license to the technology and on-going research services activities. The Company has concluded that the license is not a separate unit of accounting as it does not have stand-alone value to Shire apart from the research services to be performed pursuant to the Agreement. As a result, the Company will recognize revenue from the upfront payment on a straight-line basis over a six-year initial research term during which the Company will perform research services. As of December 31, 2012, the Company has deferred revenue of \$11.1 million related to this Agreement.

Revenues recognized under the agreement with Shire for the twelve months ended December 31, 2012, were as follows (in thousands):

	Year ended December 31, 2012
<b>Revenues related to Shire Collaboration:</b>	
Amortization of upfront fee	\$ 1,986
Research services	9,026
<b>Total</b>	<b>\$ 11,012</b>

Related costs and expenses incurred under the Shire agreement were \$7.7 million during the twelve months ended December 31, 2012.

**Table of Contents*****Agreement with Sigma-Aldrich Corporation in Laboratory Research Reagents, Transgenic Animal and Commercial Protein Production Cell-line Engineering***

In July 2007, Sangamo entered into a license agreement with Sigma. Under the license agreement, Sangamo agreed to provide Sigma with access to its proprietary ZFP technology and the exclusive right to use the technology to develop and commercialize research reagent 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 agreed to conduct a three-year research program to develop laboratory research reagents using Sangamo's ZFP technology during which time Sangamo agreed to assist Sigma in connection with its efforts to market and sell services employing the Company's ZFP technology in the research field. Sangamo has transferred the ZFP manufacturing technology to Sigma.

In October 2009, Sangamo expanded its license agreement with Sigma. In addition to the original terms of the license agreement, Sigma received exclusive rights to develop and distribute ZFP-modified cell lines for commercial production of protein pharmaceuticals and certain ZFP-engineered transgenic animals for commercial applications. Under the terms of the agreement, Sigma made an upfront cash payment of \$20.0 million consisting of a \$4.9 million purchase of 636,133 shares of Sangamo common stock, valued at \$4.9 million, and a \$15.1 million upfront license fee. The upfront license fee was recognized on a straight-line basis from the effective date of the expanded license through July 2010, which represents the period over which Sangamo was obligated to perform research services for Sigma. Sangamo is also eligible to receive commercial license fees of \$5.0 million based upon a percentage of net sales and sublicensing revenue and thereafter a reduced royalty rate of 10.5% of net sales and sublicensing revenue. In addition, upon the achievement of certain cumulative commercial milestones Sigma will make milestone payments to Sangamo up to an aggregate of \$25.0 million.

		Year ended December 31,	
	2012	2011	2010
Revenue related to Sigma Collaboration:			
Royalty revenues	\$ 1,288	\$ 938	\$ 734
License fee and milestone revenues	1,000	671	11,574
Total	2,288	1,609	12,308

Related costs and expenses incurred under the Sigma agreement were \$0.3 million, \$0.5 million and \$1.2 million during 2012, 2011 and 2010, respectively.

***Agreement with Dow AgroSciences in Plant Agriculture***

In October 2005, Sangamo entered into an exclusive commercial license with DAS. Under this agreement, Sangamo is providing DAS with access to its proprietary ZFP technology and the exclusive right to use the technology to modify the genomes or alter the nucleic acid or protein expression of plant cells, plants, or plant cell cultures. Sangamo has retained rights to use plants or plant-derived products to deliver ZFP transcription factors (ZFP TFs) or ZFP nucleases (ZFNs) into humans or animals for diagnostic, therapeutic, or prophylactic purposes. The Company's agreement with DAS provided for an initial three-year research term. 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 the Company's 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, development and commercialization milestone payments for each product, and royalties on sales of products. Furthermore, DAS has the right to sublicense Sangamo's ZFP technology to third parties for use in plant cells, plants, or plant cell cultures, and Sangamo will be entitled to 25% of any cash consideration



## **Table of Contents**

received by DAS under such sublicenses. In December 2010, the Company amended its agreement with DAS to extend the period of reagent manufacturing services and research services through December 31, 2012.

The agreement also provides for minimum sublicense fees each year due to Sangamo every October, provided the agreement is not terminated by DAS. Annual fees range from \$250,000 to \$3.0 million and total \$25.3 million over 11 years. The Company does not have any performance obligations with respect to the sublicensing activities to be conducted by DAS. DAS has the right to terminate the agreement at any time; accordingly, the Company's actual sublicense fees over the term of the agreement could be lower than \$25.3 million. In addition, each party may terminate the agreement upon an uncured material breach of the agreement by the other party. In the event of any termination of the agreement, all rights to use the Company's ZFP technology will revert to Sangamo, and DAS will no longer be permitted to practice Sangamo's ZFP technology or to develop or, except in limited circumstances, commercialize any products derived from the Company's ZFP technology.

Revenues under the agreement were \$4.7 million, \$4.5 million and \$4.4 million during 2012, 2011 and 2010, respectively. Related costs and expenses incurred under the agreement were \$0.6 million, \$0.9 million and \$0.7 million during 2012, 2011 and 2010, respectively.

### **Funding from Research Foundations**

#### ***California Institute for Regenerative Medicine***

In October 2009, the CIRM, a State of California entity, granted a \$14.5 million Disease Team Research Award to develop an AIDS-related lymphoma therapy based on the application of ZFN gene-editing technology in stem cells. The four year grant supports an innovative research project conducted by a multidisciplinary team of investigators, including investigators from the University of Southern California, City of Hope National Medical Center and Sangamo BioSciences. Sangamo expects to receive funding up to \$5.2 million from the total amount awarded based on expenses incurred for research and development efforts by Sangamo as prescribed in the agreement, and subject to its terms and conditions. The award is intended to substantially fund Sangamo's research and development efforts related to the agreement. The State of California has the right to receive, subject to the terms and conditions of the agreement between Sangamo and CIRM, payments from Sangamo resulting from sales of a commercial product resulting from research and development efforts supported by the grant, not to exceed two times the amount Sangamo receives in funding under the agreement with CIRM.

Revenues attributable to research and development performed under the CIRM grant agreement for AIDS-related lymphoma therapy were \$1.2 million, \$1.7 million and \$1.0 million during 2012, 2011 and 2010, respectively. Related costs during 2012, 2011 and 2010 were \$1.2 million, \$2.0 million and \$1.0 million, respectively.

#### ***CHDI Foundation, Inc.***

In April 2011, Sangamo entered into an agreement with the CHDI to develop a novel therapeutic for Huntington's disease based on Sangamo's proprietary ZFP technology. The ZFP therapeutic approach targets the gene that causes Huntington's disease, an inherited neurodegenerative disease for which there are currently no therapies available to slow the disease progression. Under the agreement with CHDI, and subject to its terms and conditions, CHDI paid the Company \$1.3 million, the total funds due under the agreement, over a period of one year which is intended to substantially fund the Company's research efforts related to the agreement. During 2012, the agreement was amended to extend the project through August 2012 and to increase total potential funding from \$1.3 million to \$2.1 million, plus reimbursement for certain direct expenses related to the project. The agreement with CHDI terminated on August 31, 2012.

**Table of Contents**

Revenues attributable to research and development performed under the CHDI collaboration agreement were \$1.1 million during 2012 and 2011. Related costs during 2012 and 2011 were \$1.1 million and \$1.2 million, respectively.

***The Juvenile Diabetes Research Foundation International***

In October 2006, Sangamo entered into an agreement with the Juvenile Diabetes Research Foundation International (JDRF) to provide financial support for one of Sangamo's Phase 2 human clinical studies of the Company's product candidate SB-509, a ZFP Therapeutic that was in development for the treatment of diabetic neuropathy. In January 2010, JDRF and Sangamo amended the agreement and, subject to its terms and conditions, JDRF agreed to provide additional funding of up to \$3.0 million for a Phase 2b trial in diabetic neuropathy.

In October 2011, the Company announced that it would not pursue additional clinical development of the SB-509 program. In March 2012, the Company received a final payment of \$0.8 million for work performed under the agreement. The Company does not expect to receive additional funding under the agreement.

Revenues attributable to research and development activities performed under the JDRF agreements were \$0.8 million, \$0.5 million and \$1.5 million during 2012, 2011 and 2010, respectively.

***The Michael J. Fox Foundation for Parkinson's Research***

In January 2007, the Company entered into a partnership with the Michael J. Fox Foundation for Parkinson's Research (MJFF) to provide financial support of the Company's program to develop ZFP TFs to activate the expression of glial cell line-derived neurotrophic factor (GDNF). Under the agreement with MJFF and subject to its terms and conditions, MJFF paid the Company \$1.0 million, the total funds due under the agreement. In June 2010, the Company received a commitment for additional funding of \$0.9 million from MJFF to support further studies of ZFP TF activators of GDNF and intended to substantially fund Sangamo research efforts related to the agreement. As of 2012 the Company has received the entire \$1.9 million in funding available under the agreements with MJFF and does not expect to receive any further funding under this agreement.

Revenues attributable to research and development performed under the MJFF agreement were \$0.4 million in 2011 and 2010. There were no such revenues in 2012.

**Funding from Other Sources*****Qualifying Therapeutic Discovery Project Program***

In October 2010, Sangamo was awarded a total of \$1.0 million in grants for four qualifying therapeutic discovery projects under the Patient Protection and Affordable Care Act. There was no such funding in 2012 or 2011.

**NOTE 5 PROPERTY AND EQUIPMENT**

Property and equipment consist of the following (in thousands):

	December 31,	
	2012	2011
Laboratory equipment	\$ 2,950	\$ 2,851
Furniture and fixtures	499	442
Leasehold improvements	1,046	1,036
	4,495	4,329
Less accumulated depreciation	(2,952)	(2,726)
	\$ 1,543	\$ 1,603



**Table of Contents**

Depreciation expense was \$0.6 million for 2012 and 2011, and \$0.7 million for 2010. In 2012, the Company disposed of \$0.5 million in fixed assets with associated accumulated depreciation of \$0.4 million. The Company recognized a \$0.1 million loss on the write-off of these assets.

**NOTE 6 COMMITMENTS**

Sangamo occupies office and laboratory space under operating leases in Richmond, California that expire in August 2014. Rent expenses were \$0.6 million for 2012, 2011 and 2010. Future minimum payments under contractual obligations at December 31, 2012 consist of the following (in thousands):

<b>Fiscal Year:</b>	<b>Operating Lease</b>
2013	616
2014	417
Thereafter	
Total minimum payments	\$ 1,033

**NOTE 7 STOCKHOLDERS EQUITY*****Preferred Stock***

The Company has 5,000,000 preferred shares authorized, which may be issued at the Board's discretion.

***Common Stock***

In April 2011, Sangamo completed an underwritten public offering of its common stock, in which the Company sold an aggregate of 6,700,000 shares of its common stock at a public offering price of \$7.70 per share. The net proceeds to Sangamo from the sale of shares in this offering, after deducting underwriting discounts and commissions and other estimated offering expenses, were approximately \$50.2 million.

***Stock Incentive Plan***

Sangamo's 2004 Stock Incentive Plan (the 2004 Plan), which supersedes the 2000 Stock Incentive Plan (the 2000 Plan), provides for the issuance of common stock and grants of options to purchase shares of common stock to employees, officers, directors and consultants. The option exercise price per share will generally not be less than 100 percent of the fair value per share of common stock on the option grant date, and the option term will not exceed ten years. If the person to whom the option is granted is a 10 percent stockholder, and the option granted qualifies as an Incentive Stock Option Grant, then the exercise price per share will not be less than 110 percent of the fair value per share of common stock on the option grant date, and the option term will not exceed five years. Options granted under the 2004 Plan generally vest over four years at a rate of 25 percent one year from the grant date and one thirty-sixth per month thereafter and expire ten years after the grant, or earlier upon employment termination. Certain options granted under the 2004 Plan to the Company's non-employee directors have been structured so that they may be exercised prior to vesting, with the related shares subject to Sangamo's right to repurchase any shares that have not vested pursuant to the vesting schedule in effect for such award at the exercise price paid if the option holder's board service terminates. Approximately 6.5 million shares were initially reserved for issuance pursuant to the 2000 Plan and the 2004 Plan. The number of shares authorized for issuance under the 2004 Plan automatically increases on the first trading day of the fiscal year by an amount equal to 3% of the total number of shares of the Company's common stock outstanding on the last trading day of the preceding fiscal year, but in no event shall any such increase exceed 1.75 million shares per year. During 2012, 2011 and 2010, 1,576,644, 1,361,332 and 1,349,832 additional shares, respectively, were authorized for issuance under the 2004 Plan pursuant to the evergreen increase feature of such plan.

**Table of Contents****Employee Stock Purchase Plan**

Sangamo's 2010 Employee Stock Purchase Plan (Purchase Plan), which supersedes the 2000 Employee Stock Purchase Plan, provides a total reserve of 2,100,000 shares of common stock for issuance under the Purchase Plan. Eligible employees may purchase common stock at 85 percent of the lesser of the fair market value of Sangamo's common stock on the first day of the applicable two-year offering period or the last day of the applicable six-month purchase period.

**Stock Option Activity**

A summary of Sangamo's stock option activity is as follows:

	Number of Shares	Weighted- Average Exercise per Share Price	Weighted Average Remaining Contractual Term (In years)	Aggregate Intrinsic Value (In thousands)
Options outstanding at December 31, 2011	8,374,190	\$ 6.28	6.78	
Options granted	1,352,150	\$ 5.38		
Options exercised	(326,688)	\$ 3.73		
Options canceled	(215,306)	\$ 7.04		
Options outstanding at December 31, 2012	9,184,346	\$ 6.21	6.46	\$ 8,821
Options vested and expected to vest at December 31, 2012	8,806,544	\$ 6.25	6.31	\$ 8,523
Options exercisable at December 31, 2012	6,435,730	\$ 6.62	5.41	\$ 6,679

Newly created shares are issued upon exercise of options. There were no shares subject to Sangamo's right of repurchase as of December 31, 2012. The intrinsic value of options exercised was \$0.6 million, \$1.0 million and \$0.5 million during 2012, 2011 and 2010, respectively.

At December 31, 2012, the aggregate intrinsic values of the outstanding and exercisable options were \$8.8 million and \$6.7 million, respectively. The aggregate intrinsic value of shares vested and expected to vest during 2012, 2011 and 2010 was \$8.5 million, \$0.1 million and \$11.2 million, respectively.

The following table summarizes information with respect to stock options outstanding at December 31, 2012:

Range of Exercise Price	Options Outstanding and Exercisable		Options Exercisable	
	Number of Shares of common stock subject to options	Weighted Average Remaining Contractual Life (In years)	Number of Shares of common stock subject to options	Weighted Average Exercise Price
\$ 2.04 \$ 3.42	366,394	8.31	107,603	\$ 2.55
\$ 3.45 \$ 3.45	1,613,813	5.94	1,613,813	\$ 3.45
\$ 3.61 \$ 5.19	1,045,182	3.67	912,138	\$ 4.47
\$ 5.26 \$ 5.30	7,500	8.03	1,500	\$ 5.30
\$ 5.35 \$ 5.35	1,126,273	6.93	838,523	\$ 5.35
\$ 5.41 \$ 5.41	1,186,650	9.93		\$
\$ 5.42 \$ 5.66	60,500	6.24	56,333	\$ 5.46
\$ 5.70 \$ 5.70	1,132,851	7.94	565,551	\$ 5.70
\$ 5.86 \$ 6.82	1,054,230	5.88	785,006	\$ 6.49

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\$ 6.88	\$14.62	1,590,953	4.80	1,555,263	\$	12.59
		9,184,346	6.46	6,435,730	\$	6.62

71

**Table of Contents****Restricted Stock Units**

During 2012, the Company issued 486,750 Restricted Stock Units (RSUs) under the Company's 2004 Stock Incentive Plan at a grant date fair value of \$5.41. These awards will vest as follows: one-third of the award will vest in a series of three successive equal annual installments. During 2011, the Company issued 550,000 RSUs under the Company's 2004 Stock Incentive Plan at a grant date fair value of \$2.55. These awards will vest as follows: one-third of the award will vest on the second anniversary of the award date and two-thirds of the award will vest on the third anniversary of the award date. During 2010, the Company issued 10,000 RSUs under the Company's 2004 Stock Incentive Plan at a grant date fair value of \$6.05. These RSUs vested in equal monthly installments over a two-year service period. Fair value of restricted stock units are estimated based upon the closing sales price of the Company's common stock on the grant date. There were 1,036,750 and 551,667 RSUs outstanding under the Company's stock option plans as of December 31, 2012 and 2011, respectively. The aggregate value of shares vested during 2012, 2011 and 2010 was \$0.1 million, \$0.2 million and \$0.1 million, respectively.

A summary of Sangamo's restricted stock unit activity is as follows:

	Number of Shares	Weighted Average Remaining Contractual Term (In years)	Aggregate Intrinsic Value (In thousands)
RSUs outstanding at December 31, 2011	551,667		
RSUs awarded	486,750		
RSUs released	(1,667)		
RSUs forfeited	0		
RSUs outstanding at December 31, 2012	1,036,750	1.76	\$ 6,231
RSUs vested and expected to vest at December 31, 2012	835,782	1.76	\$ 5,023

As of December 31, 2012, 2,749,117 shares were reserved for future awards under the Company's stock incentive plans. As of December 31, 2012, there were 1,708,315 shares of common stock reserved for future issuance under the 2010 Employee Stock Purchase Plan.

**NOTE 8 INCOME TAXES**

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of the Company's deferred tax assets are as follows (in thousands):

	December 31, 2012	2011
Deferred tax assets:		
Net operating loss carryforwards	\$ 73,129	\$ 67,395
Research and development tax credit carryforwards	6,770	6,844
Capitalized research	5	117
Stock-based compensation	7,375	7,355
Other	937	1,125
	88,216	82,836
Valuation allowance	(88,216)	(82,836)
Net deferred tax assets	\$	\$

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Realization of deferred tax assets is dependent upon future earnings, if any, the timing and amount of which are uncertain. Accordingly, the net deferred tax assets have been fully offset by a valuation allowance. The



**Table of Contents**

valuation allowance increased by \$5.4 million, \$19.7 million and \$7.4 million for the years ended December 31, 2012, 2011 and 2010, respectively. As of December 31, 2012, Sangamo had net operating loss carryforwards for federal and state income tax purposes of approximately \$187.1 million and \$163.1 million, respectively. If not utilized, the net federal and state operating loss carryforwards will begin to expire in 2013. The Company also has federal and state research tax credit carryforwards of \$5.1 million and \$5.9 million, respectively. The federal research credits will begin to expire in 2018 while the state research credits have no expiration date. Utilization of the Company's net operating loss carryforwards and research tax credit carryforwards may be subject to substantial annual limitations due to the ownership change limitations provided by the Internal Revenue Code and similar state provisions. The annual limitation could result in the expiration of the net operating loss carryforwards and research tax credit carryforwards before use.

The Company files U.S and state income tax returns with varying statutes of limitations. The tax years from 1998 forward remain open to examination due to the carryover of net operating losses or tax credits. The Company also files various foreign income tax returns with varying statutes of limitations, and the tax years from 2006 and thereafter remain open to examination.

The Company's practice is to recognize interest and/or penalties related to income tax matters in income tax expense. As of December 31, 2012, the Company had no accrued interest and/or penalties. The unrecognized tax benefits may change during the next year for items that arise in the ordinary course of business. In the event that any unrecognized tax benefits are recognized, the effective tax rate will not be affected.

The following table summarizes the activity related to the Company's unrecognized tax benefits (in thousands):

	December 31,		
	2012	2011	2010
Beginning balance	\$ 2,750	\$ 1,896	\$ 1,643
Additions based on tax positions related to the current year	153	589	253
Additions for tax positions of prior years	58	265	
Reductions for tax positions of prior years	(227)		
Ending balance	\$ 2,734	\$ 2,750	\$ 1,896

**NOTE 9 ACCOUNTS PAYABLE AND ACCRUED LIABILITIES**

Accounts payable and accrued liabilities consist of the following (in thousands):

	December 31,	
	2012	2011
Accounts payable	\$ 3,046	\$ 4,110
Accrued clinical trial expense	615	968
Accrued professional fees	238	299
Deferred rent	94	131
Other	20	7
Total accounts payable and accrued liabilities	\$ 4,013	\$ 5,515

**NOTE 10 EMPLOYEE BENEFIT PLAN**

The Company sponsors a defined-contribution savings plan under Section 401(k) of the Internal Revenue Code covering all full-time employees (Sangamo 401(k) Plan). The Sangamo 401(k) Plan is intended to qualify under Section 401 of the Internal Revenue Code.

**Table of Contents**

In 2012, the Company matched contributions by employees equal to 50% of the first 6% of employee contributions up to a limit of \$1,000. Matching funds are fully vested when contributed. Contributions to the Sangamo 401(k) Plan in the year ended December 31, 2012, were \$0.1 million. There were no such contributions in 2011 or 2010.

**NOTE 11 QUARTERLY FINANCIAL DATA (UNAUDITED)**

The following table sets forth certain unaudited quarterly financial data for the eight quarters ended December 31, 2012. The unaudited information set forth below has been prepared on the same basis as the audited information and includes all adjustments necessary to present fairly the information set forth herein. The operating results for any quarter are not indicative of results for any future period. All data is in thousands except per common share data.

	2012				2011			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Revenues	\$ 3,243	\$ 4,574	\$ 4,907	\$ 8,931	\$ 2,200	\$ 1,514	\$ 1,857	\$ 4,748
Expenses	\$ 10,526	\$ 10,318	\$ 10,709	\$ 12,300	\$ 11,801	\$ 11,795	\$ 11,431	\$ 11,113
Net loss	\$ (7,268)	\$ (5,728)	\$ (5,790)	\$ (3,478)	\$ (9,578)	\$ (10,259)	\$ (9,554)	\$ (6,359)
Net loss per share	\$ (0.13)	\$ (0.11)	\$ (0.11)	\$ (0.07)	\$ (0.21)	\$ (0.20)	\$ (0.18)	\$ (0.12)

## **Table of Contents**

### **ITEM 9 CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE**

None.

### **ITEM 9A CONTROLS AND PROCEDURES**

#### **(I) Evaluation of Disclosure Controls and Procedures**

We maintain disclosure controls and procedures to ensure that information we are required to disclose in reports that we file or submit under the Securities Exchange Act of 1934, as amended (Exchange Act) is recorded, processed, summarized and reported within the time periods specified in Securities and Exchange Commission's (SEC) rules and forms. Our management evaluated, with the participation of our chief executive officer (CEO) and our chief financial officer (CFO), the effectiveness of our disclosure controls and procedures, as such term is defined under Rule 13a-15(e) under the Exchange Act. Based on that evaluation, our CEO and CFO concluded that our disclosure controls and procedures were effective, at a reasonable assurance level, as of December 31, 2012.

#### **(II) Management's Report on Internal Control over Financial Reporting**

Internal control over financial reporting refers to the process designed by, or under the supervision of, our CEO and CFO, and effected by our Board of Directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles, and includes those policies and procedures that:

- (1) Pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets of the Company;
- (2) Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the Company are being made only in accordance with authorizations of management and directors of the Company; and
- (3) Provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the Company's assets that could have a material effect on the financial statements.

Management is responsible for establishing and maintaining an adequate internal control over financial reporting for the Company. Internal control over financial reporting cannot provide absolute assurance of achieving financial reporting objectives because of its inherent limitations. Internal control over financial reporting is a process that involves human diligence and compliance and is subject to lapses in judgment and breakdowns resulting from human failures. Internal control over financial reporting also can be circumvented by collusion or improper management override. Because of such limitations, there is a risk that material misstatements may not be prevented or detected on a timely basis by internal control over financial reporting. However, these inherent limitations are known features of the financial reporting process. Therefore, it is possible to design into the process safeguards to reduce, though not eliminate, this risk.

Under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on the framework set forth in Internal Control Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on our evaluation under the framework set forth in Internal Control Integrated Framework, our management concluded that our internal control over financial reporting was effective as of December 31, 2012. The effectiveness of our internal control over financial reporting as of December 31, 2012 has been audited by Ernst & Young LLP, an independent registered public accounting firm, as stated in their report which is included herein.

There have been no significant changes in our internal control over financial reporting that have materially affected, or are reasonably likely to materially affect internal control over financial reporting during the fiscal quarter ended December 31, 2012.



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**Table of Contents**

**(III) Report of Independent Registered Public Accounting Firm**

The Board of Directors and Stockholders

Sangamo BioSciences, Inc.

We have audited Sangamo BioSciences, Inc.'s internal control over financial reporting as of December 31, 2012, based on criteria established in *Internal Control - Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission (the COSO criteria). Sangamo BioSciences, Inc.'s management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the company's internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, Sangamo BioSciences, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2012 based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of Sangamo BioSciences, Inc. as of December 31, 2012 and 2011, and the related consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2012 and our report dated February 26, 2013 expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP

San Jose, California

February 26, 2013

**ITEM 9B OTHER INFORMATION**

None

**Table of Contents**

**PART III**

Certain information required by Part III is omitted from this Report on Form 10-K since we intend to file our definitive Proxy Statement for our next Annual Meeting of Stockholders, pursuant to Regulation 14A of the Securities Exchange Act of 1934, as amended (the 2013 Proxy Statement), no later than April 30, 2013, and certain information to be included in the 2013 Proxy Statement is incorporated herein by reference.

**ITEM 10 DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE**

The information required by this item concerning our directors, executive officers, Section 16 compliance and corporate governance matters is incorporated by reference to the information set forth in the sections titled Election of Directors, Management, and Section 16(a) Beneficial Ownership Reporting Compliance in our 2013 Proxy Statement.

**ITEM 11 EXECUTIVE COMPENSATION**

The information required by this item regarding executive compensation is incorporated by reference to the information set forth in the sections titled Executive Compensation in our 2013 Proxy Statement.

**ITEM 12 SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS**

The information required by this item regarding security ownership of certain beneficial owners and management is incorporated by reference to the information set forth in the section titled Security Ownership of Certain Beneficial Owners and Management and Equity Compensation Plans in our 2013 Proxy Statement.

**ITEM 13 CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE**

The information required by this item regarding certain relationships and related transactions is incorporated by reference to the information set forth in the section titled Certain Relationships and Related Transactions in our 2013 Proxy Statement.

**ITEM 14 PRINCIPAL ACCOUNTING FEES AND SERVICES**

The information required by this item regarding principal accounting fees and services is incorporated by reference to the information set forth in the section titled Principal Accounting Fees and Services in our 2013 Proxy Statement.

**Table of Contents**

**PART IV**

**ITEM 15 EXHIBITS AND FINANCIAL STATEMENT SCHEDULES**

(a) The following documents are included as part of this Annual Report on Form 10-K:

1. Financial Statements See Index to Consolidated Financial Statements in Item 8.
2. Financial Statement Schedules Not Applicable.
3. Exhibits See Index to Exhibits.

Table of Contents**SIGNATURES**

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, on February 26, 2013.

SANGAMO BIOSCIENCES, INC.

By: */s/* EDWARD O. LANPHIER II  
**Edward O. Lanphier II**  
*President, Chief Executive Officer and Director*

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed by the following persons on behalf of the registrant and in the capacities and on the dates indicated:

<b>Signature</b>	<b>Title</b>	<b>Date</b>
<i>/s/</i> EDWARD O. LANPHIER II  <b>Edward O. Lanphier II</b>	President, Chief Executive Officer and  Director (Principal Executive Officer)	February 26, 2013
<i>/s/</i> H. WARD WOLFF  <b>H. Ward Wolff</b>	Executive Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)	February 26, 2013
<i>/s/</i> WILLIAM R. RINGO  <b>William R. Ringo</b>	Director and Chairman of the Board	February 26, 2013
<i>/s/</i> PAUL B. CLEVELAND  <b>Paul B. Cleveland</b>	Director	February 26, 2013
<i>/s/</i> STEPHEN G. DILLY, M.B.B.S, PH.D  <b>Stephen G. Dilly, M.B.B.S, Ph.D</b>	Director	February 26, 2013
<i>/s/</i> JOHN W. LARSON  <b>John W. Larson</b>	Director	February 26, 2013
<i>/s/</i> STEVEN J. MENTO, PH.D  <b>Steven J. Mento, Ph.D</b>	Director	February 26, 2013
<i>/s/</i> SAIRA RAMASAstry  <b>Saira Ramasastry</b>	Director	February 26, 2013



**Table of Contents**

**INDEX TO EXHIBITS**

<b>Exhibit</b>	
<b>Number</b>	<b>Description of Document</b>
3.1	Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Company's Registration Statement on Form S-1/A (Registration No. 333-30134) filed April 4, 2000).
3.2	Amended and Restated Bylaws (incorporated by reference to Exhibit 3.2 to the Company's Registration Statement on Form S-1/A (Registration No. 333-30134) filed April 4, 2000).
4.1	Form of Specimen Common Stock Certificate (incorporated by reference to Exhibit 4.1 to the Company's Registration Statement on Form S-1/A (Registration No. 333-30134) filed April 4, 2000).
10.1(+)	2000 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.2 to the Company's Registration Statement on Form S-1/A (Registration No. 333-30134) filed February 24, 2000).
10.2	Form of Indemnification Agreement entered into between Sangamo and each of its directors and executive officers (incorporated by reference to Exhibit 10.4 to the Company's Registration Statement on Form S-1/A (Registration No. 333-30134) filed February 24, 2000).
10.3	Sublicense Agreement, by and between Sangamo and Johnson & Johnson, dated May 9, 1996 (incorporated by reference to Exhibit 10.3 to the Company's Annual Report on Form 10-K/A filed April 22, 2010).
10.4	Patent License Agreement between Sangamo and Massachusetts Institute of Technology, dated May 9, 1996, as amended by the First Amendment, dated December 10, 1997 (incorporated by reference to Exhibit 10.4 to the Company's Annual Report on Form 10-K/A filed April 22, 2010).
10.5	License Agreement between Sangamo and the Johns Hopkins University, dated June 25, 1995, as amended by Amendment No. 1, dated July 16, 1998 (incorporated by reference to Exhibit 10.5 to the Company's Annual Report on Form 10-K/A filed April 22, 2010).
10.6	Triple Net Laboratory Lease, between Sangamo and Point Richmond R&D Associates II, LLC, dated May 23, 1997 (incorporated by reference to Sangamo's Registration Statement on Form S-1 (Reg. No. 333-30314), as amended).
10.7(+)	Employment Agreement, between Sangamo and Edward O. Lanphier II, dated June 1, 1997 (incorporated by reference to Exhibit 10.15 to the Company's Registration Statement on Form S-1/A (Registration No. 333-30134) filed March 14, 2000).
10.8	Second Amendment to Patent License Agreement between Sangamo and Massachusetts Institute of Technology, dated December 2, 1998 (incorporated by reference to Exhibit 10.8 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
10.9	Amendment No. 2 to License Agreement between Sangamo and the Johns Hopkins University, effective as of July 26, 1999 (incorporated by reference to Exhibit 10.9 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
10.10	Third Amendment to Patent License Agreement between Sangamo and Massachusetts Institute of Technology, dated September 1, 1999 (incorporated by reference to Exhibit 10.10 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
10.11	Fourth Amendment to Patent License Agreement between Sangamo and Massachusetts Institute of Technology, effective as of February 10, 2000 (incorporated by reference to Exhibit 10.11 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
10.12	Amendment No. 3 to License Agreement between Sangamo and the Johns Hopkins University, effective as of March 10, 2000 (incorporated by reference to Exhibit 10.12 to the Company's Annual Report on Form 10-K, filed March 5, 2010).

## **Table of Contents**

### **Exhibit**

<b>Number</b>	<b>Description of Document</b>
10.13	License Agreement by and between The Scripps Research Institute and Sangamo, dated March 14, 2000 (incorporated by reference to Exhibit 10.13 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
10.14	Fifth Amendment to Patent License Agreement between Sangamo and Massachusetts Institute of Technology, effective as of December 15, 2000 (incorporated by reference to Exhibit 10.14 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
10.15(+)	2004 Stock Incentive Plan (incorporated by reference to Appendix C of the Company's Definitive Proxy Statement on Schedule 14A filed April 29, 2004).
10.16	First Amendment to Triple Net Laboratory Lease, between Sangamo and Point Richmond R&D Associates II, LLC, dated March 12, 2004 (incorporated by reference to Sangamo's Annual Report on Form 10-K for the year ended December 31, 2004).
10.17	Sixth Amendment to Patent License Agreement between Sangamo and Massachusetts Institute of Technology, dated September 1, 2005 (incorporated by reference to Exhibit 10.17 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
10.18	Research and Commercial Option License Agreement, dated October 5, 2005, between Sangamo and Dow AgroSciences LLC (incorporated by reference to Exhibit 10.23 to the Company's Annual Report on Form 10-K, filed March 16, 2006).
10.19	Research, Development and Commercialization Agreement dated October 24, 2006 between Sangamo and Juvenile Diabetes Research Foundation International (incorporated by reference to Exhibit 10.19 to the Company's Annual Report on Form 10-K, filed March 1, 2007).
10.20	Seventh Amendment to Patent License Agreement between Sangamo and Massachusetts Institute of Technology, dated October 27, 2006 (incorporated by reference to Exhibit 10.20 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
10.21	First Amendment of Research and Commercial Option License Agreement between Sangamo and Dow AgroSciences LLC, dated November 7, 2006 (incorporated by reference to Exhibit 10.21 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
10.22	Asset Purchase Agreement dated December 1, 2006 by and between Sangamo and Edwards Lifesciences LLC (incorporated by reference to the Company's Form 8-K filed on December 28, 2006).
10.23	Eighth Amendment to Patent License Agreement between Sangamo and Massachusetts Institute of Technology, dated February 1, 2007 (incorporated by reference to Exhibit 10.23 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
10.24	Research and License Agreement between Sangamo and Genentech, Inc., dated April 27, 2007 (incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q, filed August 9, 2007).
10.25	Amendment No. 4 to License Agreement between Sangamo and the Johns Hopkins University, effective as of May 21, 2007 (incorporated by reference to Exhibit 10.25 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
10.26	License Agreement between Sangamo and Sigma-Aldrich Corporation, dated July 10, 2007 (incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q, filed November 1, 2007).
10.27	Common Stock Purchase Agreement between Sangamo and Sigma-Aldrich Corporation, dated July 10, 2007 (incorporated by reference to Exhibit 10.1 to the Company's Form 8-K filed on July 10, 2007).

## **Table of Contents**

### **Exhibit**

<b>Number</b>	<b>Description of Document</b>
10.28	First Amendment of the License Agreement between Sigma-Aldrich Corporation and Sangamo, dated November 9, 2007 (incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed on November 6, 2009).
10.29	Letter Agreement between Sangamo and Sigma-Aldrich Corporation, dated February 25, 2008 (incorporated by reference to Exhibit 10.2 to the Company's Form 10-Q filed on May 9, 2008).
10.30	Second Research and License Agreement between Sangamo and Genentech, Inc., dated February 27, 2008 (incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed on May 9, 2008).
10.31	License Agreement between Sangamo and Open Monoclonal Technology, Inc., dated April 2, 2008 (incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed on August 7, 2008).
10.32	Amendment to License Agreement by and between The Scripps Research Institute and Sangamo, dated April 29, 2008 (incorporated by reference to Exhibit 10.32 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
10.33	Research and License Agreement between Sangamo and F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc., dated July 2, 2008 (incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed on November 4, 2008).
10.34(+)	Plan Amendment to 2004 Stock Incentive Plan (incorporated by reference to Exhibit 10.2 to the Company's Form 10-Q filed on August 7, 2008).
10.35	Letter Agreement between Sangamo and Sigma-Aldrich Corporation, dated July 2, 2008 (incorporated by reference to Exhibit 10.2 to the Company's Form 10-Q filed on November 4, 2008).
10.36	License Agreement between Sangamo and Pfizer Inc., dated December 19, 2008 (incorporated by reference to Exhibit 10.25 to the Company's Annual Report on Form 10-K, filed March 3, 2009).
10.37(+)	Amended and Restated Employment Agreement between Sangamo and H. Ward Wolff, dated December 31, 2008 (incorporated by reference to Exhibit 10.26 to the Company's Annual Report on Form 10-K, filed March 3, 2009).
10.38(+)	First Amendment to Employment Agreement between Sangamo and Edward O. Lanphier, dated December 31, 2008 (incorporated by reference to Exhibit 10.27 to the Company's Annual Report on Form 10-K, filed March 3, 2009).
10.39	Second Amendment of Research and Commercial Option License Agreement between Sangamo and Dow AgroSciences LLC, dated February 13, 2009 (incorporated by reference to Exhibit 10.39 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
10.40	Third Amendment of Research and Commercial Option License Agreement between Sangamo and Dow AgroSciences LLC, dated February 28, 2009 (incorporated by reference to Exhibit 10.40 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
10.41	Second Amendment of the License Agreement between Sigma-Aldrich Corporation and Sangamo, dated September 25, 2009 (incorporated by reference to Exhibit 10.2 to the Company's Form 10-Q filed on November 6, 2009).
10.42	Common Stock Purchase Agreement between Sangamo and Sigma-Aldrich Corporation, dated October 2, 2009 (incorporated by reference to Exhibit 10.3 to the Company's Form 8-K filed on October 5, 2009).
10.43	Third Amendment to the License Agreement between Sigma-Aldrich Corporation and Sangamo, dated October 2, 2009 (incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed on November 6, 2009).

## **Table of Contents**

<b>Exhibit</b>	
<b>Number</b>	<b>Description of Document</b>
10.44	First Amendment to the Research, Development and Commercialization Agreement between Sangamo and Juvenile Diabetes Research Foundation International, dated January 8, 2010 (incorporated by reference to Exhibit 10.44 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
10.45	Fourth Amendment of Research and Commercial Option License Agreement between Sangamo and Dow AgroSciences LLC, dated January 8, 2010 (incorporated by reference to Exhibit 10.45 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
10.46	Form of Non-Employee Director Restricted Stock Issuance Agreement (incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed on August 5, 2010).
10.47	Fifth Amendment of the Research and Commercial License Option Agreement between Sangamo BioSciences, Inc. and Dow AgroSciences LLC, dated May 14, 2010 (incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed on November 3, 2010).
10.48	Sixth Amendment of the Research and Commercial License Option Agreement between Sangamo BioSciences, Inc. and Dow AgroSciences LLC, dated August 27, 2010 (incorporated by reference to Exhibit 10.2 to the Company's Form 10-Q filed on November 3, 2010).
10.49	Seventh Amendment of the Research and Commercial License Option Agreement between Sangamo BioSciences, Inc. and Dow AgroSciences LLC, dated December 3, 2010 (incorporated by reference to Exhibit 10.49 to the Company's Form 10-K filed on February 16, 2011).
10.50	Letter Agreement Amendment regarding the Research and Commercial License Option Agreement between Sangamo BioSciences, Inc. and Dow AgroSciences LLC, dated December 3, 2010 (incorporated by reference to Exhibit 10.50 to the Company's Form 10-K filed on February 16, 2011).
10.51	Letter Agreement between Sangamo and Sigma-Aldrich Corporation, dated March 1, 2011 (incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed on August 5, 2011).
10.52	Letter dated May 19, 2011 from Dow AgroSciences LLC ( DAS ) to Sangamo amending the Research and Commercial License Option Agreement between DAS and Sangamo, dated as of October 1, 2005, as amended (incorporated by reference to Exhibit 10.2 to the Company's Form 10-Q filed on August 5, 2011).
10.53(+)	Amended and Restated Employment Agreement between Sangamo and Edward O. Lanphier II, dated June 21, 2011 (incorporated by reference to Exhibit 10.3 to the Company's Form 10-Q filed on August 5, 2011).
10.54(+)	Employment Agreement between Sangamo and Dr. Geoff Nichol, dated June 17, 2011 (incorporated by reference to Exhibit 10.4 to the Company's Form 10-Q filed on August 5, 2011).
10.55(+)	Amended and Restated Employment Agreement between Sangamo and H. Ward Wolff, dated December 15, 2011 (incorporated by reference to Exhibit 10.55 to Company's Form 10-K filed on February 23, 2012).
10.56(+)	Form of Restricted Stock Unit Agreement under the Company's 2004 Stock Incentive Plan (incorporated by reference to Exhibit 10.1 to the Company's Form 8-K filed on December 3, 2007).
10.57	Collaboration and License Agreement between Sangamo and Shire AG, dated January 31, 2012 (incorporated by reference to Exhibit 10.57 to the Company's Form 10-K filed on February 23, 2012).
10.58	Fourth Amendment of the License Agreement between Sangamo and Sigma-Aldrich Corporation, dated as of September 14, 2012 (incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed on November 2, 2012).

## **Table of Contents**

<b>Exhibit</b>	
<b>Number</b>	<b>Description of Document</b>
10.59	Sangamo BioSciences, Inc. Incentive Compensation Plan (incorporated by reference to Exhibit 10.1 to the Company's Form 8-K filed on June 27, 2012).
21.1	Subsidiaries of the Company (incorporated by reference to Exhibit 21.1 to the Company's Annual Report on Form 10-K, filed March 27, 2003).
23.1	Consent of Independent Registered Public Accounting Firm.
31.1	Rule 13a-14(a) Certification of Principal Executive Officer.
31.2	Rule 13a-14(a) Certification of Principal Financial Officer.
32.1	Certification Pursuant to 18 U.S.C. Section 1350.
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

Confidential treatment has been granted for certain information contained in this document pursuant to an order of the Securities and Exchange Commission. Such information has been omitted and filed separately with the Securities and Exchange Commission.

(+) Indicates management contract or compensatory plan or arrangement.