SANGAMO BIOSCIENCES INC
Form 10-K
February 25, 2015

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2014

or

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

Commission file number: 0-30171

SANGAMO BIOSCIENCES, INC.

(Exact name of registrant as specified in its charter)

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

(510) 970-6000

(Registrant's telephone number, including area code)

None

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

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

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

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

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

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 x

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 x 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 x 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. x

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	x	Accelerated filer	¨
Non-accelerated filer	¨ (Do not check if a smaller reporting company)	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 x

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, 2014 (the last business day of the registrant's most recently completed second fiscal quarter), as reported on the NASDAQ Global Select Market was $800,449,430. 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, 2015
Common Stock, $0.01 par value per share	69,170,150 shares

DOCUMENTS INCORPORATED BY REFERENCE

Document	Parts Into Which Incorporated
Proxy Statement for the 2015 Annual Meeting of Stockholders	Part III

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;
·product development and commercialization of our products;
·clinical trials;
·partnering, acquisition and other strategic transactions;
·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,” “intends,” “may,” “plans,” “seeks,” “should” and “will.” These statements reflect our current views wit 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.

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 as novel therapeutic products for unmet medical needs. Our current mission is to develop ZFP Therapeutics®, based on our proprietary ZFP technology, 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 longer-term, our goal is to integrate manufacturing, development and commercial operations to capture the value of our proprietary ZFP Therapeutic products.

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 to make ZFP nucleases (ZFNs), proteins that can be used to specifically modify DNA sequences in a variety of ways (genome editing) and ZFP transcription factors (ZFP TFs), proteins that can be used to turn genes on or off (gene regulation). 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, including a Phase 2 study (SB-728mR-T-1401) in HIV-infected subjects. We expect to present data from this program at appropriate scientific and medical meetings in 2015.

In January 2014, we established a collaborative partnership with Biogen Idec Inc. (Biogen) to research, develop and commercialize our preclinical ZFP Therapeutic development program, in hemoglobinopathies, including sickle cell disease (SCD) and beta-thalassemia. We also have a collaborative partnership with Shire International GmbH, formerly Shire AG, (Shire) to research, develop and commercialize certain of our preclinical ZFP Therapeutic development programs, including programs in hemophilia, Huntington's disease (HD) and other monogenic diseases. We have proprietary preclinical programs in several lysosomal storage disorders (LSDs). In addition, we have research stage programs in other monogenic diseases, including certain immunodeficiencies, as well as central nervous system (CNS) disorders and cancer immunotherapy.

We believe the potential commercial applications of ZFPs are broad-based and we have entered into strategic partnerships in fields outside human therapeutics to facilitate the sale or licensing of our ZFP platform as follows:

- 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 ®.
- 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.

Through our subsidiary Ceregene, Inc. (Ceregene), acquired in October 2013, we are conducting a Phase 2 clinical trial for the development of an adeno-associated virus (AAV) gene therapy (CERE 110) for the treatment of Alzheimer's disease (AD).

We have a substantial intellectual property position in the design, selection, composition and use of engineered ZFPs to support our commercial activities. As of February 4, 2015, we either owned outright or have exclusively licensed the commercial rights to approximately 667 patents issued in the United States and foreign national jurisdictions, and we have 583 patent applications owned and licensed pending worldwide, including patents acquired from Ceregene. 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, or mutation 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 of disorders have been identified that are caused by the inheritance of a single defective gene. These so-called monogenic diseases include hemophilia, HD, SCD, LSDs and many others.

Zinc finger DNA-binding proteins (ZFPs) are Naturally Occurring Transcription Factors in Humans

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 editing 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 Genome Editing 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 for any genomic target. We use the engineered ZFP DNA-binding domain linked to a functional domain. The ZFP DNA-binding domain brings the functional domain into the proximity of the gene of interest. 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 genome 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. When a pair of ZFNs is bound to the DNA in the correct orientation and spacing, the DNA sequence is cut between the ZFP binding sites. DNA binding by both ZFNs is necessary for cleavage, 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. ZFN-mediated genome editing can 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. We are also using ZFN-mediated gene disruption of the BCL11A gene in hematopoietic stem progenitor cells (HSPCs) as a potentially curative treatment for SCD and beta-thalassemia.

In contrast, if cells with a mutation in a particular gene are treated with a DNA sequence that encodes the correct gene sequence (referred to as a “donor” DNA) and with ZFNs that recognize and bind to sequences flanking the mutation, the cell’s repair machinery can use the donor as a template to correct the mutated gene. This ZFN-mediated gene correction enables the 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 certain monogenic diseases. In addition, by making the donor sequence a gene-sized segment of DNA, a new copy of a gene can also be precisely added into the genome at a specific location. The ability to precisely 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 integrating gene replacement approaches such as retroviruses, 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 (IVPRP), 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 treatment of hemophilia and LSDs which may potentially provide a single curative treatment for these diseases.

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 HD in which we are evaluating a ZFP TF designed to differentially down regulate the mutated disease-causing Huntingtin (HTT) gene, while leaving expression of the normal gene unchanged.

Figure 3:

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

To date, we and our partners have designed, engineered and assembled many thousands of 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 endonuclease domains to create highly specific ZFNs and to numerous functional domains to create gene-specific ZFP TFs and have demonstrated the ability of these proteins to enable genome editing or gene regulation, respectively, in hundreds of genes in dozens of different cell types and in whole organisms, including non-human primates, 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 from many of these studies in peer-reviewed scientific journals. ZFNs are currently being used 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 have ongoing clinical trials to evaluate the safety and efficacy of ZFNs in humans.

We have several strategies for the application of our ZFP Therapeutics depending on the disease or indication. We routinely deliver our therapeutics as nucleic acids, either as messenger RNA (mRNA) or encoded in a viral vector that the cell then uses to make the protein form of the ZFN or ZFP TF. We can deliver ZFP Therapeutics ex vivo (outside the body) to isolated cells of the blood, such as T-cells, in the case of our clinical HIV program, and HSPCs for our programs in HIV and monogenic blood diseases such as SCD 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 IVPRP programs in hemophilia and LSD, or directly into a specific tissue such as the brain as in our HD program.

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

With our ability to generate gene-specific ZFNs for genome editing or 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 and conventional gene therapy approaches, enabling us to pursue the development of therapies for a broad range of unmet medical needs.

For example, ZFP Therapeutics can:

- Provide novel activities such as genome editing 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 either repression or activation of a therapeutically relevant gene in a cell. This gives our technology a degree of flexibility not seen in other drug platforms. Our ZFN genome editing technology, which requires only brief cellular expression of ZFNs, allows the permanent correction of a mutation in a defective gene in a highly specific fashion. This provides a novel therapeutic and potentially life-long clinical benefit in the treatment of monogenic diseases, such as hemophilia. 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 editing 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 relatively low concentrations. In contrast, drugs that act on protein and RNA targets that are naturally present in higher cellular concentrations may 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 may be toxic in the concentrations required to be therapeutically effective.

THERAPEUTIC PRODUCT DEVELOPMENT

ZFP Therapeutic Product Development Programs

Figure 4:

Sangamo's Therapeutic Pipeline

Clinical Stage Programs

Product Candidate	Targeted Indication	Stage of Development	Protocol	Milestones
SB-728-T	HIV/AIDS	Phase 2	SB-728mR-T-1401	Trial initiated in 2014. Accrual completed. Initial data expected in late 2015.
		Phase 1/2	SB-728-1101 (Cytoxan pre-conditioning dose-ranging study)	Trial initiated in January 2012. Enrollment and treatment completed. Initial data presented in 2013 and Cytoxan dose-escalation completed in 2014. Data updates expected in 2015.
		Phase 1	SB-728-902, Cohorts 1-3 Cohort 5 (CCR5 delta-32 heterozygotes)	Enrollment and treatment completed, in long-term follow-up. Data presented in 2013 and 2014.
		Phase 1	SB-728-T*	Enrollment and treatment completed, in long-term follow-up. Data published+ 2014.
		Phase 2	SB-728-T* (Cytoxan pre-conditioning)	Trial expected to begin at University of Pennsylvania in 1H 2015.
SB-728-HSPC	HIV/AIDS	Phase 1	SB-728-HSPC*	Trial expected to begin at City of Hope in 1H 2015.
SB-BCLmR-HSPC	Beta-thalassemia major	Phase 1/2	SB-BCLmR-HSPC	Trial expected to begin in 1H 2015.
CERE-110 (AAV-NGF)	Alzheimer's disease	Phase 2		All subjects treated, in two year follow-up. Data expected in 2015.

Table 1: Summary of our ongoing clinical trials.

(*Investigator sponsored trial)

+ N.Eng. J. Med. 2014: 370:897-906 “Gene Editing of CCR5 in Autologous CD4 T-cells of Persons Infected with HIV.”

9

ZFP Therapeutic Clinical Stage Programs

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

HIV infection results in the death of immune system cells, particularly CD4+ 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 The United States Centers for Disease Control and Prevention (CDC) over 2.1 million people were newly infected with HIV in 2013. An estimated 1.5 million people died of AIDS-related illnesses in the same year. There are now over 35 million people living with HIV and AIDS worldwide. At the end of 2011, (the most recent data available) it is estimated that there were 1.2 million people living with HIV/AIDS in the United States, of which approximately 14% were unaware that they were infected. Approximately 48,000 new infections occurred in 2010, and more than 13,500 people with AIDS died in the United States in 2011.

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. Currently available drugs do not cure HIV infection or AIDS. 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.

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, or ART. This strategy typically combines drugs from at least three different classes of antiretroviral drugs. 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 genome 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, of both of their CCR5 gene copies (homozygous), resulting in the expression of a shortened non-functional CCR5 protein. This mutation appears to have no observable deleterious effect. Individuals who carry the CCR5 delta-32 mutation in 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 who was homozygous for this CCR5 delta-32 mutation. This approach transferred the 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 genome editing 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

CCR5 delta-32 mutation. In December 2008, in collaboration with scientists at the University of Pennsylvania, an 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. The data from this study was published in the New England Journal of Medicine in 2014 (N.Eng. J. Med. 2014: 370:897-906). The study demonstrated that the treatment was well tolerated and that ZFN-modified cells show long-term engraftment and have a survival advantage over unmodified cells during an ART treatment interruption (TI).

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 ART. 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 in the overall CD4 T-cell count and the CD4:CD8 ratio in multiple subjects.

In January 2012, we 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 circulating 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 TI. Using different approaches, both studies aim to increase the engraftment of cells that have undergone biallelic modification 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. Ten CCR5 delta-32 heterozygote subjects were accrued and treated on the SB-728-902, Cohort 5 study and a total of 21 subjects were accrued and treated on the SB-728-1101 study, a trial which evaluated the effect of increasing doses of Cytoxan conditioning prior to SB-728-T administration on engraftment of cells that have undergone biallelic ZFN modification. Data collected from the first 18 subjects treated in this study were presented at scientific meetings in 2013 and 2014 that further supported a correlation between the estimated numbers of engrafted biallelically modified cells and the reduction in viral load with one subject in the SB-728-902 study demonstrating a prolonged control of viral load for over a year and a half during TI. An additional three subjects were enrolled into SB-728-1101 for evaluation of the effect of the optimal dose of Cytoxan. We expect to present additional data from the SB-728-1101 study in 2015.

In 2014, we filed an IND application and initiated a new Phase 2 clinical trial, SB-728mR-T-1401, in which we are using electroporation of mRNA to deliver the CCR5-specific ZFNs to the isolated T-cells. This trial incorporates several modifications and improvements in the process developed from our previous studies with stem cells, including the delivery of ZFNs using mRNA which enables the administration of multiple doses of cells into the subjects. We accrued all nine subjects into the trial in 2014 and expect to have initial data from this study in late 2015.

We also have a program to investigate this approach to treat HIV in hematopoietic stem progenitor cells (HSPCs), again using electroporation of mRNA to deliver the ZFNs. We filed an IND application in 2014 and expect to begin a Phase 1 clinical trial in the first half of 2015 in subjects infected with HIV who have low CD4 counts despite successful viral control by ART, so-called immunologic non-responders. In October 2009, we and our collaborators at City of Hope Medical Center and the University of Southern California received partial funding for the preclinical development of this program from a four-year $14.5 million Disease Team Research Award granted by the California Institute for Regenerative Medicine (CIRM), a State of California entity. We have received $5.2 million in funding through December 31, 2013, which is our total prescribed amount under the agreement. In May 2014, CIRM agreed to fund a $5.6 million Strategic Partnership Award for clinical studies of this program at City of Hope.

Programs Partnered with Biogen

Hemoglobinopathies: Sickle cell disease and Beta-thalassemia

Mutations in the gene encoding beta-globin, the oxygen carrying protein of red blood cells, lead to hemoglobinopathies such as 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 which further decrease the amount of oxygen flowing to body tissues. Almost all patients with SCD have these painful vaso-occlusive crises, which can last from hours to days and may cause irreversible organ damage. Current standard of care is to manage and control symptoms, and to limit the number of crises. Treatments include administration of hydroxyurea, blood transfusions, iron-chelation therapy, pain medications and antibiotics. As of 2011, 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 greatly impaired production of healthy red blood cells despite bone marrow over activity, leading to life-threatening anemia, enlarged spleen, liver and heart, and bone abnormalities. Beta-thalassemia major is a severe form of thalassemia that requires regular, often monthly, blood transfusions and subsequent iron-chelation therapy to treat iron overload. The CDC estimates that 1,000 people have beta-thalassemia major 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 Southeast Asia, the Arabian Peninsula, Iran, Africa and Southern China.

In collaboration with Biogen, we are developing ZFP Therapeutics for both SCD and beta-thalassemia based on the use of our ZFN genome editing technology to modify a patient's own (autologous) HSPCs. Our ZFN genome editing technology enables multiple approaches to the correction of SCD and beta-thalassemia. Both diseases manifest in the months after birth, when patients switch from producing functional fetal gamma-globin to a mutant form of adult beta-globin, which results in their condition. Naturally occurring increased levels of fetal hemoglobin have been shown to reduce the severity of both SCD and beta-thalassemia disorders. In HSPCs, our genome editing technology can be used to precisely disrupt key transcriptional regulators, such as BCL11A, to reverse the switch from expression of the mutant adult beta-globin back to the production of functional fetal gamma-globin. Alternatively, the technology can be used to precisely insert a new corrected beta-globin gene to replace the defective copy.

A bone marrow transplant (BMT), of HSPCs from a “matched” related donor (allogeneic BMT) is curative for both diseases. However, this therapy is limited due to the scarcity of matched donors and the significant risk of Graft versus Host Disease (GvHD) after transplantation of the foreign cells. By performing genome editing in HSPCs that are isolated from and subsequently returned to the same patient (i.e. an autologous HSPC transplant), our approach eliminates both the need for a matched donor and the risk of acute and chronic GvHD. The goal of this approach is to develop a one-time curative treatment for SCD and beta-thalassemia.

In May 2013, we were awarded a $6.4 million CIRM Strategic Partnership Award to develop this potentially curative ZFP Therapeutic for beta-thalassemia. The four-year grant provides additional funds for preclinical studies that support an IND application and a Phase 1 clinical trial in transfusion-dependent beta-thalassemia patients. We filed our IND application for beta-thalassemia in 2014 and expect to begin the Phase 1 clinical trial in the first half of 2015. Our goal is to file an IND application in 2016 for our SCD program.

ZFP Therapeutic Preclinical 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 lead 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 and the World Federation of Hemophilia, hemophilia A occurs in about one in every 5,000 male births in the US with approximately 16,000 males currently affected in the US, and hemophilia B in about 1 in every 25,000 male births with approximately 4,000 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.

As part of our collaboration, Shire has selected four gene targets, clotting factors VII, VIII, IX and X for the development of ZFP Therapeutics to treat hemophilia. Using our ZFN technology we are pursuing two approaches in the development of these therapeutics: addition of a new correct copy of the Factor VIII or IX gene into a safe-harbor site, the Albumin gene or locus, using our In Vivo Protein Replacement Platform (IVPRP), and correction of the disease-causing mutation in the endogenous copy of the Factor VIII or IX gene. We have published data demonstrating functional correction of the human factor IX gene in the liver by direct intravenous delivery of AAV encoding ZFNs in a mouse model of the disease (Nature 475, 217–221, 14 July 2011). Preclinical studies of our IVPRP approach, have demonstrated that therapeutic levels of Factor IX could be generated in a dose-dependent manner in non-human primates (NHPs). There were no significant alterations in circulating albumin levels. Studies in mice also demonstrated stable Factor IX production for over 1 year. The IVPRP is designed to be a broadly applicable strategy for gene replacement that will provide a permanent correction for the lifetime of the patient and would reduce or eliminate the need for chronic infusions of replacement proteins or clotting factor products. Our goal is to submit IND applications for our ZFP Therapeutic program in hemophilia B in 2015, and for hemophilia A in 2016.

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 HTT gene. Most patients inherit one normal and one defective or mutant copy of the HTT gene, which caused 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. According to the Huntington’s Disease Society of America (HDSA) one in 10,000 people in the U.S. has HD (approximately 30,000 people). In addition, it is estimated that approximately 200,000 people in the U.S. are at risk of developing the disease.

Research in animal models of the disease has shown that lowering the levels of the mutant 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 2016.

Proprietary Preclinical Programs

Lysosomal Storage Disorders

Lysosomal storage disorders (LSDs) are a heterogeneous group of inherited disorders including Fabry disease, Gaucher disease, Hunter syndrome and Hurler syndrome and many others. 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 CNS. While their individual incidence tends to be rare, this group as a whole has an incidence of more than 1:5,000 live births according to the National Institute of Neurological Disorders and Stroke.

There are no cures for LSDs, and treatments have not yet been developed for many of these diseases. For certain disorders, including Gaucher, Fabry, Hunter and Hurler, enzyme replacement therapies (ERTs) are available. However, these require frequent administration, are costly and there is a risk that over time patients develop an immune response to the administered protein lessening its efficacy.

Our IVPRP has the potential to provide a broadly applicable genetic approach to enzyme replacement for several LSDs. Beginning with Hurler syndrome (mucopolysaccharidosis I or MPS I) and Hunter syndrome (mucopolysaccharidosis II or MPS II) our aim is use this approach to enable the patient’s liver to produce therapeutic quantities of the corrective enzymes, alpha-L-iduronidase and iduronate-2-sulfatase, respectively. Both Hunter and Hurler syndromes result in the accumulation of complex sugars called glycosaminoglycans that lead to a variety of problems. Symptoms are not present at birth but appear in early childhood and may include delayed development, enlarged internal organs, cardiovascular disorders, stunted growth and skeletal abnormalities in the case of Hunter syndrome, and abnormal bones in the spine, halted growth, deafness, joint disease and progressive intellectual disability in the case of Hurler syndrome.

We are in preclinical development for these proprietary programs and our goal is to file IND applications for product candidates for MPS I and MPS II in 2015 and two additional IND applications for other LSDs in 2016.

ZFP Therapeutic Research Programs

We have research stage programs in other monogenic diseases, in CNS disorders and in cancer immunotherapy.

AAV-NGF Therapeutic Clinical Stage Program

Clinical Development Programs Acquired from Ceregene

CERE-110 (AAV-NGF), a gene therapy approach for the treatment of AD designed to deliver nerve growth factor (NGF) directly to the brain using an AAV vector, was developed by Ceregene. The program and ongoing Phase 2 clinical trial were assets that we acquired from Ceregene in October 2013. In November 2013, we released preliminary data from a Phase 1 dose escalation study of CERE-110 demonstrating that surgical delivery of CERE-110 to the brain results in the long-term expression of bioactive NGF, the therapeutic protein. Clinicians also observed apparent stabilization of brain cell metabolic activity in treated subjects, as determined by PET-scans measuring glucose use, which may reflect a slowing of cell deterioration. The treatment was well-tolerated at all dose

levels. The Phase 2 clinical trial is fully accrued and is being carried out in collaboration with the Alzheimer's Disease Cooperative Study (ADCS) based at the University of California San Diego (UCSD) and funded by a grant from the National Institute on Aging (NIA). Forty-nine (49) patients with mild to moderate AD have been treated with a single administration of CERE-110 at ten clinical sites throughout the U.S. Approximately half of the patients received CERE-110 while the other half received an appropriate sham surgery control treatment. Patients are being followed for a minimum of two years with respect to safety, brain imaging as well as standard tests used in Alzheimer's clinical trials to measure cognitive function and quality of life. Enrollment was completed in March 2013 and we expect to have data from this study in 2015.

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 Biogen Idec Inc. in Human Therapeutics and Diagnostics

In January 2014, we entered into an exclusive worldwide collaboration and license agreement with Biogen to develop therapeutics for hemoglobinopathies, focused on beta-thalassemia and SCD. Under the agreement, the two companies will jointly conduct two research programs: the beta-thalassemia program and the SCD program. In the beta-thalassemia program, we are responsible for all discovery, research and development activities through the first human clinical trial. In the SCD program, both parties are responsible for research and development activities through the submission of an IND application for ZFP therapeutics intended to treat SCD. Biogen reimburses us for agreed upon internal and external program-related costs.

Under both programs, Biogen is responsible for subsequent worldwide clinical development, manufacturing and commercialization of licensed products developed under the agreement. At the end of specified research terms for each program or under certain specified circumstances, Biogen retains the right to step in and take over any of our remaining activities. Furthermore, we have an option to co-promote in the U.S. any licensed product to treat beta-thalassemia and SCD developed under the agreement, and Biogen will compensate us for such co-promotion activities. Subject to the terms of the agreement, we have granted Biogen an exclusive, royalty-bearing license, with the right to grant sublicenses, to use certain ZFP and other technology controlled by Sangamo for the purpose of researching, developing, manufacturing and commercializing licensed products developed under the agreement. We have also granted Biogen a non-exclusive, worldwide, royalty-free, fully paid license, with the right to grant sublicenses, of our interest in certain other intellectual property developed pursuant to the agreement.

Under the agreement, we received an upfront license fee of $20.0 million and are eligible to receive development milestone payments upon the achievement of specified regulatory, clinical development and commercialization milestones. The total amount of potential regulatory, clinical development, commercialization and sales milestone payments, assuming the achievement of all specified milestones in the agreement, is $293.8 million, including Phase 1 milestone payments of $7.5 million for each of the beta-thalassemia and SCD programs. In addition, we will also receive royalty payments for each licensed product that are a tiered double-digit percentage of annual net sales of each product.

The Agreement may be terminated by (i) us or Biogen for the uncured material breach of the other party, (ii) us or Biogen for the bankruptcy or other insolvency proceeding of the other party; (iii) Biogen, upon 180 days' advance written notice to us and (iv) Biogen, for certain safety reasons upon written notice to, and after consultation with, us. As a result, actual future milestone payments could be lower than the amounts stated above.

Collaboration and License Agreement with Shire International GmbH (formerly Shire AG) in Human Therapeutics and Diagnostics

In January 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 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 treating HD. 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 reimburses us for agreed upon 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. In the third quarter of 2014 we received a $1.0 million milestone payment from Shire related to toxicology studies for our hemophilia B program.

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 our proprietary ZFP technology and the exclusive right to use the technology to develop and commercialize research reagents products and services in the research field, excluding certain agricultural research uses that we previously licensed to DAS. 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. Under the terms of the agreement, we are eligible to 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. We established agreements in cell line engineering for pharmaceutical protein production with Genentech and in the development of transgenic animals with Open Monoclonal Technology, Inc. (OMT) and F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. (collectively, Roche).

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.

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. Roche 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 $5.8 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.

Funding from Research Foundations

California Institute for Regenerative Medicine

In October 2009, CIRM granted a $14.5 million Disease Team Research Award to develop an HIV therapy based on the application of ZFN genome editing technology in HSCs. 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. Through December 31, 2014, we have received total funding of $5.2 million, which is the total amount awarded to us as prescribed in the agreement. The award was 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 or our collaborators, 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.

In May 2013, CIRM granted us a $6.4 million Strategic Partnership Award to develop a potentially curative ZFP Therapeutic for beta-thalassemia based on the application of our ZFN genome editing technology in HSCs. The four year grant provides matching funds for preclinical work that will support an IND application and a Phase 1 clinical trial in transfusion-dependent beta-thalassemia patients which will be carried out at Children’s Hospital & Research Center Oakland, and City of Hope in collaboration with our partner in this program, Biogen. The State of California has the right to receive, subject to the terms and conditions of the agreement between us and CIRM, payment from us, or our collaborators, from sales of a commercial product resulting from research and development efforts supported by grants, in accordance with Title 17, California Code of Regulations, Section 100600.

In May 2014, CIRM agreed to fund a $5.6 million Strategic Partnership Award to fund clinical studies of a potentially curative ZFP Therapeutic for HIV/AIDS based on the application of our ZFN genome editing technology in HSPCs.

The four year grant provides matching funds to support evaluation of our stem cell-based ZFP Therapeutic in a clinical trial in HIV-infected individuals conducted at City of Hope.

ACQUISITION OF CEREGENE

In October 2013, we acquired Ceregene, a privately held biotechnology company focused on the development of AAV gene therapies, pursuant to an Agreement and Plan of Merger (the Merger Agreement). The acquired assets include all of Ceregene's therapeutic programs, including CERE-110, an AAV-NGF for the treatment of AD that is currently in a Phase 2 clinical trial. In addition to the clinical assets acquired, we acquired certain intellectual property rights relating to the manufacturing of AAV, and certain toxicology data and safety and efficacy data from Ceregene's human clinical trials, which will be used in the preparation and filing of IND applications for our in vivo ZFP Therapeutics, particularly those that target the brain.

Under the Merger Agreement, the aggregate consideration paid by us at closing consisted of 100,000 shares of our common stock, with an approximate fair value of $1.2 million. In addition, we may be required to make contingent earn-out payments to the stockholders of Ceregene as follows:

- If we grant a third-party license to develop and commercialize Ceregene's CERE-110 for the treatment of AD or CERE-120 for the treatment of Parkinson's diseases or HD (the Earn-Out Products), we are required to pay a double-digit percentage of any upfront and milestone payments we receive for such license, subject to certain reductions based on expenses incurred by us in the development of the Earn-Out Products; and
- If we commercialize any Earn-Out Product ourselves, we are required to pay, for each Earn-Out Product, royalty-like payments as a percentage of net sales that range in the low double-digits depending upon the amount of net sales, subject to certain reductions by us.

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, TALE (Transcription activator-like effector) proteins and CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats)/Cas editing systems, therapeutic applications of genome editing technology, enabling technologies related to our platform and the use of genome editing across a variety of applications. 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 genome editing and gene regulation from the Massachusetts Institute of Technology, Johnson & Johnson, The Scripps Research Institute, 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 12 families of patent filings. As of February 4, 2015, these patent filings have resulted in 20 issued U.S. patents and 50 granted foreign patents, with 4 currently pending U.S. patent applications and 10 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 the Massachusetts Institute of Technology, Johnson & Johnson and The Scripps Research Institute.

We have licensed intellectual property directed to the composition of two AAV vectors (AAV5 and AAV6) from the National Institute of Health and the University of Washington, respectively. The AAV5 license from the National Institute of Health is a nonexclusive license that will expire in 2021. The AAV6 license from the University of Washington is also a non-exclusive license and will expire in 2017. Additionally, Sangamo has licensed intellectual property from the National Institutes of Health (NIH) relating to methods of production of production of AAV. This license will expire in 2021.

Johns Hopkins University

We entered into a license agreement with the Johns Hopkins University, or JHU, on June 29, 1995, as subsequently amended, whereby JHU 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. This license agreement was

terminated in August 2014.

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 currently filed patent applications, the patent license agreement will terminate on or about September 23, 2025. 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 June 5, 2018. 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 4, 2015, we had 133 families of Sangamo-owned or co-owned patent filings, including 120 issued U.S. patents, 437 granted foreign patents, 90 pending U.S. patent applications and 470 pending foreign patent applications. These patent filings are directed to the design, composition and use of ZFPs, ZFNs, ZFP TFs and TALE proteins. Sangamo's acquisition of Ceregene's patent estate has also brought patent filings relating to AAV, needle technology and specific methods of treating diseases of the CNS and ocular diseases. The Sangamo Ceregene patent estate now comprises 6 patent families, comprising 14 issued U.S. patents, 26 issued foreign patents, 1 pending U.S. Patent applications and 8 pending foreign patent applications.

The earliest patents in our portfolio are set to begin expiring in 2015, with the average expiration of our currently issued patents expiring being mid-2023. However, these patents in our portfolio 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, engineered nucleases, and compositions: includes DNA target site selection and zinc finger binding domain design and nuclease domain design (see newly issued US8771986), DNA nickases (see newly issued US8703489), target site arrays, ZFP libraries databases and methods of construction, as well as methods to increase zinc finger binding specificity, nuclease activity (see newly issued US8772008 and US8772009), linker designs (see newly issued US8772453) and methods of making modified plant zinc finger proteins;
- ZFP targeted regulation of endogenous genes: methods relating to activation and inhibition of endogenous cellular genes, identification of accessible regions within chromatin, and regulation of endogenous plant genes;
- ZFP Therapeutics: Treatment of Huntington's disease (see newly issued US8841260), cancer therapeutics, treatment of head and neck cancer, glioblastoma, pain (see newly issued 8466267), modulation of cardiac contractility and methods to regulate the glucocorticoid receptor, treatments for HIV (see US8268618 and US patent publication US20120294838);

- ZFN Therapeutics: Treatments for HIV (see newly issued EP2447279 and US8871905), SCD and beta-thalassemia , In Vivo Protein Replacement Platform for treatment of hemophilia and lysosomal storage diseases (see patent publication US 20130177983 and 20140017212), genome editing (see newly issued US8524500, US8349810 and US8409861), models for Parkinson's Disease (see US patent publication US20120192301), regulation of the expression of PD1 to block PD1-dependent immune suppression in both chronic infectious diseases and malignancies (see newly issued US8563314);
- Non-Therapeutic Applications of ZFPs: Identification of genes, analysis of gene regulation, structure and biological function, methods of agricultural biotechnology, methods of altering cellular differentiation state, and methods of introducing exogenous nucleic acids of interest into a safe harbor locus;
- 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 , (see newly issued US8772025);
- Donor DNA design: Methods for designing optimal donors for transgene delivery (see newly issued EP2281050 and US 8936936);
- TALE protein methods of design and use (see newly issued US8912138); and
- Methods of use with stem cells (see newly issued US8735153).

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 U.S. 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."

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 has emerged from a re-examination procedure with minor claim modifications. In addition, an opposition has recently been filed for our issued European patent EP2281050. 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 and Other Contingent Expenses

If we are successful in the development and commercialization of our products, we will be obligated by our license agreements to make sublicensing, milestone and royalty payments to some or all of the licensors mentioned above, including payments due pursuant to the acquisition of Ceregene. 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; 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 genome editing and regulation of gene expression. We are aware of several companies focused on other methods for editing genes and regulating gene expression and a limited number of commercial and academic groups pursuing the development of ZFP gene regulation and genome editing technology. The field of applied gene regulation and genome editing 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/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.
- 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, Acceleron 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, BioMarin, bluebird bio, RegenX, Asklepios and Spark.
- Cell therapy companies developing cell-based products. Our competitors in this category may include Novartis, Adaptimmune, bluebird bio, Cellectis SA, Juno Therapeutics, Kite Pharma and Lion Biotechnologies.
- Nuclease technologies, under development for therapeutic applications of genome modification including companies such as Editas Medicine, CRISPR Therapeutics, Caribou BioSciences and Intellia Therapeutics developing the CRISPR/Cas9 system, Cellectis SA developing TALE nucleases and meganucleases, bluebird developing Homing Endonucleases and MegaTALs and Precision BioSciences, Inc. that is developing meganucleases.
- 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., Genzyme (a Sanofi Company) 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
- 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 FDA under the federal Food, Drug and Cosmetic Act. The FDA regulates, among other things, the development, testing, manufacture, safety, efficacy, record keeping, labeling, storage, approval, advertising, promotion, sale and distribution of biopharmaceutical products. The regulatory review and approval process, which includes preclinical testing and clinical trials of each product candidate, is lengthy, expensive and uncertain. Securing FDA approval requires the submission of extensive preclinical and clinical data and supporting information including manufacturing information and stability data to the FDA for each indication to establish a product candidate’s safety and efficacy. The approval process takes many years, requires the expenditure of substantial resources, involves post-marketing surveillance and may involve ongoing requirements for post-marketing studies.

Before commencing clinical investigations in humans in the United States, we must carry out preclinical testing. In addition, our proposed clinical studies that are conducted at a clinical site that carries out NIH-sponsored research require review from the Recombinant DNA Advisory Committee (RAC), which is the advisory board to the 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. In 2009, we also filed an IND for our HIV program using SB-728-T, as well as Phase 1 and Phase 1/2 clinical protocols for review by the RAC for this program. 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. In 2014, we filed an IND application for SB-728mR-T to expand our HIV program using mRNA for gene delivery to T-cells ex vivo, an IND application for use of our ZFP Therapeutic for HIV in HSPCs using mRNA delivery and an IND and RAC submission for SB-BCLmR-HSPC, using mRNA gene delivery to HSPCs, for beta-thalassemia.

As part of the acquisition of Ceregene, we acquired and assumed sponsorship of two INDs on file at FDA for the use of AAV to deliver NGF. CERE-110 is an investigational agent using AAV delivery of human NGF to the brain for the treatment of AD and is currently being evaluated in a fully enrolled Phase 2 clinical trial. CERE-120 uses AAV delivery of human neurturin to the brain for treatment of Parkinson's disease. Subjects are undergoing long-term follow-up observation after being treated in completed Phase 1 and 2 studies.

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.

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, 2015, we had 102 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.

We are conducting an on-going Phase 2 clinical trial (SB-728mR-T-1401) of our ZFP Therapeutics for the treatment of HIV/AIDS. Preliminary data from these studies demonstrates that treatment of aviremic HIV-infected subjects with SB-728-T has been well-tolerated. In addition, data from Phase 1 and several Phase 2 clinical trials of our ZFP Therapeutic, SB-509, for diabetic

neuropathy and ALS demonstrated that 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 and our investors assess the value of our technology primarily 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. In December 2013, we presented data from all cohorts of these two clinical trials. Three of seven evaluable subjects in Cohort 5 showed a decrease of greater than one log in their viral load during a sixteen week treatment interruption (TI) with one subject achieving a transiently undetectable viral load during the TI period and one subject achieving control of their viral load during TI for a prolonged period (>70 weeks as of January 2015). In subjects in which viral load decreased, a measurable anti-HIV immune response was also observed. Additional data were presented from the Company’s Phase 1 study (SB-728-902, Cohorts 1-3) that demonstrated a long-term decrease in the peripheral blood mononuclear cell (PBMC) HIV reservoir using a sensitive test for integrated HIV DNA in nine of nine subjects over a 36 month period (median decrease 0.9 logs). Additional subjects were enrolled into the SB-728-1101 study to define the optimum dose of Cytoxan required to safely enhance engraftment and an additional 12 subjects have been enrolled to further test this dose including nine subjects in an ongoing Phase 2 clinical trial (SB-728mR-T-1401) that is also testing repeat dosing of modified T-cells. 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 or similar results as those obtained in earlier trials.

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.

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 in the future, 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.

While we have stated our goal is to file IND applications for several ZFP Therapeutic programs in the future, 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 two to four new IND applications per year in the foreseeable future. The preparation and submission of IND applications requires us to conduct rigorous and time-consuming preclinical testing, 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 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 preclinical tests may produce negative or inconclusive results, which may lead us to decide, or regulators may require us, to conduct additional preclinical testing. If we cannot obtain positive results in preclinical testing, we may decide to abandon the projects altogether. In addition, our ability to complete and file certain IND applications depends on the support of our partners and the timely performance of their obligations under relevant collaboration agreements. If our partners are not able to perform such obligations or if they choose to slow down or delay the progress, we may not be able to prepare and file the intended IND applications on a timely basis or at all. 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 preclinical 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.

We have limited experience in conducting clinical trials.

Our most advanced clinical programs are ongoing Phase 2 trials to evaluate the safety and efficacy of a ZFP Therapeutic for HIV/AIDS and of AAV-NGF (CERE-110) for AD. However, the FDA will require additional clinical testing which involves significantly greater resources, commitments and expertise and so it is likely that we would need to enter into a collaborative relationship with a pharmaceutical company that could assume responsibility for late-stage development and commercialization.

We have limited experience in conducting advanced clinical trials and may not possess the necessary resources and expertise to complete such trials. We have entered into collaborative agreements with Shire and Biogen to provide funding and assistance in the development of our ZFP Therapeutics through the clinical trial process. Under the agreement with Shire, we are responsible for all

activities through submission of IND applications and European CTAs and Shire is responsible for clinical development and commercialization of products arising from the alliance. Under the agreement with Biogen, we are responsible for all research and development through the first human clinical trial for the treatment of beta-thalassemia and both parties are responsible for research and development through the submission of IND for ZFP Therapeutics to treat sickle cell disease (SCD). However, there is no guarantee that we will be able to enter into future collaborative relationships with third parties that can provide us with the funding and expertise for later stage trials.

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.

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 if 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 and Biogen, are unable or unwilling to advance our programs, or if they do not diligently pursue product approval, this may slow our progress and adversely affect our ability to generate revenues. In addition, our partners may sublicense or abandon development programs or we may have disagreements or disputes with our partners, which would cause associated product development to slow or cease. In addition, the business or operations of our partners may change significantly through restructuring, acquisition or other strategic transactions or decisions that may negatively impact their ability to advance our programs. 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 or 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 including AAV and mRNA technology. 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.

Our gene regulation and genome editing 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 genome editing. Although we have generated ZFPs for thousands of gene sequences, we have not created ZFPs for all gene sequences and may not be able do so, which could limit the usefulness of our technology. In addition, while we have demonstrated the function of engineered ZFNs and ZFP TFs in mammalian cells, yeast, insects, plants and animals, we have not yet demonstrated clinical efficacy of this technology in a controlled clinical trial 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 editing 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 genome 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 that 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 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 that 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.

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 currently rely on third parties to conduct some or all aspects of manufacturing of our ZFP Therapeutic product candidates for preclinical and clinical development. If one of our third-party manufacturers fails to perform adequately or fulfill our needs, we may be required to incur significant costs and devote significant efforts, to find new suppliers or manufacturers.

We currently have limited experience in, and we do not own facilities for, clinical-scale manufacturing of our product candidates and we rely upon third-party contract manufacturing organizations to manufacture and supply drug product for our preclinical and clinical studies. The manufacture of pharmaceutical products in compliance with the FDA's current good manufacturing practices (cGMP), requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products often encounter difficulties in production, including difficulties with production costs and yields, quality control, including stability of the product candidate and quality assurance testing, shortages of qualified personnel, as well as compliance with strictly enforced cGMP requirements, other federal and state regulatory requirements and foreign regulations. If our manufacturers were to encounter any of these difficulties or otherwise fail to comply with their obligations to us or under applicable regulations, our ability to provide study drugs in our clinical studies would be jeopardized. Any delay or interruption in the supply of clinical study materials could delay the completion of our clinical studies, increase the costs associated with maintaining our clinical study programs and, depending upon the period of delay, require us to commence new studies at significant additional expense or terminate the studies completely.

All manufacturers of our product candidates must comply with cGMP requirements enforced by the FDA through its facilities inspection program. These requirements include, among other things, quality control, quality assurance and the maintenance of records and documentation. Manufacturers of our product candidates may be unable to comply with these cGMP requirements and with other FDA, state and foreign regulatory requirements. The FDA or similar foreign regulatory agencies may also implement new standards at any time, or change their interpretation and enforcement of existing standards for manufacture, packaging or testing of products. We have little control over our manufacturers' compliance with these regulations and standards. A failure to comply with these requirements may result in fines and civil penalties, suspension of production, suspension or delay in product approval, product seizure or recall or withdrawal of product approval. If the safety of any product supplied is compromised due to our manufacturers' failure to adhere to applicable laws or for other reasons, we may not be able to obtain regulatory approval for or successfully commercialize our products and we may be held liable for any injuries sustained as a result. Any of these factors could cause a delay of clinical studies, regulatory submissions, approvals or commercialization of our product candidates, entail higher costs or impair our reputation.

Our current agreements with our suppliers do not provide for the entire supply of the drug product necessary for all anticipated clinical studies or for full scale commercialization. If we and our suppliers cannot agree to the terms and conditions for them to provide the drug product necessary for our clinical and commercial supply needs, we may not be able to manufacture the product candidate until a qualified alternative supplier is identified, which could also delay the development of, and impair our ability to commercialize, our product candidates.

The number of third-party suppliers with the necessary manufacturing and regulatory expertise and facilities is limited, and it could be expensive and take a significant amount of time to arrange for alternative suppliers, which could have a material adverse effect on our business. New suppliers of any product candidate would be required to qualify under applicable regulatory requirements and would need to have sufficient rights under applicable intellectual property laws to the method of manufacturing the product

candidate. Obtaining the necessary FDA approvals or other qualifications under applicable regulatory requirements and ensuring non-infringement of third-party intellectual property rights could result in a significant interruption of supply and could require the new manufacturer to bear significant additional costs which may be passed on to us

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 or AD 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.

We may not be able to fully realize the expected benefits from the acquisition of Ceregene, Inc., and the operation of the new business of Ceregene, Inc. may subject us to additional risks.

In October 2013, we acquired Ceregene, including all of its therapeutic programs and related intellectual property and other assets. Although we expect to realize strategic, operational and financial benefits as a result of the acquisition, we cannot be certain whether, and to what extent, such benefits will be achieved in the future. In particular, the success of the acquisition will depend on our ability to develop Ceregene's business, including the prosecution of its CERE-110 Phase 2 clinical trial, and to apply Ceregene's technology to advance our ZFP Therapeutics. There is no guarantee that any existing and future clinical trials of Ceregene's product candidates, including CERE-110 for the treatment of AD, will produce positive results, and failure to do so may adversely affect our ability to validate the AAV delivery technology and apply such technology to our ZFP products as well as negatively impact our stock price. In April 2013, Ceregene reported that its top line data for the CERE-120 Phase 2b clinical trial for Parkinson's disease did not demonstrate statistically significant efficacy in the primary endpoint. In November 2013, we presented early positive data from Phase 1 clinical trial of CERE-110 demonstrating that the drug was well-tolerated and resulted in appropriate delivery of the therapeutic. However, even if we obtain positive data from such clinical trials, there is no guarantee that the AAV delivery technology can be applied to our ZFP Therapeutics safely and effectively.

The acquisition of Ceregene also subjects us to additional operational and financial risks, including the following:

- additional costs that we may need to incur in order to conduct and complete Ceregene's therapeutic programs, including the CERE-110 Phase 2 clinical trial, and to comply with new regulatory requirements;
- difficulties acquiring and developing the necessary expertise to continue the development of AAV technologies and other acquired assets of Ceregene;
- difficulties in coordinating research and development activities;
- uncertainties in the business relationships with our collaborators and suppliers due to the acquisition;
- lack of previous experiences in conducting Phase 2 trials of a gene therapy based on AAV vector delivery system.

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.

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 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;
- CRISPR/Cas9 technology;
- TALE proteins and MegaTALs; 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 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 years ended December 31, 2014, 2013 and 2012 were $26.4 million, $26.6 million and $22.3 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 collaboration agreements, other strategic partnerships in non-therapeutic applications of our technology, federal government research grants and grants awarded by research foundations. As of December 31, 2014, we had an accumulated deficit of $328.6 million. Since our IPO in 2000, we have generated an aggregate of approximately $331.4 million in gross 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 advance our ZFP Therapeutic product candidates. 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.

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 2016, we may need to seek additional sources of capital through equity or debt financing. In addition, as we focus our efforts on proprietary human therapeutics, we will need to seek FDA approval of potential products, a process that could cost in excess of hundreds of millions of dollars per product. Furthermore, we may experience difficulties in accessing the capital market due to external factors beyond our control such as volatility in the equity markets for emerging biotechnology companies and general economic and market conditions both in the United States and abroad. 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 collaboration agreements, other collaborations in non-therapeutic applications of our technology, federal government research grants and grants awarded by research foundations. Our focus on higher-value therapeutic product development and related collaboration 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.

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 depend 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.

In January 2012, we entered into a collaborative agreement with Shire, pursuant to which we are engaging in a joint program with Shire to research, develop and commercialize human therapeutics and diagnostics for hemophilia, Huntington’s disease 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 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.

In addition, in January 2014, we entered into a collaborative agreement with Biogen for the clinical development and commercialization of therapeutics based on our ZFP technology for hemoglobinopathies, including beta-thalassemia and SCD. Under the agreement, we are responsible for all discovery, research and development activities through the first human clinical trial for the first ZFP Therapeutic developed for the treatment of beta-thalassemia. In the SCD program, both parties are responsible for research and development activities through the submission of an IND.

Under these agreements with Biogen and Shire, they will have control and broad discretion over all or certain aspects of the clinical development and commercialization of any product developed under the agreements, and we will have little, if any, influence on how these programs will be conducted. Our lack of control over the clinical development in our agreement with Biogen and Shire could cause delays or other difficulties in the development and commercialization of our product candidates, which may prevent us from completing the intended IND filings in a timely fashion and receiving any milestone, royalty payments and other benefits under the agreement. In addition,

under their respective agreement(s), Biogen and Shire have certain rights to terminate the agreements by providing us with advance notices, therefore, the actual milestone payments that we may receive under these agreements may be lower than the full amounts stated above.

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-Aldrich Corporation 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 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. Under the agreement, Sigma has 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 addition, under our license agreement with DAS relating to plant agriculture, DAS has the exclusive right to develop agricultural products using our ZFP technology in plant cells, plants or plant cell cultures. Both Sigma and DAS 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 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, CRISPR/Cas9 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.

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.

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, including the members of our senior management team, 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 twelve months ended December 31, 2014, the closing price of our common stock, as reported by the NASDAQ Global Select Market, ranged from a low of $9.85 to high of $23.86. During the fiscal year ended December 31, 2013, our common stock price fluctuated, ranging from a low of $6.15 to a high of $14.38. 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, including the equity markets for emerging biotechnology companies;
- deviations in our results of operations from the guidance given by us;
- 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;
- announcement of changes in business and operations by our collaborators and partners;
- 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;
- decreases in our cash balances; and
- changes, by one or more of Sangamo's security analysts, in recommendations, ratings or coverage of our stock.

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.

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 or our voting stock.

ITEM 1B – UNRESOLVED STAFF COMMENTS

None.

ITEM 2 – PROPERTIES

Our corporate headquarters occupies approximately 27,000 square feet of research and office space located at 501 Canal Boulevard in Richmond, California. The lease expires in August of 2019. We also entered into a lease to occupy approximately 7,700 square feet of research and office space located at 1003 West Cutting Boulevard in Richmond, California in December 2014. The lease expires in January of 2018. 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 proceedings arising in the ordinary course of business.

ITEM 4 – MINE SAFETY DISCLOSURES

Not Applicable.

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 Select 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 Select Market were as follows:

Common Stock

	Price	
	High	Low
Year ended December 31, 2014		
First Quarter	$23.86	$13.25
Second Quarter	$17.95	$11.71
Third Quarter	$16.40	$10.77
Fourth Quarter	$16.53	$9.85
Year ended December 31, 2013		
First Quarter	$10.80	$6.15
Second Quarter	$10.65	$7.31
Third Quarter	$11.28	$7.92
Fourth Quarter	$14.38	$9.18

Holders

As of February 1, 2015, there were 67 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 employees, 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.

36

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.

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

	Year Ended December 31,				
	2014	2013	2012	2011	2010
	(In thousands, except per share data)				
Statement of Operations Data:					
Total revenues	$45,870	$24,133	$21,655	$10,319	$20,805
Operating expenses:					
Research and development	56,744	36,979	31,709	32,098	33,154
General and administrative	15,677	13,800	12,144	14,042	12,586
Change in fair value of contingent liability	230	60	—	—	—
Total operating expenses	72,651	50,839	43,853	46,140	45,740
Loss from operations	(26,781)	(26,706)	(22,198)	(35,821)	(24,935)
Other income/(expense)	364	82	(66)	71	81
Net loss	$(26,417)	$(26,624)	$(22,264)	$(35,750)	$(24,854)
Basic and diluted net loss per share	$(0.39)	$(0.48)	$(0.42)	$(0.71)	$(0.55)
Shares used in computing basic and diluted net loss per share	67,022	55,974	52,741	50,512	45,167

	As of December 31,				
	2014	2013	2012	2011	2010
	(In thousands)				
Balance Sheet Data:					
Cash, cash equivalents, marketable securities, and interest receivable	$226,645	$131,814	$76,321	$84,463	$60,622
Working capital	169,997	87,143	59,575	78,488	54,222
Total assets	243,212	140,838	82,533	87,336	62,999
Accumulated deficit	(328,550)	(302,133)	(275,509)	(253,245)	(217,495)
Total stockholders' equity	206,633	121,710	64,896	80,132	55,907

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.

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 genome editing and gene regulation. 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 longer-term, our goal is to integrate manufacturing, development and commercial operations to capture the value of our proprietary ZFP Therapeutic products.

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, revenues 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 services 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 clinical trial 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 International GmbH, formerly Shire AG, (Shire) to research, develop and commercialize some of our preclinical ZFP Therapeutic development programs, including programs in hemophilia, Huntington's disease (HD) and other monogenic diseases. In January 2014, we established a collaborative partnership with Biogen Idec Inc. (Biogen) to discover, develop, seek regulatory approval for and commercialize therapeutics based on our ZFP technology for hemoglobinopathies, including beta thalassemia and sickle cell disease (SCD). We also have proprietary preclinical programs in lysosomal storage disorders (LSDs). In addition, we have research stage programs in other monogenic diseases, in central nervous system (CNS) disorders and in cancer immunotherapy.

We believe the potential commercial applications of ZFPs are broad-based and we have entered into strategic partnerships in fields outside human therapeutics to facilitate the sale or licensing of our ZFP platform as follows:

- 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 genome editing tools under the trademark CompoZr ®.
- 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.

On October 1, 2013, we acquired Ceregene, Inc. (Ceregene), a privately held biotechnology company focused on the development of adeno-associated virus (AAV) gene therapies. The acquired assets include all of Ceregene's therapeutic programs, including CERE-110, for the treatment of Alzheimer's disease (AD) that is currently in a Phase 2 clinical trial, certain intellectual property rights relating to the manufacturing of AAV, certain toxicology data and safety and efficacy data from Ceregene's human clinical trials. We believe that these additional assets provide valuable reference materials for us in the preparation and filing of IND applications for our in vivo ZFP Therapeutics, particularly those that target the brain.

For the year ended December 31, 2014, we incurred a consolidated net loss of $26.4 million, or $0.39 per share, compared to a consolidated net loss of $26.6 million, or $0.48 per share, for the same period in 2013. As of December 31, 2014, we had cash, cash equivalents, marketable securities and interest receivable totaling $226.6 million compared to $131.8 million as of December 31, 2013. As of December 31, 2014, we had an

accumulated deficit of $328.6 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.

Critical Accounting Policies and Estimates

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, we will allocate revenue to each non-contingent element based on the relative selling price of each element. When applying the relative selling price method, we determine 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 and Biogen in January 2014 were evaluated under these updated accounting standards.

Additionally, we recognize 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 our 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. We recognize 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.

Our 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.

Business Combinations

We accounted for the acquisition of Ceregene in accordance with Accounting Standards Codification (ASC) Topic 805, Business Combinations. ASC Topic 805 establishes principles and requirements for recognizing and measuring the total consideration transferred to and the assets acquired, liabilities assumed and any non-controlling interests in the acquired target in a business combination. ASC Topic 805 also provides guidance for recognizing and measuring goodwill acquired in a business combination; requires purchased in-process research and development to be capitalized at fair value as intangible assets at the time of acquisition; requires acquisition-related expenses and restructuring costs to be recognized separately from the business combination; expands the definition of what constitutes a business; and requires the acquirer to disclose information that users may need to evaluate and understand the financial effect of the business combination.

Fair Value Measurements

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 and contingent consideration liabilities are stated at their estimated fair values. The counterparties to the agreements relating to our investment securities consist of the U.S. Treasury, governmental agencies, various major corporations and financial institutions with high credit standing.

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, 2014, 2013 and 2012

Revenues

	Year Ended December 31,							
				%				%
	2014	2013	Change	Change	2013	2012	Change	Change
	(In thousands, except percentage values)							

Revenues:										
Collaboration agreements	$43,880	$21,678	$22,202	102	%	$21,678	$18,186	$3,492	19	%
Research grants	1,990	2,455	(465)	(19	%)	2,455	3,469	(1,014)	(29	%)
Total revenues	$45,870	$24,133	$21,737	90	%	$24,133	$21,655	$2,478	11	%

Total revenues consisted of revenues from collaboration agreements and research grants. We anticipate revenues over the next several years will be derived primarily from our collaboration agreements with Shire, Biogen, Sigma and DAS.

Revenues from our corporate collaboration agreements were $43.9 million in 2014, $21.7 million in 2013 and $18.2 million in 2012. The increase in revenue from collaborations in 2014 compared to 2013 was primarily due to an increase of $13.1 million in revenues from Biogen and $9.5 million in revenues from Shire related to research services and research milestones, partially offset by a decrease of $1.4 million in revenues from Sigma. The increase in revenue from collaborations in 2013 compared to 2012 was primarily due to an increase of $5.4 million in revenues from Shire, partially offset by a decrease of $1.7 million in revenues from DAS related to research and manufacturing services. Revenues related to Biogen and Shire included partial recognition of a $20.0 million and $13.0 million upfront license payment, respectively, as well as for research services provided.

Research grant revenues were $2.0 million in 2014, $2.5 million in 2013 and $3.5 million in 2012. The decrease of $0.5 million in 2014 from 2013 was primarily due to the recognition of all revenues related to funding from a 2009 research grant from the California Institute for Regenerative Medicine (CIRM) for our HIV/AIDs program. The decrease was partially offset by revenues related to new grant agreements with CIRM for our beta-thalassemia program. The decrease of $1.0 million in 2013 from 2012 was mainly due to the termination of our agreements with the CHDI Foundation, Inc. (CHDI) and the Juvenile Diabetes Research Foundation International (JDRF) in 2012. The decrease was partially offset by increased revenues related to other grant agreements.

During 2014, revenues related to Shire and Biogen represented 57% and 28%, respectively, of total revenues. During 2013, revenues related to Shire and DAS represented 68% and 12%, respectively, of total revenues. During 2012, revenues related to Shire, Sigma and DAS represented 51%, 11% and 22%, respectively, of total revenues.

Operating Expenses

	Year Ended December 31,									
	2014	2013	Change	% Change		2013	2012	Change	% Change	
	(In thousands, except percentage values)									
Operating expenses:										
Research and development	$56,744	$36,979	$19,765	53	%	$36,979	$31,709	$5,270	17	%
General and administrative	15,677	13,800	1,877	14	%	13,800	12,144	1,656	14	%
Change in fair value of contingent liability	230	60	170	283	%	60	—	60	100	%
Total operating expenses	$72,651	$50,839	$21,812	43	%	$50,839	$43,853	$6,986	16	%

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 including our programs under collaboration with Shire and Biogen. Pursuant to the terms of the agreements with Shire and Biogen, certain expenses related to research and development activities will be reimbursed to Sangamo, including employee and external research costs. The reimbursement funds received from Shire and Biogen is recognized as revenue as the costs are incurred and collection is reasonably assured. We also continue to fulfill our obligations under the terms of our non-therapeutic collaborations with Sigma and DAS. 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.

Research and development expenses were $56.7 million in 2014, $37.0 million in 2013 and $31.7 million in 2012. The increase of $19.8 million in research and development expenses in 2014 was primarily due to an increase of $16.2 million in internal and external research expenses related to our preclinical ZFP Therapeutic programs, including our programs under our collaborations with Shire and Biogen. Additionally, personnel related expenses, including salaries and stock-based compensation expenses, increased by $3.4 million in 2014 as compared to 2013.

The increase of $5.3 million in research and development expenses in 2013 was primarily due to an increase in internal and external research expenses related to our preclinical ZFP Therapeutic programs, including our programs under our collaboration with Shire, of $5.0 million. Additionally, personnel related expenses, including salaries and stock-based compensation expenses, increased by $1.2 million. These increases were partially offset by a decrease in clinical and manufacturing expenses of $1.1 million, primarily related to our HIV/AIDS program

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 preclinical and research stage programs, including our therapeutic programs under collaboration with Shire and non-therapeutic collaborations.

	Year Ended December 31, (In thousands)		
Programs	2014	2013	2012
SB-728-T clinical programs	$8,339	$7,071	$9,115
Other clinical programs	801	867	510
Preclinical and research programs	47,604	29,041	22,084
Total research and development expenses	$56,744	$36,979	$31,709

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 $15.7 million in 2014, $13.8 million in 2013 and $12.1 million in 2012. The increase in general and administrative expenses of $1.9 million in 2014 was primarily due to an increase of $1.4 million in personnel related expenses, including salaries and stock-based compensation expenses and an increase in professional services expenses of $0.4 million.

The increase of $1.7 million in 2013 from 2012 was primarily due to an increase of $0.9 million in personnel related expenses, including salaries and stock-based compensation expenses, and an increase in professional services expenses of $0.9 million.

Other income (expense), net

Other income was $0.4 million in 2014 and $0.1 million in 2013. Other expense was $0.1 million in 2012. Other income in 2014 and 2013 was comprised of interest income. The expense in 2012 was primarily related to disposal of fixed assets, partially offset by interest income of $0.1 million.

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, 2014, we had cash, cash equivalents, marketable securities and interest receivable totaling $226.6 million compared to $131.8 million as of December 31, 2013, with the increase primarily attributable to the completion of an underwritten public offering of the Company’s common stock in March 2014, in which 4,444,444

shares of Sangamo common stock were sold at a public offering price of $22.50 per share. The net proceeds to the Company from the sale of shares in this offering, after deducting underwriting discounts and commissions and other offering expenses, were approximately $93.8 million.

Our most significant use of capital pertains to salaries and benefits for our employees and external research and development expenses, such as manufacturing, clinical trials and preclinical 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, HD and other monogenic diseases based on our ZFP technology. Under the agreement, we received an upfront license fee of $13.0 million. Shire reimburses us for agreed upon costs incurred in connection with research and development activities conducted by us. We are also eligible to receive milestone payments based on our achievement of specified research, regulatory, clinical development, commercialization and sales milestones, which depends upon ours and Shire's ability to continue to progress our programs under collaboration. During the twelve months ended December 31, 2014 we recognized a $1.0 million milestone related to our hemophilia program. 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.

In January 2014, we entered into a collaboration and license agreement with Biogen, pursuant to which we are collaborating with Biogen to discover, develop, seek regulatory approval for and commercialize therapeutics based on our ZFP technology for hemoglobinopathies, including beta-thalassemia and SCD. Under the agreement with Biogen, we received an upfront license fee of $20.0 million. Biogen also reimburses us for agreed upon costs incurred in connection with research and development activities conducted by us. In addition, we are eligible to receive development milestone payments upon the achievement of specified regulatory, clinical development and commercialization milestones. We will also be eligible to receive incremental royalties for each licensed product that are a tiered double-digit percentage of annual net sales of such product, if any.

In October 2013, we acquired Ceregene's therapeutic programs, including a Phase 2 clinical trial for CERE-110 for the treatment of AD. The operations of Ceregene's business, including the conduct of clinical trials, are funded by an award granted by the NIH, and we do not expect to incur significant cash expenditure to continue such operations.

Cash Flow

Operating activities. For all periods, net cash used in operating activities primarily reflects our net operating losses adjusted for non-cash items including stock-based compensation expense. Net cash used in operating activities was $5.7 million in 2014 compared to $19.5 million in 2013. The decrease in net cash used in operations in 2014 was primarily due to an increase in deferred revenues in 2014 related to the $20.0 million upfront payment from Biogen pursuant to the collaboration and license agreement, partially offset by an increase in research and development expenses related to our preclinical research programs.

Net cash used in operating activities was $19.5 million in 2013 compared to $8.1 million in 2012. The increase in net cash used in operations in 2013 was primarily due to an increase in research and development expenses related to our preclinical research programs and an increase in deferred revenues in 2012 related to the $13.0 million upfront payment from Shire pursuant to the collaboration and license agreement.

Investing activities. Net cash used in investing activities was $100.7 million in 2014 and $68.1 million in 2013. Net cash provided by investing activities was $11.3 million in 2012. Cash flows from investing activities for all periods primarily related to purchases, sales and maturities of marketable securities.

Financing activities. Net cash provided by financing activities was $102.2 million in 2014, $76.1 million in 2013 and $1.7 million in 2012. Net cash provided by financing activities in 2014 was primarily attributable to $93.8 million in net proceeds from a public offering of the Company's common stock in March 2014, as well as proceeds from the issuance of common stock upon exercise of stock options. Net cash provided by financing activities in 2013 was primarily attributable to $69.5 million in net proceeds from a public offering of the Company's common stock in September 2013, as well as proceeds from the issuance of common stock upon exercise of stock options. Net cash provided by financing activities in 2012 primarily related to proceeds from the issuance of common stock upon exercise of stock options.

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 2016. 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 agreements with Shire and Biogen;
- 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;
- 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, 2014, we had net operating loss carryforwards for federal and state income tax purposes of approximately $330.9 million and $278.1 million, respectively. If not utilized, the net federal and state operating loss carryforwards will start to expire in 2018 and 2015, respectively. We also have federal and state research tax credit carryforwards of $6.7 million and $7.0 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, 2014, we had contractual obligations and commercial commitments as follows (in thousands):

	Payments Due by Period				
Contractual Obligations	Total	Less Than 1 Year	1-3 Years	4-5 Years	More Than 5 Years
Operating leases	$3,938	$ 865	$2,577	$496	$ —
License obligations	2,169	323	918	425	503
Total contractual obligations	$6,107	$ 1,188	$3,495	$921	$ 503

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.

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 change in interest rates would have a material negative impact on the value of our investment portfolio.

ITEM 8 – FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

SANGAMO BIOSCIENCES, INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

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, 2014 and 2013, 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, 2014. 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 financial statements referred to above present fairly, in all material respects, the consolidated financial position of Sangamo BioSciences, Inc. as of December 31, 2014 and 2013, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2014, 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), Sangamo BioSciences, Inc.'s internal control over financial reporting as of December 31, 2014, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated February 25, 2015 expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP

Redwood City, California

February 25, 2015

SANGAMO BIOSCIENCES, INC.

CONSOLIDATED BALANCE SHEETS

	December 31, 2014	December 31, 2013
	(In thousands, except share and per share amounts)	
ASSETS		
Current assets:		
Cash and cash equivalents	$6,030	$10,186
Marketable securities	172,932	82,627
Interest receivable	423	338
Accounts receivable	10,368	3,155
Prepaid expenses	623	457
Restricted cash	320	320
Other current assets	183	191
Total current assets	190,879	97,274
Marketable securities, non-current	47,260	38,663
Property and equipment, net	1,479	1,406
Intangible assets, in-process research and development	1,870	1,870
Goodwill	1,585	1,585
Other assets	139	40
Total assets	$243,212	$140,838
LIABILITIES AND STOCKHOLERS' EQUITY		
Current liabilities:		
Accounts payable and accrued liabilities	$8,704	$4,380
Accrued compensation and employee benefits	2,853	3,194
Escrow liability	275	275
Deferred revenues	9,050	2,282
Total current liabilities	20,882	10,131
Deferred revenues, non-current	13,149	6,679
Contingent consideration liability	1,800	1,570
Deferred tax liability	748	748
Total liabilities	36,579	19,128
Commitments and contingencies		
Stockholders' equity:		
Common stock, $0.01 par value; 160,000,000 and 80,000,000 shares authorized as of December 31, 2014 and December 31, 2013, respectively; 69,062,394 and 62,243,892 shares issued and outstanding at December 31, 2014 and December 31, 2013, respectively	690	622
Additional paid-in capital	534,518	423,209
Accumulated deficit	(328,550)	(302,133)
Accumulated other comprehensive income (loss)	(25)	12

Total stockholders' equity	206,633	121,710
Total liabilities and stockholders' equity	$243,212	$140,838

See accompanying Notes to Consolidated Financial Statements.

SANGAMO BIOSCIENCES, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS

	Year Ended December 31,		
	2014	2013	2012
	(In thousands, except per share amounts)		
Revenues:			
Collaboration agreements	$43,880	$21,678	$18,186
Research grants	1,990	2,455	3,469
Total revenues	45,870	24,133	21,655
Operating expenses:			
Research and development	56,744	36,979	31,709
General and administrative	15,677	13,800	12,144
Change in fair value of contingent liability	230	60	—
Total operating expenses	72,651	50,839	43,853
Loss from operations	(26,781)	(26,706)	(22,198)
Other income (expense), net	364	82	(66)
Net loss	$(26,417)	$(26,624)	$(22,264)
Basic and diluted net loss per share	$(0.39)	$(0.48)	$(0.42)
Shares used in computing basic and diluted net loss per share	67,022	55,974	52,741

See accompanying Notes to Consolidated Financial Statements.

SANGAMO BIOSCIENCES, INC.

CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS

	Year Ended December 31,		
	2014	2013	2012
	(In thousands)		
Net loss	$(26,417)	$(26,624)	$(22,264)
Change in unrealized gain (loss) on available-for-sale securities	(37)	(14)	14
Comprehensive loss	$(26,454)	$(26,638)	$(22,250)

See accompanying Notes to Consolidated Financial Statements.

SANGAMO BIOSCIENCES, INC.

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY

	Common Stock		Additional Paid-in	Accumulated	Accumulated Other Comprehensive Income/	Total Stockholders'
	Shares	Amount	Capital	Deficit	(Loss)	Equity
	(In thousands, except share data)					
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)
Balances at December 31, 2012	53,058,525	$ 531	$ 339,848	$ (275,509)	$ 26	$ 64,896
Issuance of common stock in connection with underwritten public offering, net of issuance costs	7,015,000	70	69,422	—	—	69,492
Issuance of common stock upon exercise of stock options and in connection with restricted stock units	1,889,818	19	6,099	—	—	6,118
Issuance of common stock under employee stock purchase plan	180,551	1	495	—	—	496
Issuance of common stock in connection with acquisition of Ceregene, Inc.	99,998	1	1,199	—	—	1,200
Stock-based compensation	—	—	6,146	—	—	6,146
Comprehensive loss:						
Net unrealized loss on marketable securities	—	—	—	—	(14)	(14)
Net loss	—	—	—	(26,624)	—	(26,624)
Comprehensive loss	—	—	—	—	—	(26,638)

Balances at December 31, 2013	62,243,892	$ 622	$ 423,209	$ (302,133)	$ 12	$ 121,710
Issuance of common stock in connection with underwritten public offering, net of issuance costs	4,444,444	44	93,752	—	—	93,796
Issuance of common stock upon exercise of stock options and in connection with restricted stock units	2,266,855	23	7,510	—	—	7,533
Issuance of common stock under employee stock purchase plan	107,203	1	847	—	—	848
Stock-based compensation	—	—	9,200	—	—	9,200
Comprehensive loss:						
Net unrealized loss on marketable securities	—	—	—	—	(37)	(37)
Net loss	—	—	—	(26,417)	—	(26,417)
Comprehensive loss	—	—	—	—	—	(26,454)
Balances at December 31, 2014	69,062,394	$ 690	$ 534,518	$ (328,550)	$ (25)	$ 206,633

See accompanying Notes to Consolidated Financial Statements.

SANGAMO BIOSCIENCES, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

	Year ended December 31,		
	2014	2013	2012
	(In thousands)		
Operating Activities:			
Net loss	$(26,417)	$(26,624)	$(22,264)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	549	569	660
Amortization of premium on marketable securities	1,098	912	889
Stock-based compensation	9,200	6,146	5,338
Net loss on disposal of property and equipment	—	—	123
Change in fair value of contingent consideration liability	230	60	—
Net changes in operating assets and liabilities:			
Restricted cash	—	(320)	—
Escrow liability	—	275	—
Interest receivable	(85)	(148)	141
Accounts receivable	(7,213)	1,008	(3,414)
Prepaid expenses and other assets	(258)	(160)	14
Accounts payable and accrued liabilities	4,324	269	(1,503)
Accrued compensation and employee benefits	(341)	721	800
Deferred revenues	13,238	(2,190)	11,134
Net cash used in operating activities	(5,675)	(19,482)	(8,082)
Investing Activities:			
Purchases of marketable securities	(227,802)	(118,894)	(91,428)
Maturities of marketable securities	127,765	51,129	103,470
Proceeds from sales of investments	—	—	—
Acquistion of Ceregene, Inc., net of cash received	—	79	—
Purchases of property and equipment	(621)	(432)	(723)
Net cash provided by / (used in) investing activities	(100,658)	(68,118)	11,319
Financing Activities:			
Proceeds from public offering of common stock, net of issuance costs	93,796	69,492	—
Taxes paid related to net share settlement of equity awards	(4,556)	(2,015)	—
Proceeds from issuance of common stock	12,937	8,630	1,676
Net cash provided by financing activities	102,177	76,107	1,676
Net increase / (decrease) in cash and cash equivalents	(4,156)	(11,493)	4,913
Cash and cash equivalents, beginning of period	10,186	21,679	16,766
Cash and cash equivalents, end of period	$6,030	$10,186	$21,679
Supplemental disclosure of noncash investing activities:			
Fair value of shares of common stock issued pursuant to the acquisition of Ceregene Inc.	$-	$1,200	$-

See accompanying Notes to Consolidated Financial Statements.

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 genome editing 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, 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, 2014, along with expected revenues from collaborations, strategic partnerships and research grants, will be adequate to fund its operations at least through 2016. Sangamo will need to raise substantial additional capital to fund subsequent operations and complete the development and commercialization of its products. Additional capital may not be available on terms acceptable to the Company, 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.

Sangamo acquired Ceregene, Inc. (Ceregene) in October 2013. Under the merger agreemen