

SANGAMO BIOSCIENCES INC  
Form 10-K  
February 18, 2016

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, 2015

or

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF  
1934

For the transition period from \_\_\_\_\_ to \_\_\_\_\_

Commission file number: 0-30171

SANGAMO BIOSCIENCES, INC.

(Exact name of registrant as specified in its charter)

Delaware (State or other jurisdiction of incorporation or organization)	68-0359556 (I.R.S. Employer Identification No.)
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501 Canal Boulevard,

Richmond, California (Address of principal executive offices)	94804 (Zip Code)
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(510) 970-6000

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(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

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

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

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes  No

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

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

Large accelerated filer <input checked="" type="checkbox"/>	Accelerated filer <input type="checkbox"/>
Non-accelerated filer <input type="checkbox"/> (Do not check if a smaller reporting company)	Smaller reporting company <input type="checkbox"/>

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

The aggregate market value of the voting stock held by non-affiliates of the registrant based upon the closing sale price of the common stock on June 30, 2015 (the last business day of the registrant's most recently completed second fiscal quarter), as reported on the NASDAQ Global Select Market was \$754,796,213. 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.

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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, 2016
Common Stock, \$0.01 par value per share	70,368,994 shares

DOCUMENTS INCORPORATED BY REFERENCE

Document	Parts Into Which Incorporated
Proxy Statement for the 2016 Annual Meeting of Stockholders	Part III

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## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Some statements contained in this report are forward-looking with respect to our operations, research, 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 with respect to future events and are based on assumptions and subject to risks and uncertainties. Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. We discuss many of these risks in greater detail under the headings “Risk Factors” and “Management’s Discussion and Analysis of Financial Results of Operations” in this Form 10-K. Sangamo undertakes no obligation to publicly release any revisions to forward-looking statements to reflect events or circumstances arising after the date of this report. Readers are cautioned not to place undue reliance on the forward-looking statements, which speak only as of the date of this Annual Report on Form 10-K.

ZFP Therapeutic® and Engineering Genetic Cures® are 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 the leading company in the field of therapeutic genome editing which we are applying to “Engineer Genetic Cures” for numerous gene-based diseases. As a clinical stage biopharmaceutical company we are focused on the research, development and commercialization of engineered DNA-binding proteins for therapeutic genome editing and gene regulation. Our proprietary zinc finger DNA-binding proteins (ZFP) technology enables efficient and highly specific genome editing and gene regulation and we are developing ZFP Therapeutics; novel therapeutic products for the treatment of genetic disease. We have several proprietary clinical and preclinical programs in development and have strategically partnered certain programs with biopharmaceutical companies to obtain funding for our own programs and to expedite clinical and commercial development. Our long-term goal is to forward integrate into manufacturing, development and commercial operations to more fully capture the value of our proprietary ZFP Therapeutic products.

We, and our licensed partners, are the leaders in the research, development and commercialization of ZFPs, a naturally occurring class of proteins found in humans. We have used our knowledge and expertise to develop a proprietary technology platform in both genome editing and gene regulation. ZFPs can be engineered to make ZFP nucleases (ZFNs), proteins that can be used to specifically modify DNA sequences by adding or knocking out specific genes (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 potentially have broad and fundamental applications in several areas, including human therapeutics, plant agriculture and research reagents, including the production of transgenic animals and cell-line engineering. In the process of developing this platform we have accrued significant scientific, manufacturing and regulatory capabilities and know-how that is generally applicable in the broader field of gene therapy.

The main focus for our company is the development of novel human therapeutics. Our lead ZFP Therapeutic, SB-728, a ZFN-modified autologous cell product for the treatment of HIV/AIDS, is the first therapeutic application of our ZFN genome editing technology and is being evaluated in an ongoing Phase 2 study of ZFN-modified T-cells (SB-728-T-1101, Cohort 3\*) and a Phase 1/2 study of modified hematopoietic stem cells (SB-728mR-HSPC) in HIV-infected subjects. We are also initiating Phase 1/2 studies of in vivo genome editing applications of ZFP Therapeutics for hemophilia B and MPS I, a lysosomal storage disorder (LSD). In addition, we have proprietary preclinical programs in hemophilia A and other LSDs and research stage programs in other monogenic diseases, including certain central nervous system (CNS) disorders and cancer immunotherapy.

We have established a collaborative partnership with Biogen 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 our preclinical ZFP Therapeutic development program in Huntington’s disease (HD).

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. We have a license agreement with Sigma-Aldrich Corporation (Sigma). Under this agreement, Sigma has the exclusive rights to develop and market ZFP-based laboratory research reagents marketed under the trademark CompoZr<sup>®</sup> as well as

ZFP-modified cell lines for commercial production of protein pharmaceuticals and ZFP-engineered transgenic animals. We also have a license agreement with Dow AgroSciences, LLC (DAS), a wholly owned subsidiary of Dow Chemical Corporation. Under this agreement, DAS has the exclusive rights to use our ZFP technology to modify the genomes or alter protein expression of plant cells, plants, or plant cell cultures and markets our ZFN technology under the trademark EXZACT™ Precision Technology.

We have a substantial intellectual property position in the genome editing field including the design, selection, composition and use of engineered ZFPs to support our commercial activities. As of February 1, 2016, we either owned outright or have exclusively licensed the commercial rights to approximately 760 patents issued in the United States and foreign national jurisdictions, and we have 629 patent applications owned and licensed pending worldwide. We continue to license and file new patent applications that strengthen our core and accessory patent portfolio. We believe that our intellectual property position is a critical element in our ability to research, develop and commercialize products and services based on ZFP technology across our chosen applications.



## DNA, Genes, and Proteins

DNA is present in all cells except mature red blood cells, and encodes the inherited characteristics of all living organisms. A cell's DNA is organized in chromosomes as thousands of individual units called genes. Genes encode proteins, which are assembled through the process of transcription—whereby DNA is transcribed into ribonucleic acid (RNA)—and, subsequently, translation—whereby RNA is translated into protein (Figure 1). Proteins are involved in virtually all cell functions. DNA, RNA and proteins comprise many of the targets for pharmaceutical drug discovery and therapeutic intervention.

### Figure 1:

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

The human body is composed of specialized cells that perform different functions and are thus organized into tissues and organs. All somatic cells in an individual's body contain the same set of genes. However, only a fraction of these genes are turned on, or expressed, in an individual human cell at any given time. Genes are regulated (i.e. turned on or turned off) by DNA-binding proteins called transcription factors 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 the CCR5 gene which encodes a protein that is critical for HIV infection. We are also using ZFN-mediated gene disruption of the BCL11A Enhancer in hematopoietic stem progenitor cells (HSPCs) as a single long-lasting 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 and potentially 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. Our preclinical data have been reviewed by advisory bodies such as the NIH Recombinant Advisory Committee (RAC) and regulatory bodies such as the U.S. Food and Drug Administration (FDA) and we have ongoing clinical trials to evaluate the safety and efficacy of ZFNs in humans.

We have employed 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 such as Adeno Associated Virus (AAV) 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

We believe that our ZFP technology provides a unique and proprietary basis for a broad new class of drugs that have differential technical advantages over small-molecule drugs, protein pharmaceuticals, RNA-based therapeutics, conventional gene therapy approaches and other genome editing platforms, enabling us to develop therapies for a broad range of unmet medical needs.

We can generate highly specific ZFNs for genome editing and gene regulation and have developed multiple delivery strategies to administer these therapeutics, including using mRNA, AAV, adenovirus and plasmid. As more genes and DNA sequences are linked to specific diseases, we believe that the clinical breadth and scope of our ZFP Therapeutic applications will continue to expand.

For example, ZFP Therapeutics can:

- Enable genome editing and gene regulation strategies to address novel drug targets. Engineered ZFNs enable the efficient disruption, correction or targeted addition of a gene sequence in a very precise fashion, 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 development platforms. Direct, targeted modification of the genome cannot be achieved using conventional gene therapy approaches, antisense RNA, siRNA, conventional small molecules, antibodies, or other protein. Our ZFN genome editing technology, which requires only brief cellular expression of ZFNs, enables the permanent disruption or addition of a therapeutically relevant gene in a highly targeted fashion. For example, our IVPRP strategy enables targeted insertion of a therapeutic gene into the genome of liver cells. This strategy has the potential to provide an extended or life-long clinical benefit in the treatment of monogenic diseases, such as hemophilia, without the risk of washout of therapeutic genes delivered using non-integrating vectors such as AAV or the potentially deleterious issues related to random insertion of therapeutic genes into the genome by randomly integrating viral vectors such as lentiviral vectors.
- Provide therapeutic solutions for targets that cannot be effectively addressed by existing drug modalities. The sequencing and publication of the human genome and growing information generated by genome-wide association studies have enabled the identification of both genes and regulatory sequences as potential new therapeutic targets. Many of these targets have a direct role in disease processes but cannot be bound or modulated for therapeutic purposes by small molecules, monoclonal antibodies or RNA based therapeutics. Alternative therapeutic approaches are required to modulate the biological activity of these so-called “non-druggable” targets. One such target is the BCL11A Enhancer, a regulatory sequence, which we are disrupting using ZFNs in hematopoietic stem progenitor cells (HSPCs) in order to elevate levels of fetal globin. This target is being developed in collaboration with Biogen as a therapeutic approach for a long-lasting treatment for SCD and beta-thalassemia
- Provide high specificity and selectivity for targets. ZFP Therapeutics can be designed to act with high specificity and we have published several examples of such data in high impact journals including (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 in a cell, 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, which may reduce the risk of toxicity. 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.

· Provides a genome editing platform with superior qualities for therapeutic development. Unlike other less developed bacterial-based genome editing platforms, such as CRISPR/Cas9 and TALENS, our proprietary ZFN genome editing technology is based on human proteins that have co-evolved with our complex human genome. The relative complexity of the protein-DNA interaction of our ZFN platform and the ability to engineer the entire protein-DNA interface also gives us the ability to optimize all components of our genome editing technology to drive efficient cutting with singular specificity. The ZFN-mediated mechanism is optimized for both gene insertion and gene knockout and over years of developing this platform, we have engineered our ZFN proteins to provide maximum design density (1:2 base pairs), giving us the capability to target virtually any sequence of interest and to place a ZFN

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exactly where we choose with single gene specificity. This precision is particularly critical for therapeutic gene insertion and correction. Finally, we have an established validated process for rapid development of a ZFN Therapeutic clinical lead and have taken our therapeutics through regulatory review and into human clinical studies where we are able to evaluate both the safety and efficacy of our approach.

#### THERAPEUTIC PRODUCT DEVELOPMENT

#### ZFN Therapeutic Product Development Programs

Figure 4:

Sangamo's Therapeutic Pipeline

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## Clinical Stage Programs

Product Candidate	Targeted Indication	Stage of Development	Protocol	Milestones
SB-728-T	HIV/AIDS	Phase 2	SB-728-1101 (Cytosan pre-conditioning dose-ranging study)	Cohort 3* ongoing, two of three subjects in Cohort 3* demonstrated viral load control in the absence of ART, additional five subjects will be accrued; full data expected in 2016. Enrollment and treatment of Cohorts 1-5 completed; in long-term follow-up.
		Phase 2	SB-728mR-T-1401	Accrual completed; in long-term follow-up.
		Phase 1	SB-728-902, Cohorts 1-3 Cohort 5 (CCR5 delta-32 heterozygotes)	Enrollment and treatment completed; in long-term follow-up.
		Phase 1	SB-728-T*	Enrollment and treatment completed, in long-term follow-up. Data published+ 2014.
		Phase 2	SB-728-T* (Cytosan pre-conditioning)	Trial ongoing at University of Pennsylvania.
SB-728-HSPC	HIV/AIDS	Phase 1/2	SB-728mR-HSPC*	Trial ongoing at City of Hope.
SB-FIX	Hemophilia B	Phase 1/2	SB-FIX-1501	Dose escalation study. Trial expected to begin in 1H 2016.
SB-318	Hurler Syndrome (MPS I)	Phase 1/2	SB-318-1502	Dose escalation study. Trial expected to begin in mid-2016

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.”

## ZFP Therapeutic 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 most recent data from The United States Centers for Disease Control and Prevention (CDC) over 2 million people were newly infected with HIV in 2014. An estimated 1.2 million people died of AIDS-related illnesses in the same year. There are now over 36 million people living with HIV and AIDS worldwide. At the end of 2012, (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 13% were unaware that they were infected. It is estimated that approximately 50,000 people are newly infected with HIV each year in the United States. Approximately 48,000 new infections occurred in 2010, and more than 13,700 people with AIDS died in the United States in 2012.

#### 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. While these drugs can suppress virus in the blood to undetectable levels, they cannot eliminate the reservoir of cells containing genomically-integrated HIV from the body. Hence, individuals infected 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, suppresses viral load, reduces the viral reservoir 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 HSPCs 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.

We began clinical trials in this program in late 2009 and over the past six years have conducted several studies in different populations of HIV infected subjects designed to evaluate, safety and tolerability of SB-728-T treatment. We have treated over 80 subjects and to date these studies have shown that the treatment is well-tolerated. In addition we have evaluated the effect of SB-728-T on subjects’ CD4 T-cell counts, levels of CCR5-modified T-cells, viral burden during a treatment interruption (TI) from anti-retroviral therapy (ART) and levels of HIV DNA in peripheral blood mononuclear cells as a measure of the viral reservoir. We have also studied the effect of Cytosan preconditioning on levels of cell engraftment, treatment with modified CD4 T-cells alone and treatments that include both modified CD4 and CD8 T-cells. In addition our studies have compared the effectiveness of the SB-728-T cell product when ZFNs were delivered to T-cells using either Adenovirus or mRNA and electroporation. The data have demonstrated durable engraftment and persistence of SB-728-T, ability of the ZFN-modified cells to traffic to the gut mucosa and that the modified cells have a survival advantage over unmodified cells during a TI from ART. In addition, our studies have demonstrated improvements in the overall CD4 T-cell count and the CD4:CD8 ratio in multiple subjects as well as a decrease in the viral reservoir and the ability of certain subjects to control their viral loads for prolonged periods in the absence of ART. The data from our first Phase 1 study were published in the *New England Journal of Medicine* in 2014 (*N.Eng. J. Med.* 2014: 370:897-906).

We also have a Phase 1/2 clinical study (SB-729mR-HSPC) to investigate this approach to treat HIV in hematopoietic stem progenitor cells (HSPCs), using electroporation of mRNA to deliver the ZFNs. In May 2014 California Institute for Regenerative Medicine (CIRM) agreed to fund a \$5.6 million Strategic Partnership Award for clinical studies of this program at City of Hope.

## Hemophilia B

We have a Phase 1/2 open-label, dose-escalation clinical trial in hemophilia B.

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 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.

#### Sangamo's Therapeutic Approach

We have developed a platform strategy, our In Vivo Protein Replacement Platform™ (IVPRP™), to address hemophilia A and B and other monogenic diseases that are currently treated using enzyme or protein replacement therapy. Using our ZFN genome editing technology we are adding a new therapeutic copy of the Factor VIII or IX gene precisely into a safe-harbor site, the Albumin gene or locus, and using the powerful Albumin promoter to drive expression of the newly inserted gene. We have published data demonstrating the potential utility of this platform for several different monogenic disease applications (Blood. 2015 Oct 8;126(15):1777-84).

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, thus increasing its potential usefulness in a pediatric population and would reduce or eliminate the need for chronic infusions of replacement proteins or clotting factor products. Our hemophilia B program was reviewed by the NIH Recombinant DNA Advisory Committee (RAC) and an IND application for the program was cleared by the FDA in December 2015. We expect to begin enrolling subjects into a Phase 1/2, open-label, dose-escalation clinical trial in the first half of 2016. Our goal is to file an IND application for our hemophilia A program in the second half of 2016.

### Lysosomal Storage Disorders

Lysosomal storage disorders (LSDs) are a heterogeneous group of inherited disorders including Fabry disease, Gaucher disease, Mucopolysaccharidosis type I (MPS I, Hurler syndrome) and Mucopolysaccharidosis Type II (MPS II Hunter 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 cells. These enzymes are found in structures called lysosomes which act as recycling sites in cells, breaking down unwanted material into simple products. 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, 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, MPS I and MPS II, 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 reducing its efficacy.

Our IVPRP has the potential to provide a broadly applicable genetic approach to enzyme replacement for several LSDs.

### MPS I

MPS I is caused by mutations in the gene encoding the alpha-L-iduronidase (IDUA) enzyme, resulting in a deficiency of IDUA which is required for the degradation of the glycosaminoglycans (GAGs) dermatan sulfate and heparin sulfate. The inability to degrade GAGs leads to their accumulation within the lysosomes throughout the body and individuals with this mutation experience multi-organ dysfunction and damage. Depending on the severity of the mutations and degree of residual enzyme activity, affected individuals may develop organomegaly, joint stiffness, skeletal deformities, corneal clouding, hearing loss and mental retardation. Three forms of MPS I, in order of increasing severity, include Scheie, Hurler-Scheie and Hurler syndromes. According to the National MPS Society, one in 500,000 births in the U.S. will result in Scheie syndrome, one in 115,000 births in Hurler/Scheie, and one in 100,000 births results in Hurler syndrome. There are approximately 2,000 MPS I patients in the U.S.

The current therapies for individuals with MPS I include hematopoietic stem cell transplantation (HSCT) for those with the most severe form of the disease (Hurler) and enzyme replacement therapy (ERT) for patients with the attenuated forms of the disease (Hurler-Scheie, Scheie). However, the reported mortality rate after HSCT is approximately 15% and the survival rate with successful engraftment is 56%. Most patients with milder forms of the disease receive weekly enzyme replacement therapy (ERT), usually in a doctor's office. For MPS I, IDUA infusions take on average four to six hours, however within hours, the replacement enzyme cannot be detected in the circulation. We expect to initiate a Phase 1/2 open-label, dose-escalation clinical trial in MPS I in mid-2016.

Pre-clinical Programs

MPS II

MPS II is an X-linked disorder primarily affecting males and caused by mutations in the gene encoding the iduronate-2-sulfatase (IDS) enzyme. This results in a deficiency of IDS which is required for the degradation of GAGs. The inability to degrade GAGs leads to their accumulation within the lysosomes throughout the body and individuals with this mutation experience multi-organ dysfunction and damage. Children with MPS II appear normal at birth but begin showing symptoms of developmental delay by age 2 – 3 years. Depending on the severity of the mutations and degree of residual enzyme activity, affected individuals may develop delayed development, enlarged internal organs, cardiovascular disorders, stunted growth and skeletal abnormalities and hearing loss. The disorder is progressive and symptoms range from mild (normal cognitive function) to severe (cognitively impaired). According to the National MPS Society, one in 100,000 male births in the U.S. will result in MPS II. There are approximately 500 MPS II patients in the U.S.

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The current therapy for individuals with MPS II includes weekly ERT. In contrast with Hurler syndrome, hematopoietic stem cell transplantation (HSCT) does not ameliorate neurologic symptoms.

#### Gaucher disease

Gaucher disease is caused by mutations in the gene encoding beta-glucocerebrosidase. Deficiency of this enzyme results in the accumulation of glucocerebroside and related substances in white blood cells, called macrophages, within the patient's spleen, liver, bone marrow and other organs, leading to damage to several tissues and organs within the body. Clinical manifestations of Type 1 Gaucher's disease, which occurs more frequently in people of Ashkenazi Jewish heritage, are diverse and include liver and/or spleen enlargement, skeletal weakness, bone disease, anemia, thrombocytopenia, and leukopenia but not CNS involvement. Patient symptomology may be masked or not attributed to the disease, leading to delayed diagnosis or misdiagnosis. Type 2 and 3 Gaucher disease affect the CNS. According to the National Gaucher Foundation approximately one in 50,000-75,000 live non-Ashkenazi Jewish births and one in 600 Ashkenazi Jewish births will lead to Gaucher disease. There are approximately 5,000-7,000 Gaucher patients in the US and 5,000-15,000 in Europe, however, the prevalence is likely under-reported due to delayed diagnosis or misdiagnosis. The current therapies for individuals with Gaucher disease include oral substrate inhibitor therapy once or twice a day and ERT every two weeks.

#### Fabry disease

Fabry disease is caused by mutations in the alpha galactosidase gene resulting in a deficiency of the alpha-galactosidase A enzyme and leading to the accumulation of a type of fat molecule, called globotriaosylceramide, in cells lining blood vessels in the skin and cells in the kidneys, heart, and nervous system. Patients with Fabry's disease may experience nerve pain, kidney damage, left ventricular hypertrophy and neurological damage. Symptoms may appear at any point from childhood to middle age, but their appearance largely depends on whether there is some residual enzymatic activity. The incidence of the disease is unknown but it is estimated that there are approximately 2,700 – 8,000 patients in the US. The current therapy for individuals with Fabry disease therapy is recombinant alpha-galactosidase A ERT every two weeks which leads to stabilization, but not reversal of organ damage caused by the accumulation of alpha-galactosidase A enzyme substrate.

#### Sangamo's Therapeutic Approach

Beginning with MPS I and MPS II our aim is use this approach to enable the patient's liver to produce therapeutic quantities of the corrective enzymes, IDUA and IDS, respectively.

Our third and fourth IVPRP LSD targets are Gaucher disease and Fabry disease, respectively. Similar to MPS I and MPS II, our aim is to enable the patient's liver to produce therapeutic quantities of the corrective enzymes, beta-glucocerebrosidase for Gaucher and alpha-galactosidase A for Fabry disease.

An IND application for our product candidate for MPS I was filed in 2015 and was cleared by the FDA in early February 2016. We expect to begin a Phase 1/2, open-label, dose escalation, clinical trial for this program in mid-2016. We are in preclinical development for MPS II, Gaucher disease and Fabry disease. Our goal is to file an IND application for our product candidate for MPS II in the first half of 2016 and two additional IND applications for Gaucher disease and Fabry disease in the second half of 2016.

#### 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 experience 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. 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 regulatory sequences that control the expression of 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.

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 long-lasting treatment for SCD and beta-thalassemia.

We expect to file an IND application for our beta-thalassemia program in the first half of 2016. Biogen expects to file an IND application for the SCD program in the second half of 2016.

#### Programs Partnered with Shire

##### 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 causes 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 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 15 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) approximately 30,000 people in the U.S. have HD. 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 Shire is responsible for all clinical development activities including filing the IND application.

#### ZFP Therapeutic Research Programs

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

## CORPORATE RELATIONSHIPS

We have established collaborative and strategic partnerships in non-therapeutic areas and for several of our ZFP Therapeutic programs. 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 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 the 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.

#### Amended 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 to research, develop and commercialize human therapeutics and diagnostics based on our ZFP technology. Under the agreement, we received an upfront license fee of \$13.0 million. The two companies agreed to develop potential human therapeutic or diagnostic products for seven gene targets. The initial four gene targets were 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 had the right, subject to certain limitations, to designate two additional gene targets. Pursuant to the agreement, we 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.

On September 1, 2015, the Shire Agreement was amended such that Shire agreed to return to Sangamo the exclusive, world-wide rights to gene targets for the development and commercialization of ZFP Therapeutics for hemophilia A and B. Shire retains the rights and will continue to develop a ZFP Therapeutic for Huntington's disease and a ZFP Therapeutic for one additional gene target yet to be named. Sangamo will provide certain target feasibility services, and upon Shire's request, certain research activities according to a research plan as agreed upon by both companies. Such research activities performed by Sangamo will be reimbursed by Shire. Shire's rights with respect to other targets contemplated in the original agreement revert to Sangamo. Under the revised agreement, each company is responsible for expenses associated with its own programs and will reimburse the other for any ongoing services provided. Shire

is responsible for reimbursement of expenses related to obligations prior to the amendment date which will be recognized as revenue as expenses are incurred. Sangamo has granted Shire a right of first negotiation to license the hemophilia A and B IVPRP programs. Under the amended agreement, Shire does not have any milestone payment obligations with respect to the retained programs, but it is required to pay single digit percentage royalties to Sangamo, up to a specified maximum cap, on the commercial sales of ZFP Therapeutic products from such programs. Under the Agreement, Sangamo has full control over, and full responsibility for the costs of, the hemophilia programs returned to the Company, subject to certain diligence obligations and Shire's right of first negotiation to obtain a license to such programs under certain circumstances. Sangamo is required to pay single digit percentage royalties to Shire, up to a specified maximum cap, on commercial sales of ZFP Therapeutic products from such returned programs.

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, effective upon at least 90 days' advance written notice.

### 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.

In October 2009 we expanded the license agreement with Sigma to include 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 were 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 25% of any sublicensing revenues. 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.

In December 2015 Ligand Pharmaceuticals Inc. (Ligand) acquired OMT. For any given OMT-derived product, Ligand 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. DAS also obtained a 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 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.

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 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 HSPCs. 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. In May 2015 Sangamo announced a consolidated development path for its beta-thalassemia and SCD programs using the "BCL11A Enhancer" target. Due to the switch to the BCL11A Enhancer strategy, CIRM and Sangamo terminated the Strategic Partnership Award as of June 30, 2015. Sangamo returned \$3.0 million in unused funds received from CIRM under the award during the three months ended September 30, 2015.

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. 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.

#### 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 genome editing and gene regulation 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, the California Institute of Technology, City of Hope and the University of Utah. These licenses grant us rights to make, use and sell ZFPs, ZFNs and ZFP TFs under 15 families of patent filings. As of February 1, 2016, these patent filings have resulted in 17 issued U.S. patents and 41 granted foreign patents, with 4 currently pending U.S. patent applications and 9 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 those licensed under agreements with the Massachusetts Institute of Technology, the University of Utah, 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.

#### 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. At the request of Sangamo, the patent license has been amended to remove some of the intellectual property in this license agreement that does not affect the development of our technology. The patent license agreement still expires upon the expiration of the last patent covered by the patent license agreement. Based on currently licensed patents, the patent license agreement will terminate on or about October 9, 2019. 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.

#### University of Utah Research Foundation

We entered into a patent license agreement with the University of Utah Research Foundation, on September 8, 2004, as subsequently amended, whereby Utah granted us a worldwide license to technology and patents relating to the use of ZFNs 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 license agreement expires on the expiration of the last patent covered by the patent license agreement. Based on currently issued patents, the license agreement will terminate on or about March 2, 2025. Utah may terminate the license agreement upon a default by us that remains uncured following written notice. We may end the agreement at any time upon 90 days 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.

#### Therapeutic Licenses

We have entered into licenses potentially useful for specific therapeutic uses of our genome editing technologies with the Regents of the University of California and the Children's Medical Center Corporation. The patents included in these licenses relate to CNS disorders and hemoglobinopathies, respectively. These license include 3 patent families, including 5 issued foreign patents, 9 issued US patents, 34 pending foreign patents and 2 pending US patents.



## Sangamo Intellectual Property

In addition to our in-licensed patent portfolio, as of February 1, 2016, we had 141 families of Sangamo-owned or co-owned patent filings, including the acquired Ceregene patent estate, which totaled approximately 144 issued U.S. patents, 510 granted foreign patents, 110 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 and CRISPR/Cas systems.

As of February 1, 2016, the earliest active patents in our portfolio are set to begin expiring in 2017, with the average expiration of our currently issued patents expiring being mid-2025. 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 US8962281), DNA nickases (see newly issued EP2313515), 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 EP2188384, US9121072, US9145565 and US9115409), linker designs and methods of making modified plant zinc finger proteins (see newly issued EP2415873 and EP2412812);
- 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, cancer therapeutics, treatment of head and neck cancer, glioblastoma, pain, modulation of cardiac contractility and methods to regulate the glucocorticoid receptor, treatments for HIV;
- Nuclease Therapeutics: Treatments for HIV, SCD and beta-thalassemia (see patent publication US20140093913, 20150132269, 20150218253 and 20140080216, In Vivo Protein Replacement Platform for treatment of hemophilia and lysosomal storage diseases (see newly issued US9150847, patent publication US 20140112896, and US20140017214), genome editing (see newly issued US9222105), models for Parkinson's Disease, regulation of the expression of PD1; Immunomodulatory therapeutics (see newly issued US8945868, US8956828 and patent publications US20140120622, US20150037304, US20140301990); Cystic Fibrosis (see newly issued US9161995); hemophilia (see newly issued US9175280 and EP2627665 and patent publication US20150159172); glioblastoma (see newly issued US9217026);
- 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, methods of transgenic animal development (see newly issued US9206404);
- Donor DNA design: Methods for designing optimal donors for transgene delivery (see newly issued US9005973, US9045763 and US9045763);
- Non-ZFP nucleases, methods of design and use (see newly issued US9150879 and patent publication US20150056705, 20150353917 and 20150307561);
- Engineering of stem cells (see patent publication US20150110762);
- Methods for genome editing (see newly issued US9200266).

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 patentable, even when newly discovered, although a cDNA corresponding to the transcription product of that gene may be.

Accordingly, U.S. patent claims to DNA sequences can cover only isolated cDNAs, 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 cDNA 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 cDNA 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 and are subject to interpretation and refinement by the court system. 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. For example, our issued European patents EP2281050, EP2171052 and EP2527435 have been opposed in Europe. We do not know what the outcome of these procedures will be. The claims of these patents may be amended such that claim scope is reduced or the patents may be revoked as a result of these procedures.

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. 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 and CRISPR/Cas 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:

- 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

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this category may include, but not be limited to, uniQure, BioMarin, bluebird bio, RegenX, Spark Therapeutics, Dimension Therapeutics, and Voyager Therapeutics.

- 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. 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., Ionis Pharmaceuticals, Inc., Genzyme (a Sanofi Company) and Regulus Therapeutics, LLC.
- Small molecules in development from both in-house drug discovery programs of pharmaceutical companies such as Pfizer, Inc., GlaxoSmithKline (GSK), Novartis, and Merck & Co., Inc., as well as from biotechnology companies with expertise and capabilities in small molecule discovery and development such as Gilead, Genzyme, and Global Blood Therapeutics which has a small molecule product in development for SCD.
- Monoclonal antibody companies and product candidates from certain biotechnology firms such as Genentech, Inc. and Amgen.

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, for licenses to proprietary technology and for subjects in our clinical trials of treatments for rare diseases. 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.
- recruit subjects into our clinical trials in a timely fashion.

#### 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 mammalian cells and animals) and clinical trials in humans followed by a formal regulatory submission and an extensive regulatory clearance process conducted 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 final drug 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.

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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.

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 in certain circumstances. 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 a small number of subjects 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, as well as certain Phase 1 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 have been engaged in clinical trials of our ZFP Therapeutic products since 2005. Since 2009 we have had an ongoing clinical program to evaluate SB-728-T, a ZFN modified autologous T-cell therapy for treatment of HIV. Within our HIV program we have an ongoing Phase 2 clinical trial SB-728-1101 Cohort 3\* as well as a Phase 1/2 clinical trial of this same approach in HSPCs. Most subjects enrolled in completed clinical trials related to this program are in long-term follow-up. In 2015 we filed a RAC submission and an IND application for SB-FIX, which uses AAV delivery of our ZFNs for correction of hemophilia B in vivo, and a RAC submission for SB-318, using the same AAV delivery system for correction of IDUA deficiency for MPS I. Phase 1/2 clinical trials for both of these programs, SB-FIX-1501 for hemophilia B and SB-318-1502 for MPS I, will begin in the first half of 2016 and mid-2016, respectively.

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, 2016, we had 119 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

An investment in our common stock involves significant risk. 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. You should carefully consider the information described in the following risk factors, together with the other information appearing elsewhere in this report, before making an investment decision regarding our common stock.

### 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 have an ongoing Phase 2 clinical trial (SB-728-1101, Cohort 3\*) of our ZFP Therapeutic, SB-728-T, for the treatment of HIV/AIDS. We also have an open Phase 1/2 clinical trial of our ZFP Therapeutic for HIV in HSPCs (SB-728mR-HSPC) and expect to initiate Phase 1/2 clinical trials of our IVPRP approach in hemophilia B and MPS I in the first half of 2016 and in mid-2016, respectively. Preliminary data demonstrate that treatment of 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 shares in our common 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 15 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 clinical program to develop SB-728-T for the treatment of HIV/AIDS which is now in Phase 2 clinical testing. 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) of their antiretroviral therapy (ART) 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). 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). We have enrolled additional subjects into the SB-728-1101 study to define the optimum dose of Cytoxin required to safely enhance engraftment and to evaluate the inclusion of modified CD8 cells as well as modified CD4 cells in the SB-728-T product. Two of three additional subjects, enrolled in Cohort 3\* of this study, have demonstrated notable reductions in viral load during a TI from ART which has lasted for over one year. 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.

#### 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.

If we are not able to obtain the necessary regulatory approval to commercialize our products or if such approval is delayed or suspended, it would have an adverse effect on our business operations and trading price of our common stock

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 withdrawals 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 effect 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. For potential marketing application approval, additional clinical testing will be required, 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, and we may need to seek partnerships or collaboration with third parties to advance these trials. We have entered into a collaborative agreement with Biogen to provide funding and assistance in the development of certain ZFP Therapeutics through the clinical trial process. 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 outside the United States. 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 may 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 to do so, which could limit the usefulness of our technology. In addition, while we have demonstrated the function of engineered ZFNs and ZFP TFs in mammalian cells, yeast, insects, plants and animals, we have not yet demonstrated clinical 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 program, 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 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 date from Phase 2 rail were reported in early 2015 and demonstrated similar findings but did not demonstrate significant signs of efficacy. In the first quarter of 2015, the Company decided to discontinue the CERE-110 and CERE-120 clinical trial programs. As such, the probability of achieving projected revenues and cash flows associated with these programs were adversely affected. There is no guarantee that the AAV delivery technology can be applied to our ZFP Therapeutics safely and effectively.

#### 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:
  - recombinant proteins;
  - gene therapy/cDNAs;
  - antisense;
  - siRNA and microRNA approaches, exon skipping;
  - small molecule drugs;
  - monoclonal antibodies;
  - CRISPR/Cas technology;
  - TALE proteins and MegaTALs
- For our Non-Therapeutic Applications:
  - For protein production: gene amplification, CRISPR/Cas technology, TALE technology, insulator technology, and mini-chromosomes;
  - For target validation: antisense, siRNA, TALE technology and CRISPR/Cas technology;
  - For plant agriculture: recombination approaches, mutagenesis approaches, TALE technology, CRISPR/Cas technology, mini-chromosomes; and
  - For transgenic animals: somatic nuclear transfer, embryonic stem cell, TALE, CRISPR/Cas 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
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license the proprietary technologies of academic and research institutions that are competitive with our technology, which may preclude us from pursuing similar opportunities.

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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 and genome editing 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 and genome editing for the prevention or treatment of human diseases. Public attitudes may be influenced by claims that gene therapy or genome editing is unsafe, and, consequently, our products may not gain the acceptance of the public or the medical community. Negative public reaction to gene therapy or genome editing in general could result in greater government regulation and stricter labeling requirements of gene based 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, 2015, 2014 and 2013 were \$40.7 million, \$26.4 million and \$26.6 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, 2015, we had an accumulated deficit of \$369.3 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 2017, 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. In September 2015 we amended the Shire agreement to restructure the collaboration, under which Shire will retain the rights to develop a ZFP Therapeutic for Huntington's disease and another target yet to be named, while returning the rights to us for the development, clinical testing and commercialization of ZFP Therapeutics for hemophilia A and B. Under the amended agreement, we will provide certain target feasibility activities and upon Shire's request, certain research activities under a research plan, agreed upon by both companies. 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 our agreement with Biogen, they have control and broad discretion over all or certain aspects of the clinical development and commercialization of any product developed under the agreement, 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 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. In September 2015 we amended our agreement with Shire pursuant to which Shire will no longer continue the clinical development of our ZFP Therapeutics for hemophilia A and B. As a result, we intend to develop these programs either ourselves or seek the support of other partners or collaborators. We may not have sufficient resources and expertise to develop these programs by ourselves, and we may not be able to identify a suitable partner or negotiate a favorable collaboration agreement to allow us to continue the development of these programs. 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 may have filed patent applications that are similar to ours, we cannot guarantee 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 that a third party may receive.

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 aspects of 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;
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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/Cas 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 skilled and qualified 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 three months ended December 31, 2015, the closing price of our common stock, as reported by the NASDAQ Global Select Market, ranged from a low of \$5.56 to high of \$9.69. During the fiscal year ended December 31, 2015, our common stock price fluctuated, ranging from a low of \$5.56 to a high of \$18.54. 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;

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- 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, or changes in our existing collaboration agreements;
- 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 of our voting stock. The application of Section 203 may, in some circumstances, deter or prevent a change in control of our company even when such change may be beneficial to our stockholders.

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 have two additional properties located in Richmond, California, including a lease to occupy approximately 7,700 square feet of research and office space that expires in January of 2018 and a build-to-suit lease to occupy approximately 41,400 square feet of space that expires five years after substantial construction is completed.

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, 2015		
First Quarter	\$18.54	\$12.64
Second Quarter	\$15.56	\$10.35
Third Quarter	\$10.86	\$5.64
Fourth Quarter	\$9.69	\$5.56
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

## Holders

As of February 1, 2016, there were 66 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.



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,				
	2015	2014	2013	2012	2011
	(In thousands, except per share data)				
<b>Statement of Operations Data:</b>					
Total revenues	\$39,539	\$45,870	\$24,133	\$21,655	\$10,319
<b>Operating expenses:</b>					
Research and development	67,198	56,974	37,039	31,709	32,098
General and administrative	19,197	15,677	13,800	12,144	14,042
Total operating expenses	86,395	72,651	50,839	43,853	46,140
Loss from operations	(46,856)	(26,781)	(26,706)	(22,198)	(35,821)
Other income/(expense)	431	364	82	(66)	71
Benefit from income taxes	5,722	—	—	—	—
Net loss	\$(40,703)	\$(26,417)	\$(26,624)	\$(22,264)	\$(35,750)
Basic and diluted net loss per share	\$(0.58)	\$(0.39)	\$(0.48)	\$(0.42)	\$(0.71)
Shares used in computing basic and diluted net loss	69,757	67,022	55,974	52,741	50,512
	As of December 31,				
	2015	2014	2013	2012	2011
	(In thousands)				
<b>Balance Sheet Data:</b>					
Cash, cash equivalents, marketable securities, and interest					
receivable	\$209,307	\$226,645	\$131,814	\$76,321	\$84,463
Working capital	192,485	169,997	87,143	59,575	78,488
Total assets	217,235	243,212	140,838	82,533	87,336
Accumulated deficit	(369,253)	(328,550)	(302,133)	(275,509)	(253,245)
Total stockholders’ equity	192,439	206,633	121,710	64,896	80,132

## 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 therapeutic genome editing and gene regulation, and we are the leaders in this field. 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. We have several proprietary clinical and preclinical programs in development and have strategically partnered certain programs with biopharmaceutical companies to expedite clinical and commercial development. Our long-term goal



is to forward integrate into manufacturing, development and commercial operations to more fully 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, and in 2016 we expect to initiate clinical trials to evaluate ZFP Therapeutics, including our hemophilia B and MPS I programs. 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 2014 we established a collaborative partnership with Biogen 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 hemophilia A and lysosomal storage disorders (LSDs). We also have established a collaborative partnership with Shire International GmbH, formerly Shire AG (Shire), to research, develop and commercialize our preclinical ZFP Therapeutic development program for Huntington's disease (HD). 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. We have a license agreement with the research reagent company Sigma-Aldrich Corporation (Sigma). Under this agreement, Sigma has the exclusive rights to develop and market ZFP-based laboratory research reagents marketed under the trademark CompoZr<sup>®</sup> as well as ZFP-modified cell lines for commercial production of protein pharmaceuticals and ZFP-engineered transgenic animals. We also have a license agreement with Dow AgroSciences, LLC (DAS), a wholly owned subsidiary of Dow Chemical Corporation. Under this agreement, DAS has the exclusive rights to use our ZFP technology to modify the genomes or alter protein expression of plant cells, plants, or plant cell cultures and markets our ZFN technology under the trademark EXZACT<sup>™</sup> Precision Technology.

For the year ended December 31, 2015, we incurred a consolidated net loss of \$40.7 million, or \$0.58 per share, compared to a consolidated net loss of \$26.4 million, or \$0.39 per share, for the same period in 2014. As of December 31, 2015, we had cash, cash equivalents, marketable securities and interest receivable totaling \$209.3 million compared to \$226.6 million as of December 31, 2014. As of December 31, 2015, we had an accumulated deficit of \$369.3 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 a portion has 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.

#### 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 Stock 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.

#### In-Process Research and Development

Intangible assets related to in-process research and development costs, or IPR&D, are considered to be indefinite-lived until the completion or abandonment of the associated research and development efforts. If and when development is complete, which generally occurs if and when regulatory approval to market a product is obtained, the associated assets would be deemed finite-lived and would then be amortized based on their respective estimated useful lives at that point in time. In the first quarter of 2015, the Company decided to discontinue the CERE-110 and CERE-120 clinical trial programs. As such, the probability of achieving projected revenues and cash flows associated with these programs were adversely affected. The Company did not believe the programs have an alternative future use for itself or other market participants. Accordingly, the Company recognized a \$1.9 million impairment charge related to these assets during the year ended December 31, 2015 and recorded to the research and development (R&D) expense line item in the consolidated statements of operations.

#### Contingent Consideration Liability

Under the merger agreement with Ceregene, the Company may be required to make contingent earn-out payments if the Company grants a third-party license to develop and commercialize certain product candidates acquired from Ceregene, or if the Company commercializes any of these product candidates itself. These earn-out payments will become payable in the period they are earned. In accordance with ASC Topic 805, the Company determined the fair value of this liability for contingent consideration on the acquisition date using a probability-weighted discounted cash flow analysis. During the year ended December 31, 2015, the recognized amount of the liability for contingent consideration decreased by \$1.8 million due to the decrease in the probability of incurring potential future royalty payments associated with the impairment of IPR&D assets acquired from Ceregene.

#### Results of Operations

Years Ended December 31, 2015, 2014 and 2013

##### Revenues

Year Ended December 31,							
2015	2014	Change	% Change	2014	2013	Change	% Change

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(In thousands, except percentage values)

Revenues:										
Collaboration agreements	\$37,844	\$43,880	\$(6,036)	(14	%)	\$43,880	\$21,678	\$22,202	102	%
Research grants	1,695	1,990	(295 )	(15	%)	1,990	2,455	(465 )	(19	%)
Total revenues	\$39,539	\$45,870	\$(6,331)	(14	%)	\$45,870	\$24,133	\$21,737	90	%

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 Biogen, Sigma and DAS.

Revenues from our corporate collaboration agreements were \$37.8 million in 2015, \$43.9 million in 2014 and \$21.7 million in 2013. The decrease in revenues from collaborations in 2015 compared to 2014 was primarily due to a decrease of \$10.2 million in revenues related to Shire research services, partially offset by an increase of \$4.0 million in royalty revenue related to our Sigma license. 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. 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 \$1.7 million in 2015, \$2.0 million in 2014 and \$2.5 million in 2013. The decrease of \$0.3 million in 2015 from 2014 was primarily due to the decrease in revenue related to funding from a research grant from CIRM for our beta-thalassemia project. The decrease was partially offset by \$0.1 million in revenue related to our new grant agreement with University of Pennsylvania for our HIV program. 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 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.

During 2015 revenues related to our collaborative agreements with Shire and Biogen represented 40% and 35%, respectively of total revenues. During 2014 revenues related to Shire and DAS represented 57% and 28%, respectively of total revenues. During 2013, revenues related to Shire, Sigma-Aldrich Corporation (Sigma) and Dow AgroSciences LLC (DAS) represented 68%, 9% and 12%, respectively, of total revenues.

### Operating Expenses

	Year Ended December 31,							
	2015	2014	Change	% Change	2014	2013	Change	% Change
	(In thousands, except percentage values)							
<b>Operating expenses:</b>								
Research and development	\$67,198	\$56,974	\$10,224	18 %	\$56,974	\$37,039	\$19,935	54 %
General and administrative	19,197	15,677	3,520	22 %	15,677	13,800	1,877	14 %
Total operating expenses	\$86,395	\$72,651	\$13,744	19 %	\$72,651	\$50,839	\$21,812	43 %

### 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 and our IVPRP programs in the clinic and if we are able to progress our earlier stage ZFP therapeutic product candidates into clinical trials including our programs under our 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 are 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 \$67.2 million in 2015, \$57.0 million in 2014 and \$37.0 million in 2013. The increase of \$10.2 million in research and development expenses in 2015 was primarily due to an increase of \$5.8 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 \$4.6 million in 2015 as compared to 2014 due to increased headcount.

The increase of \$19.9 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.

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.”



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The table below shows research and development expenses for our primary clinical development program, SB-728, 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.

Programs	Year Ended December 31, (In thousands)		
	2015	2014	2013
SB-728 clinical programs	\$7,654	\$8,339	\$7,071
Other clinical programs and non-therapeutic programs	3,031	801	867
Preclinical and research programs	56,513	47,604	29,041
Total research and development expenses	\$67,198	\$56,744	\$36,979

### 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 \$19.2 million in 2015, \$15.7 million in 2014 and \$13.8 million in 2013. The increase in general and administrative expenses of \$3.5 million in 2015 was primarily due to an increase of \$1.8 million in personnel related expenses, including salaries and stock-based compensation expenses due to increased headcount and an increase in professional services expenses of \$1.4 million.

The increase 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.

### Other income, net

Other income was \$0.4 million in 2015, \$0.4 million in 2014 and \$0.1 million in 2013. Other income in 2015, 2014 and 2013 was comprised of interest income.

### Benefit from income taxes

Benefit from income taxes were \$5.7 million in 2015. The increase was primarily due to \$5.0 million in income tax benefit recognized from the claims settlement with certain institutional investors that were beneficial owners of our common stock related to the disgorgement of short swing profits pursuant to Section 16 of the Securities Exchange Act of 1934, as amended. There was no benefit from incomes taxes in 2014 and 2013.

## 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, 2015, we had cash, cash equivalents, marketable securities and interest receivable totaling \$209.3 million compared to \$226.6 million as of December 31, 2014, with the decrease primarily attributable to our net operating loss.

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.

Under our agreement with Biogen, we received an upfront license fee of \$20.0 million in 2014. Biogen 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 January 2012 we entered into a license and collaboration agreement with Shire, under which we received an upfront license fee of \$13.0 million. In addition, Shire agreed to reimburse us for agreed upon costs incurred in connection with research and development activities that we conducted and to pay us certain milestone payments based on our achievement of specified research, regulatory, clinical development, commercialization and sales milestones, which depended upon our ability with Shire to continue to progress our programs under collaboration. We were also eligible to receive royalty payments on net sales of products developed under the collaboration, if any. On September 1, 2015, we amended the Shire agreement such that going forward, each company is responsible for expenses associated with its own programs and will reimburse the other for any ongoing services provided. Under the amended agreement, Shire does not have any milestone payment obligations to us with respect to the retained programs, but it is required to pay single digit percentage royalties to us, up to a specified maximum cap, on the commercial sales of ZFP therapeutic products from such programs. Under the Agreement, we have full control over, and full responsibility for the costs of, the hemophilia programs returned to us, subject to certain diligence obligations and Shire's right of first negotiation to obtain a license to such programs under certain circumstances. We are required to pay single digit percentage royalties to Shire, up to a specified maximum cap, on commercial sales of ZFP therapeutic products from such returned programs.

#### 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 \$33.7 million in 2015 compared to \$5.7 million in 2014. The increase in net cash used in operations in 2015 was primarily due to an increase in research and development expenses related to our preclinical research programs, decrease in deferred revenues related to the recognition of the \$20.0 million upfront payment from Biogen pursuant to the collaboration and license agreement, and benefit from income taxes related to the claim settlement, partially offset by an decrease in accounts receivable.

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.

**Investing activities.** Net cash provided by investing activities was \$77.5 million in 2015. Net cash used in investing activities was \$100.7 million in 2014 and \$68.1 million in 2013. Cash flows from investing activities for all periods was primarily related to purchases, sales and maturities of marketable securities.

**Financing activities.** Net cash provided by financing activities was \$19.7 million in 2015, \$102.2 million in 2014, and \$76.1 million in 2013. Net cash provided by financing activities in 2015 was primarily attributable to a \$14.5 million claim settlement with certain institutional investors that were beneficial owners of our common stock related to the disgorgement of short-swing profits pursuant to Section 16 of the Securities Exchange Act of 1934, as amended, as well as proceeds from the exercise of stock options. 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.

#### 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 2017. 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 a \$5.7 million benefit for income taxes for the period of December 31, 2015. As of December 31, 2015, we had net operating loss carryforwards for federal and state income tax purposes of approximately \$351.3 million and \$264.3 million, respectively. If not utilized, the net federal and state operating loss carryforwards will start to expire in 2018 and 2016, respectively. We also have federal and state research tax credit carryforwards of \$7.8 million and \$8.2 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.

#### Off Balance Sheet Arrangements

We do not have any off balance sheet arrangements as defined in Item 303(a)(4)(ii) of Regulation S-K.

#### Contractual Obligations and Commercial Commitments

As of December 31, 2015, we had contractual obligations and commercial commitments as follows (in thousands):

	Total	Payments Due by Period			
		Less Than 1 Year	1-3 Years	4-5 Years	More Than 5 Years
Contractual Obligations					
Operating leases	\$5,497	\$ 1,015	\$3,594	\$ 503	\$ 385
License obligations	1,936	313	828	405	390
Total contractual obligations	\$7,433	\$ 1,328	\$4,422	\$ 908	\$ 775

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.

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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, 2015 and 2014, 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, 2015. 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, 2015 and 2014, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2015, 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, 2015, 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 18, 2016 expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP

Redwood City, California

February 18, 2016

## SANGAMO BIOSCIENCES, INC.

## CONSOLIDATED BALANCE SHEETS

	December 31, 2015	December 31, 2014
<b>ASSETS</b>		
Current assets:		
Cash and cash equivalents	\$69,482	\$6,030
Marketable securities	139,518	172,932
Interest receivable	307	423
Accounts receivable	2,521	10,368
Prepaid expenses	754	623
Restricted cash	—	320
Other current assets	—	183
Total current assets	212,582	190,879
Marketable securities, non-current	—	47,260
Property and equipment, net	2,916	1,479
Goodwill and intangible assets, net	1,585	3,455
Other assets	152	139
Total assets	\$217,235	\$243,212
<b>LIABILITIES AND STOCKHOLDERS' EQUITY</b>		
Current liabilities:		
Accounts payable and accrued liabilities	\$8,229	\$8,704
Accrued compensation and employee benefits	2,748	2,853
Escrow liability	—	275
Deferred revenues	9,120	9,050
Total current liabilities	20,097	20,882
Deferred revenues, non-current	4,699	13,149
Contingent consideration liability	—	1,800
Deferred tax liability	—	748
Total liabilities	24,796	36,579
Commitments and contingencies		
Stockholders' equity:		
Common stock, \$0.01 par value; 160,000,000 shares authorized, 70,354,608 and 69,062,394 shares issued and outstanding at December 31, 2015, and December 31, 2014, respectively		
	703	690
Additional paid-in capital	560,989	534,518
Accumulated deficit	(369,253)	(328,550)
Accumulated other comprehensive income (loss)	—	(25 )
Total stockholders' equity	192,439	206,633
Total liabilities and stockholders' equity	\$217,235	\$243,212

See accompanying Notes to Consolidated Financial Statements.

## SANGAMO BIOSCIENCES, INC.

## CONSOLIDATED STATEMENTS OF OPERATIONS

	Year Ended December 31,		
	2015	2014	2013
	(In thousands, except per share amounts)		
<b>Revenues:</b>			
Collaboration agreements	\$37,844	\$43,880	\$21,678
Research grants	1,695	1,990	2,455
Total revenues	39,539	45,870	24,133
<b>Operating expenses:</b>			
Research and development	67,198	56,974	37,039
General and administrative	19,197	15,677	13,800
Total operating expenses	86,395	72,651	50,839
Loss from operations	(46,856)	(26,781)	(26,706)
Other income, net	431	364	82
Loss before taxes	(46,425)	(26,417)	(26,624)
Benefit from income taxes	5,722	—	—
Net loss	\$(40,703)	\$(26,417)	\$(26,624)
Basic and diluted net loss per share	\$(0.58 )	\$(0.39 )	\$(0.48 )
Shares used in computing basic and diluted net loss per share	69,757	67,022	55,974

See accompanying Notes to Consolidated Financial Statements.

SANGAMO BIOSCIENCES, INC.

CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS

	Year Ended December 31,		
	2015	2014	2013
	(In thousands)		
Net loss	\$(40,703)	\$(26,417)	\$(26,624)
Change in unrealized gain (loss) on available-for-sale securities, net of tax	25	(37)	(14)
Comprehensive loss	\$(40,678)	\$(26,454)	\$(26,638)

See accompanying Notes to Consolidated Financial Statements.





## SANGAMO BIOSCIENCES, INC.

## CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY

	Common Stock		Additional	Accumulated	Accumulated	Total
	Shares	Amount	Paid-in	Deficit	Other	Stockholders'
	(In thousands, except share data)					
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
Issuance of common stock upon exercise						
of stock options and in connection with						
restricted stock units, net of tax	1,164,033	12	4,336	—	—	4,348
Issuance of common stock under						
employee stock purchase plan	128,181	1	910	—	—	911
Stock-based compensation	—	—	11,730	—	—	11,730
Claims settlement under Section 16(b), net of tax benefit	—	—	9,495	—	—	9,495
Comprehensive loss:						
Net unrealized gain on marketable						
securities, net of tax	—	—	—	—	25	25
Net loss	—	—	—	(40,703 )	—	(40,703 )
Comprehensive loss	—	—	—	—	—	(40,678 )
Balances at December 31, 2015	70,354,608	\$ 703	\$ 560,989	\$ (369,253 )	\$ —	\$ 192,439

See accompanying Notes to Consolidated Financial Statements.

## SANGAMO BIOSCIENCES, INC.

## CONSOLIDATED STATEMENTS OF CASH FLOWS

	Year ended December 31,		
	2015	2014	2013
	(In thousands)		
<b>Operating Activities:</b>			
Net loss	\$(40,703 )	\$(26,417 )	\$(26,624 )
<b>Adjustments to reconcile net loss to net cash used in operating activities:</b>			
Depreciation and amortization	988	549	569
Amortization of premium on marketable securities	827	1,098	912
Stock-based compensation	11,730	9,200	6,146
Change in fair value of contingent consideration liability	(1,800 )	230	60
Intangible impairment	1,870	—	—
Benefit from income taxes	(5,722 )	—	—
<b>Net changes in operating assets and liabilities:</b>			
Interest receivable	116	(85 )	(148 )
Accounts receivable	7,847	(7,213 )	1,008
Prepaid expenses and other assets	376	(258 )	(480 )
Accounts payable and accrued liabilities	(764 )	4,324	544
Accrued compensation and employee benefits	(105 )	(341 )	721
Deferred revenues	(8,380 )	13,238	(2,190 )
Net cash used in operating activities	(33,720 )	(5,675 )	(19,482 )
<b>Investing Activities:</b>			
Purchases of marketable securities	(257,988)	(227,802)	(118,894)
Maturities of marketable securities	337,861	127,765	51,129
Acquisition of Ceregene, Inc., net of cash received	—	—	79
Purchases of property and equipment	(2,411 )	(621 )	(432 )
Net cash provided by / (used in) investing activities	77,462	(100,658)	(68,118 )
<b>Financing Activities:</b>			
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	(1,546 )	(4,556 )	(2,015 )
Proceeds from issuance of common stock	6,804	12,937	8,630
Claims settlement under Section 16(b)	14,452	—	—
Net cash provided by financing activities	19,710	102,177	76,107
Net increase / (decrease) in cash and cash equivalents	63,452	(4,156 )	(11,493 )
Cash and cash equivalents, beginning of period	6,030	10,186	21,679
Cash and cash equivalents, end of period	\$69,482	\$6,030	\$10,186
<b>Supplemental disclosure of noncash investing activities:</b>			
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

Overview

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 genome editing and gene regulation 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, 2015, along with expected revenues from collaborations, strategic partnerships and research grants, will be adequate to fund its operations at least through 2017. 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.

Basis of Presentation

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

Business Combinations

The Company accounted for the acquisition of Ceregene in accordance with Accounting Standards Codification (ASC) Topic 805, Business Combinations (ASC Topic 805). 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.

#### Cash and Cash Equivalents

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

As part of the acquisition of Ceregene, Sangamo was required to set aside \$0.3 million in an escrow account until April 1, 2015 at which time it was released.

#### Marketable Securities

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

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

#### 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 the Company's investment securities consist of the US Treasury, governmental agencies, various major corporations and financial institutions with high credit standing.

#### Property and Equipment

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

#### Revenue Recognition

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

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

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

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

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

For revenue agreements with multiple element arrangements, such as license and development agreements, entered into on or after January 1, 2011, the Company allocates revenue to each non-contingent element based on the relative selling price of each element. When applying the relative selling price method, the Company determines the selling price for each deliverable using VSOE of selling price or TPE of selling price. If neither exists the Company uses ESP for that deliverable. Revenue allocated is then recognized when the basic four revenue recognition criteria are met for each element. The collaboration and license agreements



entered into with Shire International GmbH, formerly Shire AG, (Shire) in January 2012 and Biogen Inc. (Biogen) in January 2014 were evaluated under these amended accounting standards.

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

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

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

During 2015 revenue related to Shire and Biogen represent 40% and 35%, respectively of total revenues. During 2014 revenues related to Shire and Biogen represented 57% and 28%, respectively of total revenues. During 2013, revenues related to Shire, Sigma-Aldrich Corporation (Sigma) and Dow AgroSciences LLC (DAS) represented 68%, 9% and 12%, respectively of total revenues. Receivables from collaborations are typically unsecured and are concentrated in the biopharmaceutical industry. Accordingly, we may be exposed to credit risk generally associated with biopharmaceutical companies or specific to our collaboration agreements. To date, we have not experienced any losses related to these receivables.

#### Research and Development Expenses

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

#### Stock-Based Compensation

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

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

### Indefinite-Lived Intangible Assets

As part of the Ceregene acquisition the Company recognized indefinite-lived intangible assets for in-process research and development and goodwill as further discussed below. ASC 350 and related updates require companies to test indefinite-lived intangible assets for impairment annually, and more frequently if indicators of impairment exist. ASC 350 includes an optional qualitative assessment for testing indefinite-lived intangible assets for impairment that permits companies to assess whether it is more likely than not (i.e., a likelihood of greater than 50%) that an indefinite-lived intangible asset is impaired. If a company concludes based on the qualitative assessment that it is not more likely than not that the fair value of an indefinite-lived intangible asset or, in the case of goodwill, that the fair value of the related reporting unit, is less than carrying value, it would not have to determine the asset's or reporting unit's fair value, as applicable.

## In-Process Research and Development

Intangible assets related to in-process research and development costs, or IPR&D, are considered to be indefinite-lived until the completion or abandonment of the associated research and development efforts. If and when development is complete, which generally occurs if and when regulatory approval to market a product is obtained, the associated assets would be deemed finite-lived and would then be amortized based on their respective estimated useful lives at that point in time. Prior to completion of the research and development efforts, the assets are considered indefinite-lived. During this period, the assets will not be amortized but will be tested for impairment on an annual basis and between annual tests if the Company becomes aware of any events occurring or changes in circumstances that would indicate a reduction in the fair value of the IPR&D projects below their respective carrying amounts. In the first quarter of 2015, the Company decided to discontinue the CERE-110 and CERE-120 clinical trial programs. As such, the probability of achieving projected revenues and cash flows associated with these programs were adversely affected. The Company did not believe the programs have an alternative future use for itself or other market participants. Accordingly, the Company recognized a \$1.9 million impairment charge related to these assets during the year ended December 31, 2015 and recorded to the research and development (R&D) expense line item in the consolidated statements of operations.

## Goodwill

Goodwill represents the excess of the consideration transferred over the estimated fair values of assets acquired and liabilities assumed in a business combination and is considered to be indefinite-lived. Goodwill is not amortized but is tested for impairment on an annual basis and between annual tests if the Company becomes aware of any events occurring or changes in circumstances that would indicate an impairment of goodwill has occurred. During the fourth quarter of 2015, the Company performed an assessment of the qualitative factors affecting the fair value of its reporting unit and concluded that it was not more likely than not that the fair value of its reporting unit was less than carrying value and that, as a result, it is not more likely than not that goodwill is impaired.

## Contingent Consideration Liability

Under the merger agreement with Ceregene, the Company may be required to make contingent earn-out payments if the Company grants a third-party license to develop and commercialize certain product candidates acquired from Ceregene, or if the Company commercializes any of these product candidates itself. These earn-out payments will become payable in the period they are earned. In accordance with ASC Topic 805, the Company determined the fair value of this liability for contingent consideration on the acquisition date using a probability-weighted discounted cash flow analysis. Future changes to the fair value of the contingent consideration will be determined each period and charged to expense in the "Changes in fair value of contingent liability" expense line item in the consolidated statements of operations under operating expenses. During the year ended December 31, 2015, the recognized amount of the liability for contingent consideration decreased by \$1.8 million due to the decrease in the probability of incurring potential future royalty payments associated with the impairment of IPR&D assets acquired from Ceregene.

## Income Taxes

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

## Net Loss Per Share

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

Because Sangamo is in a net loss position, diluted net loss per share excludes the effects of common stock equivalents consisting of options and restricted stock units, which are all anti-dilutive. All stock options and restricted stock units outstanding were excluded from the calculation of diluted net loss per share for all periods presented. Stock options and restricted stock units outstanding at the end of 2015, 2014 and 2013 were 9,008,185, 8,905,782, and 9,469,521, respectively.

#### Segments

The Company operates in one segment. Management uses one measure of profitability and does not segregate its business for internal reporting. As of December 31, 2015 and 2014, all of the Company's assets were maintained in the U.S. For the years ended December 31, 2015, 2014 and 2013, substantially all the Company's revenues and operating expenses were generated and incurred in the U.S.

## Recent Accounting Pronouncements

During 2015 the FASB issued ASU 2015-17 as part of their simplification initiative. The amendments to ASC 740 eliminate the requirement that an entity must separate deferred tax liabilities and assets between current and noncurrent amounts in a classified balance sheet. Rather, deferred taxes will be presented as noncurrent under the new standard. While the rule takes effect in 2017 for public companies, early adoption is permitted, including for December 31, 2015 year-end financial statements. The Company is electing to early adopt the pronouncement and include a prospective presentation in their year-end financial statements. By electing to file prospectively to all deferred tax liabilities and assets the Company has included a statement in Footnote 11 that prior periods were not retrospectively adjusted, the nature of and reason for the change in accounting principle.

In August 2014, the Financial Accounting Standards Board issued Accounting Standards Update (ASU) No. 2014-15, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern (ASU 2014-15). ASU 2014-15 requires management to evaluate whether there is substantial doubt about an entity's ability to continue as a going concern and to provide related footnote disclosures. In doing so, companies will have reduced diversity in the timing and content of footnote disclosures than under the current guidance. ASU 2014-15 is effective for the Company in the first quarter of 2016 with early adoption permitted. The Company does not believe the impact of adopting ASU 2014-15 on its consolidated financial statements will be material

In May 2014 the Financial Accounting Standards Board issued ASU 2014-09, Revenue from Contracts with Customers (ASU 2014-09). This standard outlines a single comprehensive model for entities to use in accounting for revenue arising from contracts with customers and supersedes most current revenue recognition guidance, including industry-specific guidance. The main principle of ASU 2014-09 is to recognize revenues when promised goods or services are transferred to customers in an amount that reflects the consideration that is expected to be received for those goods or services. ASU 2014-09 provides companies with two implementation methods: (i) apply the standard retrospectively to each prior reporting period presented (full retrospective application); or (ii) apply the standard retrospectively with the cumulative effect of initially applying the standard as an adjustment to the opening balance of retained earnings of the annual reporting period that includes the date of initial application (modified retrospective application). This guidance is effective for annual reporting periods beginning after December 15, 2017, including interim periods within that reporting period. The Company is currently in the process of evaluating the impact of the pending adoption of ASU 2014-09 on its consolidated financial statements.

## NOTE 2 –FAIR VALUE MEASUREMENT

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

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

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

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

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

	December 31, 2015			
	Fair Value Measurements			
	Total	Level 1	Level 2	Level 3
<b>Assets:</b>				
Cash equivalents:				
Money market funds	\$25,070	\$25,070	\$—	\$—
Commercial paper securities	2,000	2,000	—	—
U.S. government sponsored entity debt securities	38,867	38,867	—	—
Total	65,937	65,937	—	—
Marketable securities:				
Commercial paper securities	30,717	—	30,717	—
Corporate debt securities	17,263	—	17,263	—
U.S. government sponsored entity debt securities	91,538	—	91,538	—
Total	139,518	—	139,518	—
Total cash equivalents and marketable securities	\$205,455	\$65,937	\$139,518	\$—

	December 31, 2014			
	Fair Value Measurements			
	Total	Level 1	Level 2	Level 3
<b>Assets:</b>				
Cash equivalents:				
Money market funds	\$3,182	\$3,182	\$—	\$—
Total	3,182	3,182	—	—
Marketable securities:				
Commercial paper securities	33,748	—	33,748	—
Corporate debt securities	22,813	—	22,813	—
U.S. government sponsored entity debt securities	163,631	—	163,631	—
Total	220,192	—	220,192	—
Total cash equivalents and marketable securities	\$223,374	\$3,182	\$220,192	\$—
<b>Liabilities:</b>				
Contingent consideration liability	\$1,800	\$—	\$—	\$1,800
Total	\$1,800	\$—	\$—	\$1,800

## Investments

The Company generally classifies its marketable securities as Level 2. Instruments are classified as Level 2 when observable market prices for identical securities that are traded in less active markets are used. When observable market prices for identical securities are not available, such instruments are priced using benchmark curves, benchmarking of like securities, sector groupings, matrix pricing and valuation models. These valuation models are proprietary to the pricing providers or brokers and incorporate a number of inputs, including, listed in approximate order of priority: benchmark yields, reported trades, broker/dealer quotes, issuer spreads, two-sided markets, benchmark securities, bids, offers and reference data including market research publications. For certain security

types, additional inputs may be used, or some of the standard inputs may not be applicable. Evaluators may prioritize inputs differently on any given day for any security based on market conditions, and not all inputs listed are available for use in the evaluation process for each security evaluation on any given day.

#### Contingent Consideration Liability

In October 2013 the Company acquired Ceregene and recorded a liability for the estimated fair value of contingent consideration payments to former Ceregene stockholders, as outlined under the terms of the merger agreement with Ceregene. These contingent payments are owed if the Company grants a third-party license to develop and commercialize certain product candidates acquired from Ceregene, or if the Company commercializes any of such product candidates itself. The fair value of this liability is estimated using a probability-weighted discounted cash flow analysis. Such valuations require significant estimates and assumptions including but not limited to: determining the timing and estimated costs to complete the in-process projects, projecting regulatory approvals, estimating future cash flows and developing appropriate discount rates. The Company has classified this liability as Level 3.



Subsequent changes in the fair value of this contingent consideration liability are recorded to the research and development expense line item in the consolidated statements of operations as operating expenses. During the year ended December 31, 2015, the recognized amount of the liability for contingent consideration decreased by \$1.8 million due to the decrease in the probability of incurring potential future royalty payments associated with the impairment of IPR&D assets acquired from Ceregene (see Note 6).

The following sets forth the changes in the estimated fair value for our contingent consideration liability classified as Level 3 (in thousands):

Fair value as of December 31, 2013	\$ 1,570
Change in fair value	230
Fair value as of December 31, 2014	1,800
Change in fair value	(1,800)
Fair value as of December 31, 2015	\$—

### NOTE 3 – MARKETABLE SECURITIES

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

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized (Losses)	Estimated Fair Value
<b>December 31, 2015</b>				
Cash equivalents:				
Money market funds	\$ 25,070	\$ —	\$ —	\$ 25,070
Commercial paper securities	2,000	—	—	2,000
U.S. government sponsored entity debt securities	38,866	1	—	38,867
Total	65,936	1	—	65,937
Available-for-sale securities:				
Commercial paper securities	\$ 30,667	\$ 50	\$ —	\$ 30,717
Corporate debt securities	17,275	—	(12 )	17,263
U.S. government sponsored entity debt securities	91,562	—	(24 )	91,538
Total	139,504	50	(36 )	139,518
Total cash equivalents and available-for-sale securities	\$ 205,440	\$ 51	\$ (36 )	\$ 205,455
<b>December 31, 2014</b>				
Cash equivalents:				
Money market funds	\$ 3,182	\$ —	\$ —	\$ 3,182
Total	3,182	—	—	3,182
Available-for-sale securities:				
Commercial paper securities	\$ 33,715	\$ 33	\$ —	\$ 33,748
Corporate debt securities	22,831	—	(18 )	22,813
U.S. government sponsored entity debt securities	163,671	—	(40 )	163,631
Total	220,217	33	(58 )	220,192

Total cash equivalents and available-for-sale securities \$223,399 \$ 33 \$ (58 ) \$223,374

As of December 31, 2015, all of the Company's investments had maturity dates within two years. All of the Company's available-for-sale securities mature within the next twelve months of the date of the balance sheet. The Company had no material realized losses or other-than-temporary impairments of available-for-sale securities for the years ended December 31, 2015, 2014 and 2013. Sangamo has the intent and ability to hold the investment for a period of time sufficient to allow for any anticipated recovery in the market value. No investments were other-than-temporarily impaired.

## NOTE 4 – STOCK-BASED COMPENSATION

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

	Year Ended December 31,		
	2015	2014	2013
Research and development	\$6,444	\$5,064	\$3,204
General and administrative	5,286	4,136	2,942
Total stock-based compensation expense	\$11,730	\$9,200	\$6,146

As of December 31, 2015, total stock-based compensation expense related to unvested stock options to be recognized in future periods was \$18.3 million, which is expected to be expensed over a weighted-average period of 2.94 years. As of December 31, 2015, total stock-based compensation expense related to unvested RSUs to be recognized in future periods was \$8.1 million, which is expected to be expensed over a weighted-average period of 2.34 years. There was no capitalized stock-based employee compensation expense as of December 31, 2015.

## Valuation Assumptions

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

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

The weighted-average estimated fair value per share of options granted during 2015, 2014 and 2013 was \$5.72, \$8.16 and \$8.29, respectively based upon the assumptions used in the Black-Scholes valuation model. The assumptions used for estimating the fair value of the employee stock options are as follows:

	Year Ended December 31,		
	2015	2014	2013
Risk-free interest rate	1.46-1.58%	1.70%	1.50-1.88%
Expected life of option (in years)	5.25-5.38	5.33	5.36-5.38
Expected dividend yield of stock	0%	0	% 0
Expected volatility	0.66-0.67	0.69	0.88

Employees purchased approximately 128,181, 107,203, and 180,551 shares of common stock through the 2010 Purchase Plan at an average exercise price of \$7.10, \$7.92 and \$2.75 per share during 2015, 2014 and 2013, respectively.

The weighted-average estimated fair value of shares purchased under the Company's ESPP during 2015, 2014 and 2013 were \$4.42, \$3.25 and \$1.47, respectively based upon the assumptions used in the Black-Scholes valuation model. The weighted-average assumptions used for estimating the fair value of the ESPP purchase rights are as follows:

	Year Ended December 31,		
	2015	2014	2013
Risk-free interest rate	0.06-0.05%	0.30%	0.05-0.61%
Expected life of option (in years)	0.5-2.0	0.5-2.0	0.5-2.0
Expected dividend yield of stock	0%	0	% 0 %
Expected volatility	0.55-0.70	0.75	0.51-0.85

NOTE 5 – MAJOR CUSTOMERS, PARTNERSHIPS AND STRATEGIC ALLIANCES

Collaboration Agreements

Collaboration and License Agreement with Biogen, Inc. in Human Therapeutics

In January 2014 the Company entered into a Global Research, Development and Commercialization Collaboration and License Agreement (the “Biogen Agreement”) with Biogen, pursuant to which Sangamo and Biogen collaborate to discover, develop, seek

regulatory approval for and commercialize therapeutics based on Sangamo's zinc finger DNA-binding protein (ZFP) technology for hemoglobinopathies, including beta-thalassemia and sickle cell disease (SCD).

Under the Biogen Agreement, Sangamo and Biogen jointly conduct two research programs: the beta-thalassemia program and the SCD program. For the beta-thalassemia program, Sangamo is responsible for all discovery, research and development activities through the first human clinical trial for the first ZFP Therapeutic developed under the Biogen Agreement for the treatment of beta-thalassemia. For the SCD program, both parties are responsible for research and development activities through the submission of an Investigational New Drug (IND) application for ZFP Therapeutics intended to treat SCD. For both programs, Biogen is responsible for subsequent world-wide clinical development, manufacturing and commercialization of licensed products developed under the Biogen Agreement. At the end of the specified research terms for each program or under certain specified circumstances, Biogen retains the right to step in and take over any remaining activities of Sangamo. Furthermore, Sangamo has an option to co-promote in the United States any licensed product to treat beta-thalassemia and SCD developed under the Biogen Agreement, and Biogen agrees to compensate Sangamo for such co-promotion activities.

Sangamo received an upfront license fee of \$20.0 million upon entering into the Biogen Agreement. In addition, the Company will also be eligible to receive \$126.3 million in payments upon the achievement of specified research, regulatory, clinical development milestones, as well as \$167.5 million in payments upon the achievement of specified commercialization and sales milestones. Biogen reimburses Sangamo for agreed upon costs incurred in connection with research and development activities conducted by Sangamo. In addition, Sangamo is eligible to receive contingent payments upon the achievement of specified regulatory, clinical development, commercialization and sales milestones. The total amount of potential regulatory, clinical development, commercialization and sales contingent payments, assuming the achievement of all specified milestone events in the Biogen Agreement, is \$293.8 million, including Phase 1 contingent payments of \$7.5 million for each of the beta-thalassemia and SCD programs. In addition, if products are commercialized under the Biogen Agreement, Biogen will pay Sangamo incremental royalties for each licensed product that are a tiered double-digit percentage of annual net sales of such product. To date, no milestone payments have been received and no products have been approved and therefore no royalty fees have been earned under the Biogen Agreement.

All contingent payments under the Biogen Agreement, when earned, will be non-refundable and non-creditable. The Company has evaluated the contingent payments under the Biogen Agreement based on the authoritative guidance for research and development milestones and determined that certain of these payments meet the definition of a milestone and that all such milestones are evaluated to determine if they are considered substantive milestones. Milestones are considered substantive if they are related to events (i) that can be achieved based in whole or in part on either the Company's performance or on the occurrence of a specific outcome resulting from the Company's performance, (ii) for which there was substantive uncertainty at the date the agreement was entered into that the event would be achieved and (iii) that would result in additional payments being due to the Company. Accordingly, consideration received for the achievement of milestones that are determined to be substantive will be recognized as revenue in their entirety in the period when the milestones are achieved and collectability is reasonably assured. Revenue for the achievement of milestones that are not substantive will be recognized over the remaining period of the Biogen Agreement, assuming all other applicable revenue recognition criteria have been met.

Subject to the terms of the Biogen Agreement, Sangamo grants 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 Biogen Agreement. Sangamo also grants Biogen a non-exclusive, world-wide, royalty free, fully paid license, with the right to grant sublicenses, of Sangamo's interest in certain other intellectual property developed pursuant to the Biogen Agreement.

The Company has identified the deliverables within the arrangement as a license to the technology and on-going research services activities. The Company has concluded that the license is not a separate unit of accounting as it does

not have stand-alone value to Biogen apart from the research services to be performed pursuant to the Biogen Agreement. As a result, the Company will recognize revenue from the upfront payment on a straight-line basis over a forty-month estimated initial research term during which the Company will perform research services. As of December 31, 2015, the Company has deferred revenue of \$8.6 million related to the Biogen Agreement.

Revenues recognized under the Biogen Agreement for the years ended December 31, 2015 and 2014 are as follows (in thousands):

	Year ended December 31,	
	2015	2014
Revenue related to Biogen Collaboration:		
Recognition of upfront fee	\$6,176	\$5,313
Research services	7,769	7,751
Total	\$13,945	\$13,064

Related costs and expenses incurred under the Biogen agreement related to the beta-thalassemia project, which is co-funded with California Institute for Regenerative Medicine (CIRM), were \$6.5 million and \$5.2 million during the years ended December 31, 2015 and December 31, 2014, respectively. Related costs and expenses for other projects including SCD under the Biogen agreement were \$2.9 million and \$3.5 million during the years ended December 31, 2015 and December 31, 2014, respectively.

#### Collaboration and License Agreement with Shire International GmbH, formerly Shire AG, in Human Therapeutics and Diagnostics

In January 2012 the Company entered into a Collaboration and License Agreement with Shire (the "Shire Agreement"), pursuant to which the Company and Shire collaborate to research, develop and commercialize human therapeutics and diagnostics for monogenic diseases based on Sangamo's novel ZFP technology. This agreement was amended on September 1, 2015.

Under the original Shire Agreement, the Company and Shire agreed to develop potential human therapeutic or diagnostic products for seven gene targets. The initial four gene targets selected were blood clotting Factors VII, VIII, IX and X, and products developed for such initial gene targets will be used for treating or diagnosing hemophilia A and B. In June 2012 Shire selected a fifth gene target for the development of a ZFP Therapeutic for Huntington's disease. Shire had the right, subject to certain limitations, to designate two additional gene targets. Pursuant to the Shire Agreement, the Company granted Shire an exclusive, world-wide, royalty-bearing license, with the right to grant sublicenses, to use Sangamo's ZFP technology for the purpose of developing and commercializing human therapeutic and diagnostic products for the gene targets.

Under the terms of the Shire Agreement, the Company was responsible for all research activities through the submission of an IND or European Clinical Trial Application (CTA), while Shire was 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 reimbursed Sangamo for agreed upon internal and external program-related research costs. The Company received an upfront license fee of \$13.0 million upon entering into the Shire Agreement in 2012. In 2014 Sangamo recognized a \$1.0 million milestone payment related to the hemophilia program.

On September 1, 2015, the Shire Agreement was amended such that Shire agreed to return to Sangamo the exclusive, world-wide rights to gene targets for the development and commercialization of ZFP Therapeutics for hemophilia A and B. Shire retains the rights and will continue to develop a ZFP Therapeutic for Huntington's disease and a ZFP Therapeutic for one additional gene target yet to be named. Sangamo will provide certain target feasibility services, and upon Shire's request, certain research activities according to a research plan as agreed upon by both companies. Such research activities performed by Sangamo will be reimbursed by Shire. Shire's rights with respect to other targets contemplated in the original agreement revert to Sangamo. Under the revised agreement, each company is responsible for expenses associated with its own programs and will reimburse the other for any ongoing services provided. Shire was responsible for reimbursement of \$4.0 million related to obligations prior to the amendment date which is being recognized in revenue as expenses are incurred. During the 12 months ended December 31, 2015, \$3.4 million was incurred and recognized related to prior obligations. Sangamo has granted Shire a right of first negotiation to license the hemophilia A and B programs. Under the amended agreement, Shire does not have any milestone payment obligations with respect to the retained programs, but it is required to pay single digit percentage royalties to Sangamo, up to a specified maximum cap, on the commercial sales of ZFP therapeutic products from such programs. Under the Agreement, Sangamo has full control over, and full responsibility for the costs of, the hemophilia programs returned to us, subject to certain diligence obligations and Shire's right of first negotiation to obtain a license to such programs under certain circumstances. The Company is required to pay single digit percentage royalties to Shire, up to a specified maximum cap, on commercial sales of ZFP therapeutic products from such returned programs.

The Company has identified the deliverables within the amended arrangement as a license to the technology and on-going research services activities. The Company has concluded that the license is not a separate unit of accounting as it does not have stand-alone value to Shire apart from the research services to be performed pursuant to the Shire amendment. Sangamo continues to be responsible for research activities related to our licensed technology with Shire under the amendment. As a result, the Company will continue to recognize revenue from the upfront payment received upon entering into the original Shire agreement in 2012 on a straight-line basis over the six-year initial research term during which the Company expects to perform research services. As of December 31, 2015, the Company has deferred revenue of \$5.1 million related to the Shire Agreement.



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Revenues recognized under the Shire Agreement for the years ended December 31, 2015, 2014 and 2013, were as follows (in thousands):

	Year ended December 31,		
	2015	2014	2013
Revenue related to Shire Collaboration:			
Recognition of upfront fee	\$2,167	\$2,167	\$2,167
Recognition of milestone	—	1,000	—
Research services	13,584	22,765	14,286
Total	\$15,751	\$25,932	\$16,453

Related costs and expenses incurred under the Shire agreement were \$13.5 million, \$21.1 million and \$14.2 million during the twelve months ended December 31, 2015, 2014 and 2013, respectively.

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

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

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

Revenues recognized under the agreement with Sigma for the years ended December 31, 2015, 2014 and 2013, were as follows (in thousands):

	Year ended December 31,		
	2015	2014	2013
Revenue related to Sigma Collaboration:			
Royalty revenues	\$390	\$344	\$824
License fee and milestone revenues	4,463	448	1,351
Total	\$4,853	\$792	\$2,175

Related costs and expenses incurred under the Sigma agreement were \$0.4 million, \$0.1 million and \$0.2 million during 2015, 2014 and 2013, respectively

#### Agreement with Dow AgroSciences in Plant Agriculture

In October 2005 Sangamo entered into an exclusive commercial license with Dow AgroSciences, LLC (DAS). Under this agreement, Sangamo is providing DAS with access to its proprietary ZFP technology and the exclusive right to use the technology to modify the genomes or alter the nucleic acid or protein expression of plant cells, plants, or plant cell cultures. Sangamo has retained rights to use plants or plant-derived products to deliver ZFP transcription factors (ZFP TFs) or ZFP nucleases (ZFNs) into humans or animals for diagnostic, therapeutic or prophylactic purposes. The Company's agreement with DAS provided for an initial three year research term. In June 2008 DAS exercised its option under the agreement to obtain a commercial license to sell products incorporating or derived from plant cells generated using the Company's ZFP technology, including agricultural crops, industrial products and plant-derived biopharmaceuticals. The exercise of the option triggered a one-time commercial license fee of \$6.0 million, payment of the remaining \$2.3 million of the previously agreed upon \$4.0 million in research milestones, development and commercialization milestone payments for each product, and royalties on sales of products. Furthermore, DAS has the right to

sublicense Sangamo's ZFP technology to third parties for use in plant cells, plants, or plant cell cultures, and Sangamo will be entitled to 25% of any cash consideration received by DAS under such sublicenses. In December 2010 the Company amended its agreement with DAS to extend the period of reagent manufacturing services and research services through December 31, 2012.

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

Revenues under the agreement with DAS were \$3.0 million during 2015, 2014 and 2013, respectively. Related costs and expenses incurred under the agreement with DAS were \$0.0 million during 2015 and 2014, respectively and \$0.4 million during 2013.

#### Funding from Research Foundations

##### California Institute for Regenerative Medicine - HIV

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 its ZFN genome editing technology in hematopoietic stem progenitor cells (HSPCs). The four year grant provides matching funds to support evaluation of the Company's stem cell-based ZFP Therapeutic in a clinical trial in HIV-infected individuals conducted at City of Hope.

Revenues attributable to research and development performed under the CIRM grant agreements for HIV/AIDS were \$0.0 million, during 2015 and 2014, respectively and \$1.2 million during 2013. Related costs were \$1.7 million in 2015 and \$1.8 million in 2014 and 2013, respectively.

##### California Institute for Regenerative Medicine - Beta-Thalassemia

In May 2013 CIRM granted the Company a \$6.4 million Strategic Partnership Award to develop a potentially curative ZFP Therapeutic for beta-thalassemia based on the application of its ZFN genome editing technology in HSPCs. 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. The State of California has the right to receive, subject to the terms and conditions of the agreement between Sangamo and CIRM, payments from Sangamo, or its collaborators, from sales of a commercial product resulting from research and development efforts supported by the grant, in accordance with Title 17, California Code of Regulations, Section 100600.

In May 2015 Sangamo announced a consolidated development path for its beta-thalassemia and SCD programs using the "BCL11A Enhancer" target. Due to the switch to the BCL11A Enhancer strategy, CIRM and Sangamo terminated the Strategic Partnership Award as of June 30, 2015. Sangamo returned \$3.0 million in unused funds received from CIRM under the award during the three months ended September 30, 2015

Revenue attributable to research and development performed under the CIRM grant agreement for beta-thalassemia were \$1.2 million, \$1.4 million and \$0.1 million in 2015, 2014 and 2013, respectively. Related costs during 2015, 2014 and 2013 were \$1.2 million, \$1.1 million and \$0.4 million, respectively.

NOTE 6 – ACQUISITION OF CEREGENE

In August 2013, Sangamo acquired all the outstanding shares of Ceregene, a privately held biotechnology company focused on the development of AAV gene therapies. The acquired assets included 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, that were be used in the preparation and filing of IND applications for Sangamo's in vivo ZFP Therapeutics, particularly those that target the brain. The acquisition closed in October 2013 (the Closing Date).

The aggregate consideration transferred or transferable by Sangamo to former Ceregene stockholders at closing consisted of 100,000 shares of Sangamo common stock, with an approximate fair value of \$1.2 million and a contingent earn-out of \$1.5 million on the Closing Date. Sangamo was not required to make the contingent earn-out payments (the Earn-Out Payments) to the stockholders of Ceregene as Sangamo has not pursued the development of Ceregene's AAV gene therapies as the Company decided to discontinue CERE-110 and CERE-120 clinical trial programs.

Also on the Closing Date, Sangamo, Ceregene and certain of Ceregene's stockholders entered into an indemnity escrow agreement, pursuant to which \$0.3 million of Ceregene remaining cash was deposited in an escrow account and released subsequent to April 1, 2015 for the benefit of Sangamo to satisfy indemnity obligations of the stockholders under the Merger Agreement.

#### In-Process Research and Development

Intangible assets include IPR&D, which consists of Ceregene's two clinical product candidates, CERE-110 for the treatment of AD and CERE-120 for the treatment of Parkinson's disease. The Company determined that the combined Closing Date estimated fair values of CERE-110 and CERE-120 was \$1.9 million. The Company used an income approach, which is a measurement of the present value of the net economic benefit or cost expected to be derived from an asset or liability, to measure the fair value of these two product candidates. Under the income approach, an intangible asset's fair value is equal to the present value of the incremental after-tax cash flows (excess earnings) attributable solely to the intangible asset over its remaining useful life. In the first quarter of 2015, the Company decided to discontinue the CERE-110 and CERE-120 clinical trial programs. As such, the probability of achieving projected revenues and cash flows associated with these programs were adversely affected. The Company does not believe the programs have an alternative future use for itself or other market participants. Accordingly, during the year ended December 31, 2015, the Company recognized a \$1.9 million impairment charge related to these assets

#### Goodwill

The excess of the consideration transferred over the fair values assigned to the assets acquired and liabilities assumed was \$1.6 million, which represents the goodwill resulting from the acquisition. Goodwill represents benefits that Sangamo believes will result from combining its operations with the operations of Ceregene and any intangible assets that do not qualify for separate recognition, as well as any future, yet unidentified products. The Company tests goodwill for impairment on an annual basis or sooner, if deemed necessary. There have been no changes to the assets acquired or liabilities assumed, including goodwill, since the Closing Date

#### Liability for Contingent Consideration

In addition the Company was required to make contingent Earn-Out Payments in the future if the Company grants a third-party license to develop and commercialize products based on the technology acquired from Ceregene (the "Earn-out Products") or if the Company commercializes any Earn-Out Products itself. The fair value of the liability for the contingent consideration recognized on the Closing Date was \$1.5 million. The Company determined the fair value of the liability for the contingent consideration based on a probability-weighted discounted cash flow analysis. During the year ended December 31, 2015, the recognized amount of the liability for contingent consideration decreased by \$1.8 million due to the decrease in the probability of incurring potential future royalty payments associated with the impairment of the in-process research and development (IPR&D) assets acquired from Ceregene (see Note 7).

#### NOTE 7 – INTANGIBLE ASSETS

Intangible assets for IPR&D consist of two clinical product candidates from our acquisition of Ceregene. IPR&D is an intangible asset classified as indefinite-lived until the completion or abandonment of the associated research and development effort, and will be amortized over an estimated useful life to be determined at the date the project is completed. If the project is abandoned, the IPR&D will be expensed at the time such determination is made.

The carrying values of these intangibles assets are as follows (in thousands):

	Year ended December 31, 201 <del>3</del> 014
CERE-110 for the treatment of Alzheimer's disease	\$—\$1,640
CERE-120 for the treatment of Parkinson's disease	— 230
Total identifiable intangible assets	\$—\$1,870

In the first quarter of 2015, the Company decided to discontinue the CERE-110 and CERE-120 clinical trial programs. As such, the probability of achieving projected revenues and cash flows associated with these programs were adversely affected. The Company does not believe the programs have an alternative future use for itself or other market participants. Accordingly, during the year ended December 31, 2015, the Company recognized a \$1.9 million impairment charge related to these assets. The impairment is recorded in research and development expense in the accompanying condensed consolidated statements of operations.

## NOTE 8 – PROPERTY AND EQUIPMENT

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

	December 31,	
	2015	2014
Laboratory equipment	\$5,801	\$3,665
Furniture and fixtures	652	550
Leasehold improvements	1,309	1,163
	7,762	5,378
Less accumulated depreciation and amortization	(4,846)	(3,899)
	\$2,916	\$1,479

Depreciation and amortization expense was \$1.0 million in 2015, \$0.5 million in 2014 and \$0.6 million for 2013.

## NOTE 9 – COMMITMENTS AND CONTINGENCIES

Sangamo occupies office and laboratory space under operating leases in Richmond, California. In August 2013 Sangamo amended its lease agreement wherein the lease was extended through August 2019. We have two additional properties located in Richmond, CA, including a lease to occupy approximately 7,700 square feet of research and office space that expires in January 2018 and a build-to-suit lease to occupy approximately 41,400 square feet of space that expires five years after substantial construction is completed. The rent expense was \$0.9 million in 2015, \$0.7 million in 2014, and \$0.7 million in 2013. Future minimum payments under contractual obligations at December 31, 2015 consist of the following (in thousands):

Fiscal Year:	Operating Leases
2016	\$ 1,015
2017	1,388
2018	1,222
2019	984
2020	503
Thereafter	385
Total minimum payments	\$ 5,497

Contingencies

Sangamo is not 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

#### NOTE 10 – STOCKHOLDERS’ EQUITY

##### Preferred Stock

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

##### Common Stock

On March 25, 2014, Sangamo completed an underwritten public offering of its common stock, in which the Company sold an aggregate of 4,444,444 shares of its common stock at a public offering price of \$22.50 per share. The net proceeds to Sangamo from the sale of shares in this offering, after deducting underwriting discounts and commissions and other offering expenses, were approximately \$93.8 million. On September 23, 2013, Sangamo completed an underwritten public offering of its common stock, in which the Company sold an aggregate of 7,015,000 shares of its common stock, including 915,000 shares issued to the Underwriters pursuant to a 30-day overallotment option, at a public offering price of \$10.58 per share. The net proceeds to Sangamo from the sale of shares in this offering, after deducting underwriting discounts and commissions and other offering expenses, were approximately \$69.5 million.



## Stock Incentive Plan

In April 2013 Sangamo's board of directors adopted, subject to stockholder approval, the Company's 2013 Stock Incentive Plan (the 2013 Plan) as the successor to the Company's 2004 Stock Incentive Plan (the 2004 Plan). At the Annual Meeting of Stockholders held on June 12, 2013, the 2013 Plan was approved by the Company's stockholders and became effective. In connection with the approval by stockholders of the 2013 Plan, outstanding awards under the 2004 Plan were transferred to the 2013 Plan. The 2004 Plan was terminated and no further awards will be made pursuant to the 2004 Plan.

Under the 2013 Plan, the exercise price per share of options granted will generally not be less than 100 percent of the fair value per share of common stock on the grant date, and the option term will not exceed ten years. If the person to whom the option is granted is a 10 percent stockholder, and the option granted qualifies as an Incentive Stock Option Grant, then the exercise price per share will not be less than 110 percent of the fair value per share of common stock on the grant date, and the option term will not exceed five years. Options granted under the 2013 Plan generally vest over four years at a rate of 25 percent one year from the grant date and one thirty-sixth per month thereafter and expire ten years after the grant, or earlier upon employment termination. Certain options previously granted under the 2004 Plan to the Company's non-employee directors are structured so that they may be exercised prior to vesting, with the related shares subject to Sangamo's right to repurchase any shares that have not vested pursuant to the vesting schedule in effect for such award at the exercise price paid if the option holder's board service terminates. Approximately 14.1 million shares were initially reserved for issuance under the 2013 Plan, including 9.7 million shares of common stock subject to outstanding awards previously granted under the 2004 Plan that were transferred to the 2013 Plan, and an additional 4.4 million shares of common stock.

The number of shares of common stock reserved for issuance under the 2013 Plan will be reduced: (i) on a 1-for-1 basis for each share of common stock subject to a stock option or stock appreciation right granted under the plan, (ii) on a 1-for-1 basis for each share of common stock issued pursuant to a full value award granted under the plan prior to the plan effective date, and (iii) by a fixed ratio of 1.33 shares of common stock for each share of common stock issued pursuant to a full-value award granted under the plan on or after the plan effective date.

Shares subject to any outstanding options or other awards under the 2013 Plan that expire or otherwise terminate prior to the issuance of the shares subject to those options or awards will be available for subsequent issuance under the 2013 Plan. Any unvested shares issued under the 2013 Plan that the Company subsequently purchases, pursuant to repurchase rights under the 2013 Plan, will be added back to the number of shares reserved for issuance under the 2013 Plan on a 1-for-1 basis or a 1.33-for-1 basis (depending on the ratio at which the share reserve was debited for the original award) and will accordingly be available for subsequent issuance in accordance with the terms of the plan.

In June 2015 Sangamo's stockholders were asked to vote to approve the amendment and restatement of our 2013 Stock Incentive Plan in order to increase the number of shares in our common stock reserved for issuance over the term of the 2013 Plan by 5,300,000 shares. At the Annual Meeting of Stockholders held on June 22, 2015, the amendment and restatement of our 2013 Stock Incentive Plan was approved by the Company's stockholders and became effective.

## Employee Stock Purchase Plan

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

## Stock Option Activity

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

	Number of Shares	Weighted- Average Exercise per Share Price	Weighted Average Remaining Contractual Term (In years)	Aggregate Intrinsic Value (In thousands)
Options outstanding at December 31, 2014	8,006,380	\$ 8.90		
Options granted	1,628,402	\$ 9.95		
Options exercised	(949,252 )	\$ 6.21		
Options canceled	(508,162 )	\$ 11.91		
Options outstanding at December 31, 2015	8,177,368	\$ 9.24	6.56	\$ 14,074
Options vested and expected to vest at December 31, 2015	7,752,480	\$ 9.15	6.40	\$ 14,042
Options exercisable at December 31, 2015	4,950,680	\$ 7.97	4.92	\$ 13,119

Newly created shares are issued upon exercise of options. There were no shares subject to Sangamo's right of repurchase as of December 31, 2015. The intrinsic value of options exercised was \$6.4 million, \$20.4 million and \$8.9 million during 2015, 2014 and 2013, respectively.

At December 31, 2015, the aggregate intrinsic values of the outstanding and exercisable options were \$14.1 million and \$13.1 million, respectively. The aggregate intrinsic value of options vested and expected to vest as of December 31, 2015, 2014 and 2013 was \$14.0 million, \$49.4 million and \$54.9 million, respectively. The aggregate estimated fair value of stock options granted to employees that vested during the years ended December 31, 2015, 2014 and 2013 was \$1.4 million, \$0.5 million and \$0.5 million, respectively.

The following table summarizes information with respect to stock options outstanding at December 31, 2015:

Range of Exercise Price	Options Outstanding and Exercisable Number of Shares of common stock subject to options	Weighted Average Remaining Contractual Life (In years)	Options Exercisable Number of Shares of common stock subject to options	Weighted Average Exercise Price
\$2.55 – \$5.35	1,486,569	3.72	1,484,693	\$ 4.35
\$5.41 – \$5.41	826,984	6.79	598,837	\$ 5.41
\$5.42 – \$5.94	1,001,858	5.07	1,001,858	\$ 5.76
\$6.05 – \$9.40	308,171	6.16	193,003	\$ 7.00
\$9.41 – \$9.41	1,229,402	9.94	—	\$ —

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\$9.45 – \$12.12	967,099	7.82	472,328	\$ 11.87
\$12.23 – \$13.99	702,135	4.31	521,809	\$ 13.83
\$14.07 – \$14.07	1,019,650	8.91	258,665	\$ 14.07
\$14.15 – \$19.80	629,500	5.66	416,862	\$ 14.69
\$23.02 – \$23.02	6,000	8.21	2,625	\$ 23.02
	8,177,368	6.56	4,950,680	\$ 7.97

Restricted Stock Units

During 2015, 2014 and 2013, the Company awarded 446,000, 488,000, and 392,500 Restricted Stock Units (RSUs), respectively. The RSUs awarded in 2015, 2014 and 2013 had an average grant date fair value of \$9.45, \$14.05 and \$12.12, respectively. These awards will vest as follows: one-third of the award will vest in a series of three successive equal annual installments. The aggregate value of shares vested during 2015, 2014 and 2013 was \$3.5 million, \$9.1 million and \$4.1 million, respectively.

A summary of Sangamo's RSU activity is as follows:

	Number of Shares	Weighted Average Remaining Contractual Term (In years)	Aggregate Intrinsic Value (In thousands)
RSUs outstanding at December 31, 2014	899,402		
RSUs awarded	446,000		
RSUs released	(387,588)		
RSUs forfeited	(126,997)		
RSUs outstanding at December 31, 2015	830,817	1.63	\$ 7,585
RSUs vested and expected to vest at December 31, 2015	718,502	1.61	\$ 6,560

RSUs that vested in 2015, 2014 and 2013 were net-share settled such that the Company withheld shares with value equivalent to the employees' minimum statutory obligation for the applicable income and other employment taxes, and remitted the cash to the appropriate taxing authorities. The total shares withheld were approximately 172,807, 309,102, and 167,138 for 2015, 2014 and 2013, respectively and were based on the value of the RSUs on their respective issuance dates as determined by the Company's closing stock price. Total payments for the employees' tax obligations to taxing authorities were \$1.5 million, \$4.6 million and \$2.0 million in 2015, 2014 and 2013, respectively and are reflected as a financing activity within the consolidated statements of cash flows. These net-share settlements had the effect of share repurchases by the Company as they reduced and retired the number of shares that would have otherwise been issued as a result of the vesting and did not represent an expense to the Company.

As of December 31, 2015, there were 4,508,405 shares reserved for future awards under the Company's 2013 Plan and 1,292,379 shares of common stock reserved for future issuance under the Purchase Plan.

#### NOTE 11 – INCOME TAXES

The benefit for income taxes consisted of the following (in thousands):

	Year ended December 31,		
	2015	2014	2013
Benefit for income taxes:			
Current:			
Federal	\$—	\$ —	\$ —
State	—	—	—
Subtotal	—	—	—
Deferred:			
Federal	\$(5,563)	\$ —	\$ —

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State	(159 )	—	—
Subtotal	(5,722)		
Income tax benefit	\$(5,722)	\$ —	\$ —

The difference between the benefit for income taxes and the amount computed by applying the federal statutory income tax rate (34%) to loss before taxes is explained as follows (in thousands):

	Year ended December 31,		
	2015	2014	2013
Tax at federal statutory rate	\$(15,785)	\$(8,982)	\$(9,052)
State taxes, net	4,840	(822 )	(4,004 )
Non-deductible stock compensation	1,085	(148 )	(598 )
Research credits	(814 )	(320 )	(280 )
Change in valuation allowance	5,043	9,778	14,261
Other	(91 )	494	(327 )
Income tax benefit	\$(5,722 )	\$—	\$—

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

	December 31,	
	2015	2014
<b>Assets:</b>		
Deferred tax assets:		
Net operating loss carryforwards	\$93,824	\$90,921
Research and development tax credit carryforwards	9,979	8,646
Stock-based compensation	6,853	8,171
Deferred revenue	4,479	2,690
Other	2,807	2,471
Total deferred tax asset	117,942	112,899
Valuation allowance	(117,942)	(112,899)
Net deferred tax assets	\$—	\$—
<b>Liabilities:</b>		
Net deferred tax liability related to intangible assets	—	(748 )
Total deferred tax liability	\$—	\$(748 )

In October 2013, we acquired Ceregene. The Company recorded goodwill and intangible assets as part of accounting for the acquisition of Ceregene. A portion of the intangible assets acquired were for the use in a particular research and development project IPR&D and are considered indefinite-lived assets with no tax basis. In 2015, the Company impaired these intangible assets and reversed the corresponding deferred tax liability.

In 2015 the Company received a \$14.5 million disgorgement settlement that was recognized as additional paid-in capital. The disgorgement settlement was recognized net of taxes of \$9.5 million, which resulted in an income tax benefit of \$5.0 million being recognized in the accompanying consolidated statements of operations for the year ended December 31, 2015.

The changes in the fair value of the unrealized gain/loss on securities investment are recorded as a component of accumulated other comprehensive income, net of a provision for income taxes.

Realization of deferred tax assets is dependent upon future earnings, if any, the timing and amount of which are uncertain. Accordingly, the net deferred tax assets have been fully offset by a valuation allowance. The valuation allowance increased by \$5.0 million, \$9.8 million and \$14.9 million for the years ended December 31, 2015, 2014 and 2013, respectively. As of December 31, 2015, Sangamo had net operating loss carryforwards for federal and state income tax purposes of approximately \$351.3 million and \$264.3 million, respectively. If not utilized, the net federal and state operating loss carryforwards will start to expire in 2018 and 2016 respectively. The Company also has federal and state research tax credit carryforwards of \$7.8 million and \$8.2 million, respectively. The federal research credits will begin to expire in 2018 while the state research credits have no expiration date. Utilization of the Company's net operating loss carryforwards and research tax credit carryforwards may be subject to substantial annual limitations due to the ownership change limitations provided by the Internal Revenue Code and similar state provisions. The annual limitation could result in the expiration of the net operating loss carryforwards and research tax credit carryforwards before utilization.

The Company files federal and state income tax returns with varying statutes of limitations. The tax years from 2000 forward remain open to examination due to the carryover of net operating losses or tax credits. The Company also files a UK income tax return, and the tax years from 2008 and thereafter remain open to examination.

The Company's practice is to recognize interest and/or penalties related to income tax matters in income tax expense. As of December 31, 2015, the Company had no accrued interest and/or penalties. The unrecognized tax benefits may change during the next year for items that arise in the ordinary course of business. In the event that any unrecognized tax benefits are recognized, the effective tax rate will not be affected.

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

	December 31,		
	2015	2014	2013
Beginning balance	\$3,438	\$3,182	\$2,735
Additions based on tax positions related to the current year	557	228	294
Additions for tax positions of prior years	4,335	28	153
Reductions for tax positions of prior years	—	—	—
Ending balance	\$8,330	\$3,438	\$3,182

#### NOTE 12 – ACCOUNTS PAYABLE AND ACCRUED LIABILITIES

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

	December 31,	
	2015	2014
Accounts payable	\$3,905	\$5,525
Accrued research and development expenses	3,624	2,435
Accrued professional fees	356	531
Deferred rent	196	129
Other	148	84
Total accounts payable and accrued liabilities	\$8,229	\$8,704

#### NOTE 13 – EMPLOYEE BENEFIT PLAN

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

The Company matched contributions by employees equal to 50% of the first 6% of employee contributions up to a limit of \$3,000 in 2015 and \$2,000 in 2014. Matching funds are fully vested when contributed. Contributions to the Sangamo 401(k) Plan by the Company were \$0.3 million, \$0.2 million, and \$0.1 million for years ended December 31, 2015, 2014 and 2013, respectively.

#### NOTE 14 – QUARTERLY FINANCIAL DATA (UNAUDITED)



The following table sets forth certain unaudited quarterly financial data for the eight quarters ended December 31, 2015. The unaudited information set forth below has been prepared on the same basis as the audited information and includes all adjustments necessary to present fairly the information set forth herein. The operating results for any quarter are not indicative of results for any future period. All data is in thousands except per common share data.

	2015				2014			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Revenues	\$13,491	\$8,358	\$8,569	\$9,121	\$8,116	\$10,385	\$12,417	\$14,952
Expenses	\$19,712	\$20,635	\$21,254	\$24,794	\$15,727	\$17,432	\$20,071	\$19,421
Net loss	\$(5,319)	\$(12,126)	\$(9,245)	\$(14,013)	\$(7,572)	\$(6,981)	\$(7,545)	\$(4,319)
Net loss per share	\$(0.08)	\$(0.17)	\$(0.13)	\$(0.20)	\$(0.12)	\$(0.10)	\$(0.11)	\$(0.06)

#### NOTE 15 – BUILD-TO-SUIT LEASE

In December 2015 the Company entered into a long-term property lease which includes construction by the lessor of a building with approximately 41,400 square feet of space, in Richmond, California. The lease agreement expires five years after substantial completion of the building, which is estimated to be completed in late 2016. The Company has two options to extend the lease term for up to a combined additional ten years.

The Company is deemed, for accounting purposes only, to be the owner of the entire project including the building shell, even though it is not the legal owner. In connection with the Company's accounting for this transaction, the Company will capitalize costs of construction as a build-to-suit property within property and equipment, net, and recognize a corresponding build-to-suit lease obligation for the same amount. As of December 31, 2015 no costs were capitalized or liabilities recognized related to this lease.

Upon construction a portion of the monthly lease payment will be allocated to land rent and recorded as an operating lease expense and the non-interest portion of the amortized lease payments to the landlord related to the rent of the building will be applied to reduce the build-to-suit lease obligation.

#### NOTE 16 – CLAIMS SETTLEMENT

In September 2015 the Company received \$14.5 million as a settlement with certain institutional investors that were beneficial owners of Sangamo's common stock related to the disgorgement of short-swing profits pursuant to Section 16(b) of the Securities Exchange Act of 1934, as amended. The settlement of \$9.5 million, net of a \$5.0 million income tax benefit and certain expenses, was recognized as additional paid-in capital.

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

None.

ITEM 9A – CONTROLS AND PROCEDURES

(I) Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures to ensure that information we are required to disclose in reports that we file or submit under the Securities Exchange Act of 1934, as amended (Exchange Act) is recorded, processed, summarized and reported within the time periods specified in Securities and Exchange Commission's (SEC) rules and forms. Our management evaluated, with the participation of our chief executive officer (CEO) and our chief financial officer (CFO), the effectiveness of our disclosure controls and procedures, as such term is defined under Rule 13a-15(e) under the Exchange Act. Based on that evaluation, our CEO and CFO concluded that our disclosure controls and procedures were effective, at a reasonable assurance level, as of December 31, 2015.

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

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

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

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

Under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on the framework set forth in the "Internal Control—Integrated Framework" issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework). Based on our evaluation under the framework set forth in "Internal Control—Integrated Framework," our management concluded that our internal control

over financial reporting was effective as of December 31, 2015. The effectiveness of our internal control over financial reporting as of December 31, 2015 has been audited by Ernst & Young LLP, an independent registered public accounting firm, as stated in their report which is included herein.

There have been no significant changes in our internal control over financial reporting that have materially affected, or are reasonably likely to materially affect internal control over financial reporting during the fiscal quarter ended December 31, 2015.

(III) Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders

Sangamo BioSciences, Inc.

We have audited Sangamo BioSciences, Inc.'s internal control over financial reporting as of December 31, 2015, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). Sangamo BioSciences, Inc.'s management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the company's internal control over financial reporting based on our audit.

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

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

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

In our opinion, Sangamo BioSciences, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2015, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of Sangamo BioSciences, Inc. as of December 31, 2015 and 2014, 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, 2015 of Sangamo BioSciences, Inc. and our report dated February 18, 2016 expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP

Redwood City, California

February 18, 2016

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ITEM 9B – OTHER INFORMATION

None

PART III

Certain information required by Part III is omitted from this Report on Form 10-K since we intend to file our definitive Proxy Statement for our next Annual Meeting of Stockholders, pursuant to Regulation 14A of the Securities Exchange Act of 1934, as amended (the 2016 Proxy Statement), no later than April 30, 2016, and certain information to be included in the 2016 Proxy Statement is incorporated herein by reference.

ITEM 10 – DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this item concerning our directors, executive officers, Section 16 compliance and corporate governance matters is incorporated by reference to the information set forth in the sections titled “Election of Directors,” “Management,” and “Section 16(a) Beneficial Ownership Reporting Compliance” in our 2016 Proxy Statement.

ITEM 11 – EXECUTIVE COMPENSATION

The information required by this item regarding executive compensation is incorporated by reference to the information set forth in the sections titled “Executive Compensation” in our 2016 Proxy Statement.

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

The information required by this item regarding security ownership of certain beneficial owners and management is incorporated by reference to the information set forth in the section titled “Security Ownership of Certain Beneficial Owners and Management” and “Equity Compensation Plans” in our 2016 Proxy Statement.

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

The information required by this item regarding certain relationships and related transactions is incorporated by reference to the information set forth in the section titled “Certain Relationships and Related Transactions” in our 2016 Proxy Statement.

ITEM 14 – PRINCIPAL ACCOUNTING FEES AND SERVICES

The information required by this item regarding principal accounting fees and services is incorporated by reference to the information set forth in the section titled “Principal Accounting Fees and Services” in our 2016 Proxy Statement.

PART IV

ITEM 15 – EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

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

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



## SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, on February 18, 2016.

SANGAMO BIOSCIENCES, INC.

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

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

Signature	Title	Date
/ S / EDWARD O. LANPHIER II Edward O. Lanphier II	President, Chief Executive Officer and Director (Principal Executive Officer)	February 18, 2016
/ S / H. WARD WOLFF H. Ward Wolff	Executive Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)	February 18, 2016
/ S / WILLIAM R. RINGO William R. Ringo	Director and Chairman of the Board	February 18, 2016
/ S / PAUL B. CLEVELAND Paul B. Cleveland	Director	February 18, 2016
/ S / STEPHEN G. DILLY, M.B.B.S, PH.D Stephen G. Dilly, M.B.B.S, Ph.D	Director	February 18, 2016
/ S / JOHN W. LARSON John W. Larson	Director	February 18, 2016
/ S / STEVEN J. MENTO, PH.D Steven J. Mento, Ph.D	Director	February 18, 2016
/ S / H. Stewart Parker H. Stewart Parker	Director	February 18, 2016
/ S / SAIRA RAMASASTRY Saira Ramasastry	Director	February 18, 2016



INDEX TO EXHIBITS

Exhibit Number	Description of Document
3.1	Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Company's Registration Statement on Form S-1/A (Registration No. 333-30134) filed April 4, 2000).
3.2	Amended and Restated Bylaws (incorporated by reference to Exhibit 3.2 to the Company's Registration Statement on Form S-1/A (Registration No. 333-30134) filed April 4, 2000).
3.3	Certificate of Amendment of Seventh Amended and Restated Certificate of Incorporation of Sangamo BioSciences, Inc. (incorporated by reference to Exhibit 3.1 to the Company's Form 8-K, filed April 22, 2014).
3.4	Second Amended and Restated Bylaws (incorporated by reference to Exhibit 3.1 to the Company's Form 10-Q, filed October 28, 2014).
4.1	Form of Specimen Common Stock Certificate (incorporated by reference to Exhibit 4.1 to the Company's Registration Statement on Form S-1/A (Registration No. 333-30134) filed April 4, 2000).
4.2	Form of Senior Debt Indenture (incorporated by reference to Exhibit 4.10 to the Company's Registration Statement on Form S-3 (Registration No. 333-194126) filed February 25, 2014).
4.3	Form of Subordinated Debt Indenture (incorporated by reference to Exhibit 4.12 to the Company's Registration Statement on Form S-3 (Registration No. 333-194126) filed February 25, 2014).
10.1(+)	2000 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.2 to the Company's Registration Statement on Form S-1/A (Registration No. 333-30134) filed February 24, 2000).
10.2	Form of Indemnification Agreement (incorporated by reference to Exhibit 10.24 to the Company's Quarterly Report on Form 10-Q filed August 6, 2015).
10.3	Sublicense Agreement, by and between Sangamo and Johnson & Johnson, dated May 9, 1996 (incorporated by reference to Exhibit 10.3 to the Company's Annual Report on Form 10-K/A filed April 22, 2010).
10.4	Patent License Agreement between Sangamo and Massachusetts Institute of Technology, dated May 9, 1996, as amended by the First Amendment, dated December 10, 1997 (incorporated by reference to Exhibit 10.4 to the Company's Annual Report on Form 10-K/A filed April 22, 2010).
10.5	License Agreement between Sangamo and the Johns Hopkins University, dated June 25, 1995, as amended by Amendment No. 1, dated July 16, 1998 (incorporated by reference to Exhibit 10.5 to the Company's Annual Report on Form 10-K/A filed April 22, 2010).
10.6	Triple Net Laboratory Lease, between Sangamo and Point Richmond R&D Associates II, LLC, dated May 23, 1997 (incorporated by reference to Sangamo's Registration Statement on Form S-1 (Reg. No. 333-30314), as amended).
10.7(+)	

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Employment Agreement, between Sangamo and Edward O. Lanphier II, dated June 1, 1997 (incorporated by reference to Exhibit 10.15 to the Company's Registration Statement on Form S-1/A (Registration No. 333-30134) filed March 14, 2000).

- 10.8† Second Amendment to Patent License Agreement between Sangamo and Massachusetts Institute of Technology, dated December 2, 1998 (incorporated by reference to Exhibit 10.8 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
- 10.9 Amendment No. 2 to License Agreement between Sangamo and the Johns Hopkins University, effective as of July 26, 1999 (incorporated by reference to Exhibit 10.9 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
- 10.10† Third Amendment to Patent License Agreement between Sangamo and Massachusetts Institute of Technology, dated September 1, 1999 (incorporated by reference to Exhibit 10.10 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
- 10.11 Fourth Amendment to Patent License Agreement between Sangamo and Massachusetts Institute of Technology, effective as of February 10, 2000 (incorporated by reference to Exhibit 10.11 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
- 10.12 Amendment No. 3 to License Agreement between Sangamo and the Johns Hopkins University, effective as of March 10, 2000 (incorporated by reference to Exhibit 10.12 to the Company's Annual Report on Form 10-K, filed March 5, 2010).

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Exhibit

Number Description of Document

- 10.13 License Agreement by and between The Scripps Research Institute and Sangamo, dated March 14, 2000 (incorporated by reference to Exhibit 10.13 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
- 10.14† Fifth Amendment to Patent License Agreement between Sangamo and Massachusetts Institute of Technology, effective as of December 15, 2000 (incorporated by reference to Exhibit 10.14 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
- 10.15 First Amendment to Triple Net Laboratory Lease, between Sangamo and Point Richmond R&D Associates II, LLC, dated March 12, 2004 (incorporated by reference to Sangamo's Annual Report on Form 10-K for the year ended December 31, 2004).
- 10.16† Sixth Amendment to Patent License Agreement between Sangamo and Massachusetts Institute of Technology, dated September 1, 2005 (incorporated by reference to Exhibit 10.17 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
- 10.17† Research and Commercial Option License Agreement, dated October 5, 2005, between Sangamo and Dow AgroSciences LLC (incorporated by reference to Exhibit 10.23 to the Company's Annual Report on Form 10-K, filed March 16, 2006).
- 10.18† Research, Development and Commercialization Agreement dated October 24, 2006 between Sangamo and Juvenile Diabetes Research Foundation International (incorporated by reference to Exhibit 10.19 to the Company's Annual Report on Form 10-K, filed March 1, 2007).
- 10.19† Seventh Amendment to Patent License Agreement between Sangamo and Massachusetts Institute of Technology, dated October 27, 2006 (incorporated by reference to Exhibit 10.20 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
- 10.20 First Amendment of Research and Commercial Option License Agreement between Sangamo and Dow AgroSciences LLC, dated November 7, 2006 (incorporated by reference to Exhibit 10.21 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
- 10.21 Eighth Amendment to Patent License Agreement between Sangamo and Massachusetts Institute of Technology, dated February 1, 2007 (incorporated by reference to Exhibit 10.23 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
- 10.22† Research and License Agreement between Sangamo and Genentech, Inc., dated April 27, 2007 (incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q, filed August 9, 2007).
- 10.23† Amendment No. 4 to License Agreement between Sangamo and the Johns Hopkins University, effective as of May 21, 2007 (incorporated by reference to Exhibit 10.25 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
- 10.24† License Agreement between Sangamo and Sigma-Aldrich Corporation, dated July 10, 2007 (incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q, filed November 1, 2007).
- 10.25 First Amendment of the License Agreement between Sigma-Aldrich Corporation and Sangamo, dated November 9, 2007 (incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed on November 6, 2009).

- 10.26† Letter Agreement between Sangamo and Sigma-Aldrich Corporation, dated February 25, 2008 (incorporated by reference to Exhibit 10.2 to the Company's Form 10-Q filed on May 9, 2008).
- 10.27† Second Research and License Agreement between Sangamo and Genentech, Inc., dated February 27, 2008 (incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed on May 9, 2008).
- 10.29† License Agreement between Sangamo and Open Monoclonal Technology, Inc., dated April 2, 2008 (incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed on August 7, 2008).
- 10.29 Amendment to License Agreement by and between The Scripps Research Institute and Sangamo, dated April 29, 2008 (incorporated by reference to Exhibit 10.32 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
- 10.30† Research and License Agreement between Sangamo and F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc., dated July 2, 2008 (incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed on November 4, 2008).
- 10.31† Letter Agreement between Sangamo and Sigma-Aldrich Corporation, dated July 2, 2008 (incorporated by reference to Exhibit 10.2 to the Company's Form 10-Q filed on November 4, 2008).
- 10.32† License Agreement between Sangamo and Pfizer Inc., dated December 19, 2008 (incorporated by reference to Exhibit 10.25 to the Company's Annual Report on Form 10-K, filed March 3, 2009).

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Exhibit Number	Description of Document
10.33(+)	Amended and Restated Employment Agreement between Sangamo and H. Ward Wolff, dated December 31, 2008 (incorporated by reference to Exhibit 10.26 to the Company's Annual Report on Form 10-K, filed March 3, 2009).
10.34(+)	First Amendment to Employment Agreement between Sangamo and Edward O. Lanphier, dated December 31, 2008 (incorporated by reference to Exhibit 10.27 to the Company's Annual Report on Form 10-K, filed March 3, 2009).
10.35†	Second Amendment of Research and Commercial Option License Agreement between Sangamo and Dow AgroSciences LLC, dated February 13, 2009 (incorporated by reference to Exhibit 10.39 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
10.36	Third Amendment of Research and Commercial Option License Agreement between Sangamo and Dow AgroSciences LLC, dated February 28, 2009 (incorporated by reference to Exhibit 10.40 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
10.37†	Second Amendment of the License Agreement between Sigma-Aldrich Corporation and Sangamo, dated September 25, 2009 (incorporated by reference to Exhibit 10.2 to the Company's Form 10-Q filed on November 6, 2009).
10.38†	Third Amendment to the License Agreement between Sigma-Aldrich Corporation and Sangamo, dated October 2, 2009 (incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed on November 6, 2009).
10.39†	First Amendment to the Research, Development and Commercialization Agreement between Sangamo and Juvenile Diabetes Research Foundation International, dated January 8, 2010 (incorporated by reference to Exhibit 10.44 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
10.40	Fourth Amendment of Research and Commercial Option License Agreement between Sangamo and Dow AgroSciences LLC, dated January 8, 2010 (incorporated by reference to Exhibit 10.45 to the Company's Annual Report on Form 10-K, filed March 5, 2010).
10.41	Form of Non-Employee Director Restricted Stock Issuance Agreement (incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed on August 5, 2010).
10.42	Fifth Amendment of the Research and Commercial License Option Agreement between Sangamo BioSciences, Inc. and Dow AgroSciences LLC, dated May 14, 2010 (incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed on November 3, 2010).
10.43†	Sixth Amendment of the Research and Commercial License Option Agreement between Sangamo BioSciences, Inc. and Dow AgroSciences LLC, dated August 27, 2010 (incorporated by reference to Exhibit 10.2 to the Company's Form 10-Q filed on November 3, 2010).
10.44†	Seventh Amendment of the Research and Commercial License Option Agreement between Sangamo BioSciences, Inc. and Dow AgroSciences LLC, dated December 3, 2010 (incorporated by reference to Exhibit 10.49 to the Company's Form 10-K filed on February 16, 2011).
10.45†	

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Letter Agreement Amendment regarding the Research and Commercial License Option Agreement between Sangamo BioSciences, Inc. and Dow AgroSciences LLC, dated December 3, 2010 (incorporated by reference to Exhibit 10.50 to the Company's Form 10-K filed on February 16, 2011).

- 10.46† Letter Agreement between Sangamo and Sigma-Aldrich Corporation, dated March 1, 2011 (incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed on August 5, 2011).
- 10.47† Letter dated May 19, 2011 from Dow AgroSciences LLC ("DAS") to Sangamo amending the Research and Commercial License Option Agreement between DAS and Sangamo, dated as of October 1, 2005, as amended (incorporated by reference to Exhibit 10.2 to the Company's Form 10-Q filed on August 5, 2011).
- 10.48(+) Amended and Restated Employment Agreement between Sangamo and Edward O. Lanphier II, dated June 21, 2011 (incorporated by reference to Exhibit 10.3 to the Company's Form 10-Q filed on August 5, 2011).
- 10.49(+) Employment Agreement between Sangamo and Dr. Geoff Nichol, dated June 17, 2011 (incorporated by reference to Exhibit 10.4 to the Company's Form 10-Q filed on August 5, 2011).
- 10.50(+) Amended and Restated Employment Agreement between Sangamo and H. Ward Wolff, dated December 15, 2011 (incorporated by reference to Exhibit 10.55 to Company's Form 10-K filed on February 23, 2012).
- 10.51(+) Form of Restricted Stock Unit Agreement under the Company's 2004 Stock Incentive Plan (incorporated by reference to Exhibit 10.1 to the Company's Form 8-K filed on December 3, 2007).



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Exhibit Number	Description of Document
10.52†	Collaboration and License Agreement between Sangamo and Shire AG, dated January 31, 2012 (incorporated by reference to Exhibit 10.57 to the Company's Form 10-K filed on February 23, 2012).
10.53	Fourth Amendment of the License Agreement between Sangamo and Sigma-Aldrich Corporation, dated as of September 14, 2012 (incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q filed on November 2, 2012).
10.54	Sangamo BioSciences, Inc. Incentive Compensation Plan (incorporated by reference to Exhibit 10.1 to the Company's Form 8-K filed on June 27, 2012).
10.55	Agreement and Plan of Merger by and among Sangamo BioSciences, Inc., Merger Sub and Ceregene and the Stockholders' Representative (incorporated by reference to the Company's Form 8-K filed on October 7, 2013).
10.56	Sangamo BioSciences, Inc. 2013 Stock Incentive Plan (incorporated by reference to Appendix A to Sangamo's proxy statement on Schedule 14-A filed with the SEC on April 25, 2013).
10.57	Consent Letter from Sigma-Aldrich Co. LLC to the Company dated September 25, 2014 (incorporated by reference to Exhibit 10.2 to the Company's Form 10-Q, filed October 28, 2014).
10.58†	Global Research, Development and Commercialization Collaboration and License Agreement between Sangamo BioSciences, Inc. and Biogen Idec Ma Inc. dated as of January 8, 2014 (incorporated by reference to Exhibit 10.1 to the Company's Form 10-Q, filed May 7, 2014).
10.59	Amendment of 2013 Stock Incentive Plan on Reduction of Share Reserve (incorporated by reference to Exhibit 10.2 to the Company's Form 10-Q, filed May 7, 2014).
10.60	Ninth Amendment dated as of March 14, 2014 to License Agreement between Sangamo BioSciences, Inc. and Massachusetts Institute of Technology dated May 9, 1996 (incorporated by reference to Exhibit 10.3 to the Company's Form 10-Q, filed October 28, 2014).
10.61	Sangamo BioSciences, Inc. Amended and Restated 2013 Stock Incentive Plan (incorporated by reference to Exhibit 10.1 to the Company's Form 8-K filed with the SEC on June 25, 2015).
10.62†	Seventh Amendment to the License Agreement, dated as of January 1, 2015, between the Company and Sigma Aldrich Co., LLC(incorporated by reference to Exhibit 10.1 to the Company's Form 8-K filed with the SEC on August 6, 2015)
10.62†	Amended and Restated Collaboration and License Agreement, dated September 1, 2015, between the Company and Shire International GMBH (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed on October 30, 2015).
10.63++	Letter Amendment dated December 14, 2015 to Global Research, Development and Commercialization Collaboration and License Agreement, dated January 8, 2014 between the Company and Biogen.
12.1	Computation of Ratio of Earnings to Fixed Charges (incorporated by reference to Exhibit 12.1 to the Company's Post-Effective Amendment No. 1 to the Registration Statement on Form S-3 (Registration No. 333-194126) filed February 18, 2016).

- 21.1 Subsidiaries of the Company
- 23.1 Consent of Independent Registered Public Accounting Firm.
- 31.1 Rule 13a-14(a) Certification of Principal Executive Officer.
- 31.2 Rule 13a-14(a) Certification of Principal Financial Officer.
- 32.1 Certification Pursuant to 18 U.S.C. Section 1350.

101.INS XBRL Instance Document

101.SCH XBRL Taxonomy Extension Schema Document

101.CAL XBRL Taxonomy Extension Calculation Linkbase Document

101.DEF XBRL Taxonomy Extension Definition Linkbase Document

101.LAB XBRL Taxonomy Extension Label Linkbase Document

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Exhibit

Number Description of Document

101.PRE XBRL Taxonomy Extension Presentation Linkbase Document

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

++ Confidential treatment has been requested for certain information contained in this document. Such information has been omitted and filed separately with the Securities and Exchange Commission.

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

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