SANGAMO BIOSCIENCES INC
Form 10-K
March 16, 2006

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UNITED STATES SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

þ ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d)
OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2005

OR

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

Commission file number: 0-30171

SANGAMO BIOSCIENCES, INC.
(Exact name of registrant as specified in its charter)

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

(510) 970-6000
(Registrant s telephone number, including area code)

None
(Former name, former address and former fiscal year, if changed since last report)

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

Title of each class	**Name of each exchange on which registered**
None	

Securities registered pursuant to Section 12(g) of the Act: Common Stock, $0.01 par value per share

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

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

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

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. o

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer. See definition of accelerated filer and large accelerated filer in Rule 12b-2 of the ExchangeAct.
Large accelerated filer o Accelerated filer þ Non-accelerated filer o

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

As of June 30, 2005, the aggregate market value of the registrant s common stock held by non-affiliates of the registrant was $58,453,331 based on the closing sale price as reported on the National Association of Securities Dealers Automated Quotation System National Market System.

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 14, 2006**
Common Stock, $0.01 par value per share	**30,672,183 shares**

DOCUMENTS INCORPORATED BY REFERENCE

Document	**Parts Into Which Incorporated**
Proxy Statement for the 2006 Annual Meeting of Stockholders	**Part III**

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

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

our strategy;

product development and commercialization of our products;

clinical trials;

revenues from existing and new collaborations;

our research and development and other expenses;

sufficiency of our cash resources;

our operational and legal risks; and

our plans, objectives, expectations and intentions and any other statements that are not historical facts.

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

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PART I

Item 1. *Business*

Company Overview and Business Strategy

Background

Sangamo BioSciences is developing a new class of human therapeutics. We are a leader in the research, development, and commercialization of DNA-binding proteins for the therapeutic regulation and modification of disease-related genes. Our proprietary technology platform is based on the engineering of a naturally occurring class of proteins referred to as zinc finger DNA-binding proteins (ZFPs). We believe that ZFPs can be targeted to virtually any gene in the human genome or the genome of any other organism. Our scientists use engineered ZFPs to make ZFP transcription factors, or ZFP TFsTM, which are proteins that bind to DNA and are able to turn genes on or off (see Figure A). Additionally, ZFPs may be engineered to create zinc finger nucleases, or ZFNsTM. Engineered ZFNs can be used to cut genomic DNA at a pre-selected sequence location, facilitating either ZFN-mediated correction of genes that contain disease-causing mutations, or disruption of genes that facilitate or are responsible for disease pathology.

The pharmaceutical industry has invested billions of dollars to discover and validate new drug targets over the last decade. While there have been several notable successes, in many cases it has proven difficult to identify small-molecule drugs, monoclonal antibodies or recombinant proteins that can therapeutically modulate these targets in man. We believe that our ZFP technology platform constitutes a new therapeutic approach enabling the regulation or modification of therapeutically generated gene targets that have proven intractable to conventional methods of drug discovery. By developing ZFP TherapeuticTM products based on regulation or modification of such targets at the DNA level, Sangamo is focused on establishing a new therapeutic product development technology platform for a new class of drugs. In November 2005, we completed the enrollment and treatment of the first Phase 1 clinical trial of a ZFP Therapeutic (SB-509) in patients with diabetic neuropathy and we plan to initiate a Phase 2 trial of SB-509 in 2006. In addition, one of our corporate partners, Edwards Lifesciences (Edwards), has initiated two Phase 1 clinical studies to evaluate the safety and preliminary efficacy of a proprietary Sangamo ZFP Therapeutic, EW-A-401, for the treatment of peripheral artery disease (PAD). Sangamo has also initiated preclinical animal studies of ZFP Therapeutics in congestive heart failure, nerve regeneration, age-related macular degeneration and neuropathic pain. In addition, we have research-stage programs in HIV, X-linked severe combined immunodeficiency (X-linked SCID), hemophilia and hemoglobinopathies, cancer and cancer immunotherapy.

While we intend to invest the majority of our financial and scientific resources in the human therapeutic applications of our ZFP technology, we believe the potential commercial applications of ZFPs are broad-based and range from human therapeutics and drug discovery to pharmaceutical protein production and the engineering of commercial crop plants. In October 2005, we announced a Research License and Commercial Option Agreement with Dow AgroSciences, LLC (DAS), a wholly owned indirect subsidiary of Dow Chemical Corporation. Under the agreement, Sangamo is providing DAS with access to Sangamo s ZFP technology and the exclusive right to use it to modify the genomes or alter the nucleic acid or protein expression of plant cells, plants, or plant cell cultures. We have retained rights to use plants or plant-derived products to deliver ZFP transcription factors or nucleases into human or animals for diagnostic, therapeutic, or prophylactic purposes. In addition, we seek to capitalize on the ZFP platform by facilitating the sale or licensing of ZFP TFs or ZFNs to companies working in other fields including protein production and drug discovery. For instance, Sangamo is supplying its pharmaceutical partners Medarex Inc. and, recently, Pfizer Inc, Novo Nordisk, Novartis and Amgen with ZFP engineered cells for the enhanced production of therapeutic proteins, an advance that could substantially increase the efficiency of pharmaceutical protein production.

Sangamo has also provided companies such as LifeScan, a Johnson & Johnson company, with ZFP TFs to aid in the development of new therapeutic treatments for diabetes in the emerging field of regenerative medicine.

We have amassed a substantial intellectual property position in the design, selection, composition, and use of engineered ZFPs to support all of these commercial activities. We either own outright or have licensed the commercial rights to approximately 107 patents issued in the United States and foreign national jurisdictions, and we have 178 patent applications pending worldwide. We continue to license and file new patent applications that

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strengthen our core and accessory patent portfolio. We believe that our proprietary position will protect our ability to research, develop, and commercialize products and services based on ZFP technology across our chosen applications.

Over the last four years, we have increasingly focused our company on ZFP Therapeutic product development and have recruited experienced scientists and managers with substantial product development experience. We are also building our capabilities in preclinical development, regulatory affairs and clinical research and are applying these capabilities across our product development programs.

DNA, Genes, and Transcription Factors

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

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

Transcription factors are proteins that bind to DNA and regulate gene expression. A transcription factor recognizes and binds to a specific DNA sequence within or near a particular gene and causes that gene to be activated or repressed. In higher organisms, transcription factors typically comprise two principal domains: the first is a DNA-binding domain, which recognizes a target DNA sequence and thereby directs the transcription factor to the proper chromosomal location; the second is a functional domain that causes the target gene to be activated or repressed (see Figure A). The two-component structure of our engineered ZFP TFs is modeled on this naturally occurring structure of transcription factors in all higher organisms.

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Figure A
The Two Domain Structure of a ZFP Therapeutic

Engineered Zinc Finger Protein Transcription Factors (ZFP TFs) for Therapeutic Gene Regulation

Consistent with the two domain structure of ZFP TFs, we take a modular approach to their design. The recognition domain is typically composed of three or more zinc fingers; each individual finger recognizes and binds to a three base pair sequence of DNA, and multiple fingers can be linked together to recognize longer stretches of DNA. By modifying the amino acids of a ZFP that directly interact with DNA, we can engineer novel ZFPs capable of recognizing pre-selected DNA sequences within, or near, virtually any gene.

The ZFP DNA-binding domain is coupled to a functional domain, creating a ZFP TF capable of controlling or regulating a target gene in the desired manner. For instance, an activation domain causes a target gene to be turned on. Alternatively, a repression domain causes the gene to be turned off. We believe that we can control the duration of the effects of ZFP TFs by several methods. ZFP TFs may be delivered by using different gene transfer systems that allow them to be briefly (transiently) or continuously expressed in a cell. We can also engineer ZFP TFs with functional domains that allow their activity to be controlled by the administration of a small-molecule drug. Finally, we can engineer ZFP TFs with repression domains that are able to reduce gene expression and, in some cases, even silence their target genes.

To date, we have designed, engineered, and assembled several thousand ZFPs and have tested many of these proteins for their affinity, or tightness of binding to their DNA target, as well as their specificity, or preference for their intended DNA target. We have developed methods for the design, selection, and assembly of ZFPs capable of binding to a wide spectrum of DNA sequences and genes. We have linked ZFPs to numerous functional domains to create gene-specific ZFP TFs and have demonstrated the ability of these ZFP TFs to regulate hundreds of genes in dozens of different cell types and directly in whole organisms, including mice, rats, rabbits, pigs, plants, fruit flies, worms, and yeast. Sangamo scientists and collaborators have published data in peer-reviewed scientific journals on the transcriptional function of ZFP TFs and the resulting changes in the behavior of the target cell, tissue, or organism.

Engineered ZFNs for Therapeutic Gene Modification: Gene Correction and Gene Disruption

The ZFP DNA-binding domain may also be coupled to the cleavage domain of a restriction endonuclease an enzyme that cuts DNA creating a zinc finger nuclease or ZFN. Using the DNA binding domain of an

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engineered ZFP to target the nuclease to a chosen location, we can design a ZFN to generate a physical break at a defined location of a target gene. This targeted break in the DNA can be manipulated to effect two different outcomes, either to facilitate the replacement of the disease-causing mutation with a normal or corrected DNA sequence or to disrupt the disease-related gene resulting in the expression of a truncated or non-functional protein. We believe that ZFN-mediated gene correction will allow 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 monogenic diseases such as X-linked severe combined immunodeficiency (X-linked SCID) and sickle cell anemia. Similarly, ZFN-mediated gene modification may permit the targeted disruption of a gene that is involved in disease pathology such as disruption of the CCR5 gene to treat HIV infection.

ZFP Therapeutic Gene Correction of Monogenic Disease

Genetic diseases such as X-linked SCID, sickle cell anemia, and ß-thalassemia are caused by deleterious DNA sequence mutations within single genes. Gene Correction is the process by which a mutation, or disease-causing DNA sequence, can be repaired with the correct DNA sequence, restoring normal gene function. Our engineered ZFPs can be attached to nuclease domains to create ZFNs. The ZFN is able to recognize its intended gene target through its engineered (ZFP) DNA-binding domain (Figure A). However, instead of regulating the expression of the target gene (as with a ZFP TF), the ZFN causes the gene to be cut near the ZFP binding site, triggering a repair process and facilitating the correction of the DNA sequence at the site of the mutation. A segment of DNA or donor sequence that encodes the correct gene sequence is also introduced into the cell to provide a template for the correction of the cellular gene.

The process Sangamo uses for gene correction takes advantage of a natural process which is called homologous recombination (HR). While gene correction has been pursued in academic research laboratories for over a decade, its clinical application has been limited by the low efficiency of HR, the biological process of gene repair. HR occurs naturally at a rate of approximately once in every one million cells receiving the DNA donor sequence; this rate is too low to be of clinical use. However, we have shown in research published in the scientific journal *Nature* (**Nature** June 2005. vol: 435; pp 646-651) that the use of engineered ZFNs to cleave the target gene near the defective sequence can increase the efficiency of targeted HR by several thousand fold. The data published in Nature demonstrated the use of engineered ZFN s to correct errors in the DNA sequence of the IL2-R gamma gene, the gene that is defective in X-linked SCID. Correction was achieved in a significant percentage of treated cells without the need for selection. Importantly, gene correction was permanent and eliminated the need for integration of any foreign DNA sequence, a cause of problems in certain gene therapy studies. ZFP Therapeutic gene correction is a revolutionary technical approach to gene repair because ZFNs can be engineered to recognize virtually any target gene in the human genome. We are working to generate the preclinical data necessary to evaluate the potential utility of this approach for X-linked SCID, hemophilia and hemoglobinopathies such as sickle cell anemia and #-thalassemia. In addition, our ZFNs can be used to target the insertion of a DNA sequence into a specific site in a genome, which may also be applied to gene correction.

ZFP Therapeutic Gene Disruption for Infectious Diseases

ZFNs can also be used to disrupt a gene sequence. This may have therapeutic applications in diseases such as HIV viral infections. To effect ZFN-mediated gene disruption, ZFNs are introduced into cells without an added DNA donor sequence. Under these circumstances, introduction of a double stranded break in the cellular gene prompts the cell s repair machinery to rejoin the two broken ends of the DNA, with disruption of the gene s normal coding sequence occurring at a certain frequency. This disruption results in a shortened or non-functional protein product. In the case of HIV we are using this approach to disrupt the gene that encodes a cellular protein, CCR5, which is a co-factor for HIV infection of T-cells and other cells of the immune system.

A New Class of Human Therapeutics

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

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Following the genomics revolution of the 1990s, the sequencing and publication of the human genome, and the industrialization of genomics-based drug discovery, pharmaceutical and biotechnology companies have validated and characterized hundreds of new drug targets. However, these companies have had mixed results in translating these targets into lead product candidates or products which have advanced through clinical trials. There are many new drug targets which, although they have a clear role in disease processes, cannot be bound or modulated for therapeutic purposes by small molecules with drug-like properties. Alternative therapeutic approaches may be required to modulate the biological activity of these so-called non-druggable targets. This may create a significant clinical and commercial opportunity for the therapeutic regulation or modification of disease-associated genes using engineered ZFP TFs or ZFNs.

ZFP Therapeutics provide a new approach to non-druggable targets. ZFP TFs act through a mechanism that is unique among biological drugs: direct regulation of the disease gene as opposed to the RNA or protein target encoded by that gene. ZFNs can be used to directly correct or modify a gene. Thus, a protein target which may be intractable to small molecule control can instead be turned up, turned down or modified at the DNA level. Engineered ZFP TFs are the only class of therapeutic molecules that act directly through the regulation of gene expression at the DNA level and ZFNs provide the means for specific and efficient gene modification. This mode of action is not available to antisense RNA, siRNA, which act by interfering with the expression of cellular RNA, or conventional small molecules, antibodies, or other protein pharmaceuticals which act at the protein level.

Therefore, we believe that ZFP Therapeutics provide a unique and proprietary approach to therapeutic design and have significant competitive advantages over small-molecule drugs, protein pharmaceuticals, and conventional gene therapy:

- ZFP Therapeutics act at the DNA level to regulate or modify gene expression, allowing direct modulation of the gene;
- ZFP Therapeutics circumvent the non-druggable properties of many drug targets;
- ZFP TFs can either activate or repress therapeutic gene targets;
- ZFP TFs can activate or repress the expression of all variant proteins (isoforms) encoded by a particular gene;
- ZFP TFs may themselves be expressed either transiently, for acute indications, or longer term, for chronic conditions;
- ZFNs can be used to correct genes responsible for monogenic diseases or disrupt genes involved in disease processes; and
- Permanent gene correction, insertion or disruption requires only transient cellular expression of ZFNs.

THERAPEUTIC PRODUCT DEVELOPMENT

Product Development Strategy

Over the last several years, we have shown that ZFP TFs can be engineered to bind their target genes with a defined level of affinity and specificity and can regulate or modify these targets in a way that causes the desired effect at the levels of target cell, tissue, and organism. We have extended these results to preclinical animal models of disease, including mice, rats, rabbits, and pigs. We have published much of these data in peer-reviewed journals. In January 2005, we submitted some of these data to the United States Food & Drug Administration (FDA) along with preclinical

toxicology and biodistribution data as part of an IND application to support Sangamo s first Phase 1 clinical study of a ZFP Therapeutic. This trial was a single blind, placebo-controlled, dose-escalation study designed to investigate the safety and preliminary efficacy of a ZFP TF formulation, SB-509. SB-509 is designed to up-regulate the expression of vascular endothelial growth factor A (VEGF-A) in patients with mild to moderate diabetic neuropathy (DN). In May 2005, we announced that this Phase 1 clinical trial had begun and in November 2005 we reported that we had competed subject enrollment and treatment in the trial. We expect to present data from this Phase 1 trial in the first half of 2006 and we plan to initiate a Phase 2 trial in DN in the second half of 2006. Our partner, Edwards Lifesciences has two Phase 1 trials of a ZFP Therapeutic in progress. The first, in the intermittent

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claudication (IC) stage of PAD at the National Heart, Lung and Blood Institute (NHLBI), National Institutes of Health (NIH) and a second trial in the more severe form of PAD, critical limb ischemia (CLI), at Duke University Medical Center. Edwards has stated that they will begin a Phase 2 trial in CLI in 2006. We are developing the additional preclinical data to support the development of ZFP Therapeutics for cardiovascular disease, infectious diseases including HIV infection, neuropathic pain, nerve regeneration, cancer, and monogenic diseases including X-linked SCID and hemophilia and hemoglobinopathies such as sickle cell anemia and #-thalassemia.

Product Development Programs

In addition to our Phase 1 clinical trial in DN and Edwards two Phase 1 clinical trials in PAD, we currently have seven preclinical-stage programs (i.e., lead ZFP TF molecules in animal efficacy studies) as well as several research-stage programs (i.e., cell-based testing to identify and optimize lead ZFP TF or ZFN molecules for testing in animals).

Clinical Indication	Development Stage	Therapeutic Approach	Comments
Diabetic neuropathy (DN)	Phase 1 clinical trial enrollment competed November 2005	ZFP TF (SB-509) up-regulation of VEGF-A to protect and induce growth of neuronal and glial cells	Evidence from animal models suggests that up-regulation of endogenous VEGF-A directly induces the growth and repair of neuronal and glial cells. Trial is designed to evaluate product safety and preliminary trends in efficacy. Data will be presented in 2006. We expect to initiate Phase 2 trial in the second half of 2006.
Peripheral artery disease (PAD) Intermittent claudication	Phase 1 clinical trial ongoing at NHLBI, NIH	ZFP TF (EW-A-401) up-regulation of VEGF-A to induce angiogenesis, or blood vessel formation, in the lower extremities	Sponsored by our partner, Edwards Lifesciences; evaluating product safety and preliminary evidence of increase in blood flow in lower extremities of patients with intermittent claudication.
Peripheral artery disease (PAD) Critical limb ischemia	Phase 1 trial ongoing at Duke University Medical School	ZFP TF (EW-A-401) up-regulation of VEGF-A to induce angiogenesis, or blood vessel formation, in the lower extremities	Sponsored by our partner, Edwards Lifesciences; primarily evaluating product safety but also changes in progenitor cell populations to determine the extent to which tissue repair can be accomplished. Edwards

			expects to initiate a Phase 2 trial in 2006.
Ischemic heart disease (IHD)	Preclinical (animal efficacy)	ZFP TF up-regulation of VEGF-A to induce angiogenesis in the ischemic heart	Sponsored by our partner, Edwards Lifesciences; currently evaluating the preclinical efficacy of up-regulation of VEGF-A in animal models.
Human immunodeficiency virus (HIV) infection and Acquired immune deficiency syndrome (AIDS)	Preclinical (cell-based studies)	ZFN-mediated disruption of CCR5 gene in circulating T- cells, mononuclear cells and stem cells from patients infected with HIV	A well-documented mutation in CCR5 (CCR5 ß32) exists in humans and confers resistance to HIV infection. Sangamo scientists currently optimizing use of ZFN gene disruption to recapitulate the effects of this mutation in immune cells.

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Clinical Indication	Development Stage	Therapeutic Approach	Comments
Congestive heart failure (CHF)	Preclinical (animal efficacy)	ZFP TF down- regulation of phospholamban (PLN) to increase the contractility of heart muscle	Evidence from cellular and transgenic animal models suggests that phospholamban plays a critical role in congestive heart failure. Sangamo scientists currently evaluating the preclinical efficacy of PLN repression to increase the contractility of heart muscle in a rat model of congestive heart failure.
Neuropathic pain (initial indication: severe cancer-related pain)	Preclinical (animal efficacy)	ZFP TF down- regulation of cell surface receptors involved in pain signaling	Several pain targets have been identified and validated. Sangamo scientists are currently evaluating various formulations of ZFP TFs for the down-regulation of cell surface receptor (TrkA), and ion-channel (PN3) to choose the optimal ZFP TF and target receptor.
Nerve regeneration (nerve crush and spinal cord injury, amyotrophic lateral sclerosis (ALS)	Preclinical (animal efficacy)	ZFP TF up-regulation of VEGF-A to induce nerve regeneration	Sangamo scientists and collaborators are evaluating delivery methods and dosing of ZFP TF in models of nerve crush and spinal cord injury.
Age-related macular degeneration (AMD)	Preclinical (animal efficacy)	ZFP TF antiangiogenic approach; ZFP TF mediated up-regulation of PEDF and down regulation of VEGF-A in the eye	Sangamo scientists are evaluating a single and a combination of ZFP TFs to inhibit angiogenesis in the eye.
Cancer	Preclinical (cell-based studies)	ZFP TF mediated up-regulation of PEDF and GM-CSF	GM-CSF is a powerful stimulator of the immune system and PEDF is a potent antiangiogenic factor. Sangamo scientists are evaluating the combination of ZFP TFs as a means to stimulate a

	cell-mediated, antitumor response and reduce the vascularization of the tumor mass.

Table 1. Clinical indications currently targeted by Sangamo s clinical and preclinical ZFP Therapeutic product development programs.

Diabetic Neuropathy (DN)

Diabetic peripheral sensory and motor neuropathy is one of the most frequent complications of diabetes. Symptoms include numbness, tingling sensations and pain particularly in the toes or feet. This may be gradually replaced by loss of sensation and motor function as nerve damage progresses. Ulcers and sores may appear on numb areas of the foot or leg because pressure or injury goes unnoticed. Despite adequate treatment, these areas of trauma frequently become infected and this infection may spread to the bone, necessitating amputation of the leg or foot. More than 60% of non-traumatic lower-limb amputations in the United States occur among people with diabetes. In the period from 2000 to 2001 this translated to approximately 82,000 amputations. The American Diabetes Association estimates that there are approximately 18.3 million people with diabetes in the United States and that of those about 60% to 70% have mild to severe forms of neuropathy. According to the Centers for Disease Control (CDC), diabetes is becoming more common in the United States. From 1980 through 2002, the number of Americans with diabetes more than doubled.

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Apart from rigorous control of blood glucose, the only therapies approved by the FDA for the treatment of diabetic neuropathy are analgesics and antidepressants that address only the symptoms and do not retard or reverse the progression of the disease. VEGF-A has been demonstrated to have direct neuroproliferative, neuroregenerative and neuroprotective properties. Administration of recombinant VEGF-A or the cDNA encoding VEGF-A has been observed to retard or partially reverse the condition in preclinical animal models of diabetic neuropathy. We have completed preclinical studies of VEGF-A activation in similar preclinical models to confirm and extend these findings by using our ZFP Therapeutic SB-509, which is designed to up-regulate the endogenous VEGF-A gene. In January 2005, Sangamo filed an IND with the FDA for SB-509 for the treatment of mild to moderate diabetic neuropathy. We have completed enrollment and treatment of a Phase 1, single blind, dose-escalation trial to measure the laboratory and clinical safety of SB-509. We expect to present data from this trial in the first half of 2006 and to initiate a Phase 2 clinical trial of SB-509 in the second half of 2006.

Peripheral Artery Disease (PAD)

PAD is the result of inadequate arterial blood flow to the lower extremities. It is seen as a spectrum of disease, beginning with asymptomatic reduction in blood flow to the leg; followed by the development of intermittent claudication, which limits walking distance; followed by foot pain in the absence of exercise, so-called resting pain; finally leading to tissue damage and severely impaired mobility a stage known as critical limb ischemia. The condition affects 8-12 million people in the United States. Eighty percent of these patients have intermittent claudication and do not progress to resting pain or critical limb ischemia. This program to develop a formulation of a ZFP TF, EW-A-401, an activator of VEGF-A for therapeutic angiogenesis is funded and managed by our partner, Edwards Lifesciences. Edwards filed an IND application in February 2004 and initiated a Phase 1 clinical trial at the National Heart Lung and Blood Institute (NHLBI) at the National Institutes of Health (NIH) in August, 2004 for EW-A-401 to treat intermittent claudication. In June 2005, Edwards announced that they had also initiated a Phase 1 human clinical trial for EW-A-401 for critical limb ischemia, the more severe form of PAD, at Duke University Medical Center.

Ischemic Heart Disease (IHD)

IHD results from inadequate blood flow to the heart. The most common manifestation of this disease is angina, or the onset of chest pain with exercise. Macrovascular therapy, in the form of percutaneous coronary intervention (angioplasty) or coronary artery bypass grafting, is available to treat angina, and approximately 1.1 million revascularization procedures are carried out in the United States each year. However, patients with downstream blood flow restrictions often do not fully benefit from these interventions. We have developed a ZFP TF designed to up-regulate the expression of VEGF-A for therapeutic angiogenesis for the potential treatment of post-myocardial ischemic heart disease.The IHD program is funded and managed by our partner, Edwards Lifesciences, who have stated that they expect to complete preclinical animal efficacy studies in 2005 and, based upon those data, expect to initiate a human clinical trial to evaluate safety of a ZFP TF activator of VEGF-A in post-myocardial IHD.

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

According to worldaidsday.org, in 2005, over 3.0 million people were infected with HIV, and there are now over 40.0 million people world-wide living with HIV and AIDS. An estimated 3.0 million people died of AIDS in the same year. The CDC estimates that, in the United States alone, there were 1.0 million people living with HIV/AIDS, 44,000 new infections and 16,000 deaths in 2004.

HIV infection results in the death of immune system cells and thus leads to AIDS, a condition in which the body s immune system is depleted to such a degree that the patient is unable to fight off common infections. Ultimately, these patients succumb to opportunistic infections or cancers. CCR5 is the co-receptor for HIV entry into T-cells and, if CCR5 is not expressed on their surface, HIV cannot infect these cells. A population of individuals that is immune to

HIV infection, despite multiple exposures to the virus, has been identified and extensively studied. They have a natural mutation, CCR5delta32, that results in the expression of a shortened, or truncated, and non-functional CCR5 protein. This mutation appears to have no observable deleterious effect on the growth or survival of these individuals. We are using our ZFN-mediated gene disruption technology to disrupt the CCR5 gene in cells of a patient s immune system to make these cells permanently resistant to HIV infection. The aim is to provide a

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population of HIV-resistant cells that can fight HIV and opportunistic infections. In collaboration with scientists at the University of Pennsylvania and Children s Hospital, Los Angeles, we are pursuing both ex-and in-vivo approaches in T-cells and hematopoietic stem cells.

Congestive Heart Failure (CHF)

CHF is a gradual and long-term loss of pumping capacity by the heart that results in the backup of blood and fluid (edema) in the lungs and other tissues and organs. This fluid congestion can cause shortness of breath, coughing, swelling of the abdomen and extremities, fatigue, kidney damage, and kidney failure. The incidence and prevalence of CHF are increasing with approximately 550,000 new cases in the United States each year and a current patient population of more than 5 million Americans. There is strong scientific evidence to suggest that down-regulation of the gene encoding phospholamban (PLN) in the heart can improve the contractility of heart muscle in mammalian animal models of CHF. We have identified a lead ZFP TF repressor of PLN expression for the CHF program and have ongoing preclinical studies in rodent models of CHF.

Neuropathic Pain (Cancer Pain)

Neuropathic pain comprises a set of chronic pain disorders that cannot be connected to a physical trauma, as is the case with acute pain. There are several million patients with neuropathic pain in the United States including late-stage cancer patients. Studies have shown that 90% of patients with advanced cancer experience severe pain, and that pain occurs in 30% of all cancer patients regardless of the stage of the disease. Pain usually increases as cancer progresses. The most common cancer pain is from tumors that metastasize to the bone. As many as 60-80% of cancer patients with bone metastasis experience severe pain. The second most common cancer pain is caused by tumors infiltrating nerves. Tumors near neural structures may cause the most severe pain. The few drugs currently being used to treat pain in these patients show marginal efficacy and can have very significant side effects. Chronic pain is a major and underserved market opportunity and is now an area of intense focus by pharmaceutical researchers owing to the discovery of several new pain-related pathways and drug targets. Recent studies have shown that in chronic pain, certain proteins in nerve cell membranes are up-regulated or over-expressed. Our scientists have identified ZFP TF product candidates that repress the expression of two of these pain targets in cell-based models. We are incorporating these ZFP TFs into gene transfer vectors for continued testing in pain models during 2006.

Nerve Regeneration

Nerves are fragile and can be damaged by disease, pressure, stretching, or cutting. While recent advances in emergency care and rehabilitation allow many patients suffering from a nerve injury or neurodegenerative disease to survive for longer periods and live with their condition, there are currently no therapeutic options for restoring nerve function. The spectrum of direct nerve injuries ranges from pinched nerves, e.g. sciatica, to outright spinal cord severance. Neurodegenerative conditions include such disorders as amyotrophic lateral sclerosis (ALS), also called Lou Gehrig s disease, which is a progressive, fatal neurological disease affecting as many as 30,000 Americans, with 5,600 new cases occurring in the United States each year. VEGF-A has been demonstrated to have direct neuroproliferative, neuroregenerative and neuroprotective properties. Evidence from preclinical and clinical studies using VEGF-A suggests that the targeted up-regulation of VEGF-A could be a viable approach to the treatment of degenerative nerve disease, crush injuries and may eventually be extended to spinal cord injury. In collaboration with several academic labs, we are evaluating ZFP TFs that activate the VEGF-A gene in pre-clinical animal efficacy models of nerve damage and disease.

Age-related Macular Degeneration (AMD)

AMD is the leading cause of blindness in the United States. The wet form of the disease is responsible for most (90%) of the severe loss of vision and is caused by growth of abnormal blood vessels under the central part of the retina or macula. These new blood vessels may then bleed and leak fluid, causing the macula to bulge or lift up, thus distorting or destroying central vision. The Macular Degeneration Foundation estimates that there are approximately 200,000 new cases of wet macular degeneration in the United States each year. Each year 1.2 million of the estimated 12 million people in the US with macular degeneration will suffer severe central vision loss. Each

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year 200,000 individuals will lose all central vision in one or both eyes. Sangamo scientists are developing ZFP TFs to inhibit blood vessel growth, or angiogenesis, within the eye. They have identified ZFP TFs that can activate the expression of the gene for Pigment Epithelium Derived Factor (PEDF), a factor known to inhibit the growth of blood vessels and ZFP TFs that can inhibit the expression of VEGF-A, a potent angiogenic factor. These ZFP TFs are being tested individually and in combination in preclinical animal models of AMD.

Cancer

The American Cancer Society estimates that the incidence of new cancer cases was approximately 1.3 million in 2004, with 565,500 cancer deaths, accounting for 1 of every 4 deaths in the United States. An increasing number of genes are being identified that appear to be important to the development and spread of many forms of cancer. We believe our ZFP technology has potential applications in cancer therapy, both in regulating endogenous genes and in activating the body s natural mechanisms for fighting disease. Sangamo scientists are engineering adenoviral vectors to deliver ZFP TFs that can simultaneously up-regulate granulocyte macrophage colony-stimulating factor (GM-CSF) and pigment epithelial derived factor (PEDF). GM-CSF is a powerful immunostimulator and has been shown to augment anti-tumor immune responses. PEDF is a potent antiangiogenic factor that blocks the angiogenic function of VEGF. We believe that this approach may be used to treat cancer both at the tumor site and systemically by engaging the immune system and reducing the blood supply that supports tumor growth.

ZFP Therapeutic Research Programs

Sangamo has several research stage programs in progress in gene modification. These initiatives include programs in the hemoglobinopathies (e.g. sickle cell anemia and ß-thalassemia) and in immune system disorders such as X-linked severe combined immunodeficiency (X-linked SCID) and hemophilia.

Product Development Resources and Infrastructure

As Sangamo continues to progress as a clinical development-stage biotechnology company, we are building our gene delivery capabilities and our capabilities in regulatory affairs, quality assurance and clinical research. Appointments in these areas included the hiring, in August 2004, of Dale Ando, M.D. as Vice President, Therapeutic Development and Chief Medical Officer. Dr. Ando has held senior positions in therapeutic product development in several biotechnology companies and has served on the National Institutes of Health (NIH) Recombinant DNA Advisory Committee (NIH RAC) and the Adenoviral Safety Committee. We are establishing regulatory affairs, quality assurance and clinical research expertise internally, while relying on third-party contract manufacturers of ZFP Therapeutic products and contract research organizations for toxicology and initial clinical studies. This will serve to minimize our investment in fixed capital while maximizing our flexibility in the selection of gene transfer systems for the delivery of ZFP TF and ZFN genes. Our manufacturing and quality assurance personnel oversee and audit the manufacturing and testing of our experimental products at third-party facilities.

CORPORATE RELATIONSHIPS

We are applying our ZFP technology platform to several commercial applications in which our products provide Sangamo and our strategic partners and collaborators with potential technical, competitive, and economic advantages. Where and when appropriate, we have established and will continue to pursue ZFP Therapeutic strategic partnerships and Enabling Technology collaborations with selected pharmaceutical and biotechnology companies to fund internal research and development activities and to assist in product development and commercialization. In December 2004, we hired David Ichikawa as Senior Vice President, Business Development. Mr. Ichikawa has more than 20 years of industry experience with both pharmaceutical and biotechnology companies in various commercial areas.

We believe the advancement of our first ZFP Therapeutics into clinical trials in 2004 and 2005 has come at a timely point in the evolution of the worldwide pharmaceutical industry. Large pharmaceutical companies face revenue growth challenges that compel them to in-license or acquire emerging therapeutic technologies. The advancement of AFP Therapeutics into Phase 1 clinical trials may bring attention to our other AFP Therapeutic

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programs and to the potential of ZFP Therapeutics to address the non-druggable, yet high-value drug targets residing within pharmaceutical research laboratories today.

Strategic Partnership with Edwards Lifesciences Corporation

In January 2000, we announced a therapeutic product development collaboration with Edwards Lifesciences Corporation. Under the agreement, we have licensed to Edwards, on a worldwide, exclusive basis, ZFP Therapeutics for use in the activation of VEGFs and VEGF receptors in ischemic cardiovascular and vascular disease. Edwards purchased a $5.0 million note that converted, together with accrued interest, into 333,333 shares of common stock at the time of our initial public offering (IPO) at the IPO price. In March 2000, Edwards purchased a $7.5 million convertible note in exchange for a right of first refusal for three years to negotiate a license for additional ZFP Therapeutics in cardiovascular and peripheral vascular diseases. That right of first refusal was not exercised and terminated in March 2003. Together with accrued interest, this note converted into common stock at the time of our IPO at the IPO price. Through 2001, we received $2.0 million in research funding from Edwards and a $1.4 million milestone payment for delivery of a lead ZFP Therapeutic product candidate. In November 2002, Edwards signed an amendment to the original agreement and agreed to provide up to $3.5 million in research and development funding, including $2.95 million for research and development activities performed in 2002 and 2003. The filing of the IND for PAD in 2004, and the achievement of other research-related milestones in 2003, triggered a total of $1.0 million in milestone payments from Edwards Lifesciences in the first quarter of 2004.

There were no revenues attributable to milestone achievement and collaborative research and development performed under the Edwards agreement during 2005. Revenues were $615,000 and $1.5 million for 2004 and 2003, respectively. There were no related costs and expenses incurred for services performed under the Edwards agreement for either 2005 or 2004. Costs and expenses under the agreement were $1.4 million for 2003. We have no future commitments related to these agreements. Revenues attributable to milestone achievement and collaborative research and development performed under the Edwards agreement were 0%, 47% and 59% for 2005, 2004 and 2003, respectively, of total revenues earned by Sangamo. As of December 31, 2005 and 2004, there were no amounts owed the Company under the Edwards agreements.

Our license agreement with Edwards Lifesciences provides Edwards with worldwide, exclusive rights for ZFP Therapeutics for the activation of VEGF and VEGF receptors for the treatment and prevention of ischemic cardiovascular and vascular disease in humans. We have retained all rights to use our technology for all therapeutic applications of VEGF activation outside of the treatment and prevention of ischemic cardiovascular and vascular disease in humans. During the first quarter of 2005, Sangamo commenced a Phase 1 clinical trial for the treatment of diabetic neuropathy using a ZFP Therapeutic for the activation of VEGF. Edwards has stated that its rights include diabetic neuropathy and consequently our activities relating to diabetic neuropathy constitute a breach of the agreement. We strongly disagree with the Edwards assertion because diabetic neuropathy is a neurological disease and not an ischemic vascular disease and therefore is outside the scope of the Edwards license. Sangamo and Edwards are in discussions regarding this issue.

In the future, Sangamo may receive milestone payments and royalties under this agreement. We have received $2.5 million in milestone payments to date and we could receive $27.0 million in additional milestone payments under the agreement if all future milestones are met for the first product developed under the agreement. Any subsequent products developed under the agreement may generate up to $15.0 million in milestone payments each. We would also receive royalties on any sales of products generated under the agreement and these royalty obligations would continue until the expiration of the last-to-expire patent covering products developed under the agreement on a country-by-country basis. Based on currently issued patents, these royalty obligations would last through January 12, 2019. The development of any products is subject to numerous risks and no assurance can be given that any products will successfully be developed under this agreement. See Risk Factors Our gene regulation technology is relatively

new, and if we are unable to use this technology in all our intended applications, it would limit our revenue opportunities.

Under the Sangamo-Edwards agreement, we were responsible for advancing product candidates into preclinical animal testing. Edwards has responsibility for preclinical development, regulatory affairs, clinical development, and the sales and marketing of ZFP Therapeutic products developed under the agreement. Sangamo may

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receive milestone payments in connection with the development and commercialization of the first product under this agreement and may also receive royalties on product sales. As part of the November 2002 amendment to our original agreement, Edwards Lifesciences also entered into a joint collaboration with us to evaluate ZFP TFs for the regulation of a second therapeutic gene target, phospholamban (PLN), for the treatment of congestive heart failure. Under the amended agreement, Sangamo granted Edwards a right of first refusal to Sangamo s ZFP TFs for the regulation of PLN. This right of first refusal terminated on June 30, 2004. On August 14, 2003 Edwards and Sangamo entered into a third amendment to the original license agreement. Under this amendment, Sangamo received payment for research and development milestones associated with the VEGF and PLN programs.

There is no assurance that the companies will achieve the development and commercialization milestones anticipated in these agreements. Edwards has the right to terminate the agreement at any time upon 90 days written notice. In the event of termination, we retain all payments previously received as well as the right to develop and commercialize all related products.

Agreement with LifeScan for Regenerative Medicine

In September 2004, we announced that we had entered into a research agreement with LifeScan, Inc., a Johnson & Johnson company. The agreement provides LifeScan with our ZFP TFs for use in a program to develop therapeutic cell lines as a potential treatment for diabetes. In December 2004, and again in September 2005, this agreement was expanded to include additional targets important in diabetes. The agreements represented our first collaboration in the field of regenerative medicine. During 2005 and 2004, revenues attributable to collaborative research and development performed under the LifeScan agreements were $365,000 and $85,000, respectively. Related costs and expenses associated with research and development performed under the LifeScan agreements were $69,000 in 2005 and $5,000 in 2004.

Enabling Technology Programs

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

As the emphasis of our pharmaceutical research and development has shifted away from target validation to the downstream bottlenecks of the drug discovery process, we have refocused our Enabling Technology products and services on supplying our partners with our ZFP technology to enhance the production of pharmaceutical proteins.

Enabling Technology Collaborations for Pharmaceutical Protein Production

In 2003 the world wide sales of protein pharmaceuticals totaled over $32 billion. Industry experts believe that antibody drugs may generate sales in excess of $6 billion in 2005, and it is thought that if 10% of the antibody drugs currently in clinical trials prove successful, total sales could reach $45 billion by 2009 (source: Scrip Reports: PJB Publications, 2004).

Sangamo scientists have demonstrated that ZFP-engineered mammalian cells may be used to increase the yield of systems used for pharmaceutical protein production.

We have established several research collaborations in this area. In December 2004, we announced a research collaboration agreement with Pfizer Inc to use our ZFP technology to develop enhanced cell lines for protein pharmaceutical production. The scope of this agreement was expanded in January 2006 and provided further research funding from Pfizer to develop additional cell lines for enhanced protein production. Under the terms of the

agreement, Pfizer is funding research at Sangamo and Sangamo will provide our proprietary ZFP technology for Pfizer to assess its feasibility for use in mammalian cell-based protein production. We are generating novel cell lines and vector systems for enhanced protein production as well as novel technology for rapid creation of new production cell lines. During the first quarter of 2006 and first quarter of 2005, we received $775,000 and $500,000 in research-related funding under our agreements with Pfizer. Revenues attributable to collaborative research and development performed under the Pfizer agreement were $790,000 and $42,000 during 2005 and 2004,

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respectively. Related costs and expenses incurred under the Pfizer agreements were $154,000 during 2005. There were no costs or expenses incurred under the Pfizer agreement during 2004. As of December 31, 2005 and 2004 accounts receivable from Pfizer represented 80% and 88%, respectively, of our total accounts receivable balance.

In January 2005 Sangamo also announced an agreement with Amgen and in September 2005 a similar agreement with Novo Nordisk A/S. Sangamo is providing its ZFP technology to several companies including Amgen, Novartis and Novo Nordisk for evaluation of its use in developing enhanced cell lines for protein production.

Plant Agriculture Agreements

Sangamo scientists and collaborators have shown that ZFP TFs and ZFNs can be used to regulate and modify genes in plants with similar efficacy to that shown in various mammalian cells and organisms. 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, are more resistant to herbicides, pesticides, and plant pathogens; and 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. Effective as of October 1, 2005, we entered into a Research License and Commercial Option Agreement with Dow AgroSciences LLC (DAS), a wholly owned indirect subsidiary of Dow Chemical Corporation. Under this agreement, we will provide DAS with access to our proprietary ZFP technology and the exclusive right to use our ZFP technology to modify the genomes or alter the nucleic acid or protein expression of plant cells, plants, or plant cell cultures. We will retain rights to use plants or plant-derived products to deliver ZFP TFs or ZPF nucleases (ZFNs) into human or animals for diagnostic, therapeutic, or prophylactic purposes.

Our agreement with DAS provides for an initial three-year research term during which time we will work together to validate and optimize the application of our ZFP technology to plants, plant cells and plant cell cultures. A joint committee having equal representation from both companies will oversee this research. During the initial three-year research term, DAS will have the option to obtain a commercial license to sell products incorporating or derived from plant cells generated using our ZFP technology, including agricultural crops, industrial products and plant-derived biopharmaceuticals. This commercial license will be exclusive for all such products other than animal and human health products. In the event that DAS exercises this option, DAS may elect to extend the research program beyond the initial three-year term on a year-to-year basis.

Pursuant to the Research License and Commercial Option Agreement, DAS made an initial cash payment to us of $7.5 million and agreed to purchase up to $4.0 million of our common stock in the next financing transaction meeting certain criteria. In November 2005, the Company sold approximately 1.0 million shares of common stock to DAS at a price of $3.85 per share, resulting in proceeds of $3.9 million. In addition, DAS will provide between $4.0 and $6.0 million in research funding over the initial three-year research term and may make an additional payment of up to $4.0 million in research milestone payments to us during this same period, depending on the success of the research program. In the event that DAS elects to extend the research program beyond the initial three-year term, DAS will provide additional research funding. If DAS exercises its option to obtain a commercial license, we will be entitled to full payment of the $4.0 million in research milestones, a one-time exercise fee of $6.0 million, minimum annual payments of up to $25.25 million, development and commercialization milestone payments for each product, and royalties on sales of products. Furthermore, DAS will have 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 have agreed to supply DAS and its sublicensees with ZFP TFs and/or ZFNs for both research and commercial use. If DAS exercises its option to obtain a commercial license, DAS may request that we transfer, at DAS s expense, the ZFP manufacturing technology to DAS or to a mutually agreed-upon contract manufacturer.

The Research License and Commercial Option Agreement will terminate automatically if DAS fails to exercise its option for a commercial license by the end of the initial three-year research term. DAS may also terminate the agreement at the end of the second year of the initial research term if the joint committee overseeing the research determines that disappointing research results have made it unlikely that DAS will exercise the option; we are guaranteed to receive $4.0 million in research funding from DAS prior to such a termination. Following

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DAS s exercise of the option and payment of the exercise fee, DAS may terminate the agreement at any time. In addition, each party may terminate the agreement upon an uncured material breach of the other party. In the event of any termination of the agreement, all rights to use our ZFP technology will revert to us, and DAS will no longer be permitted to practice our ZFP technology or to develop or, except in limited circumstances, commercialize any products derived from our ZFP technology. Revenues related to the research license under the DAS agreement are being recognized ratably over the initial three year research term of the agreement and were $625,000 during 2005. Revenues attributable to collaborative research and development performed under the DAS agreement were $51,000 during 2005. Related costs and expenses incurred under the DAS agreement were $51,000 during 2005.

INTELLECTUAL PROPERTY AND TECHNOLOGY LICENSES

Our success and ability to compete is dependent in part on the protection of our proprietary technology and information. We rely on a combination of patent, copyright, trademark, and trade secret laws, as well as confidentiality agreements, materials transfer agreements and licensing agreements to establish and protect our proprietary rights.

We have licensed intellectual property directed to the design, selection, and use of ZFPs, ZFP TFs and ZFNs for gene regulation and modification from the Massachusetts Institute of Technology (MIT), Johnson and Johnson, The Scripps Research Institute (TSRI), Johns Hopkins University, Harvard University, the Medical Research Council, the California Institute of Technology, and the University of Utah. These licenses grant us rights to make, use, and sell ZFPs and ZFP TFs under 11 families of patent filings. All of these patent families have been filed in the United States, and seven have been filed internationally in selected countries. As of January 1, 2006, these patent filings have resulted in 15 issued U.S. patents and 10 granted foreign patents. We believe these licensed patents and patent applications include several of the early and important patent filings directed to design, selection, composition, and use of ZFPs, ZFP TFs, and ZFNs.

As of December 31, 2005, we had 55 families of Sangamo-owned patent filings, including 23 issued U.S. patents, 53 granted foreign patents, 70 pending U.S. patent applications and 75 pending foreign patent applications. These patent filings are directed to improvements in the design, composition, and use of ZFPs, ZFP TFs, and ZFNs. In the aggregate, we believe that our licensed patents and patent applications, as well as the issued Sangamo patents and pending Sangamo patent applications, will provide us with a substantial proprietary position in our commercial development of ZFP technology. The following tables provide information regarding our U.S. patents and the U.S. patents we have licensed:

Sangamo-Owned US Patents

Patent No.	Subject	Issue Date	Expiration Date
6,013,453	Binding proteins for recognition of DNA	January 11, 2000	August 17, 2015
6,453,242	Selection of Sites for Targeting by Zinc Finger Proteins and Methods of Designing Zinc Finger Proteins to Bind to Preselected Sites	September 17, 2002	January 12, 2019
6,492,117	Zinc Finger Proteins Capable of Binding DNA Quadruplexes	December 10, 2002	July 12, 2020
6,503,717		January 7, 2003	December 6, 2020

	Methods of Using Randomized Libraries of Zinc Finger Proteins for the Identification of Gene Function		
6,511,808	Methods for Designing Exogenous Regulatory Molecules	January 28, 2003	April 27, 2021
6,534,261	Regulation of Endogenous Gene Expression in Cells Using Zinc Finger Proteins	March 18, 2003	January 12, 2019
6,599,692	Functional Genomics Using Zinc Finger Proteins	July 29, 2003	September 14, 2019
6,607,882	Regulation of Endogenous Gene Expression in Cells Using Zinc Finger Proteins	August 19, 2003	January 12, 2019

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Patent No.	Subject	Issue Date	Expiration Date
6,610,489	Pharmacogenomics and Identification of Drug Targets by Reconstruction of Signal Transduction Pathways Based on Sequences of Accessible Regions.	August 26, 2003	April 27, 2021
6,689,558	Cells for Drug Discovery	February 10, 2004	February 8, 2021
6,706,470	Gene Switches	March 16, 2004	May 30, 2020
6,733,970	Screening System for Zinc Finger Polypeptides for a Desired Binding Ability	May 11, 2004	November 9, 2019
6,746,838	Nucleic Acid Binding Proteins (ZFP Design Rules)	June 8, 2004	May 26, 2018
6,777,185	Functional Genomics Using Zinc Finger Proteins	August 17, 2004	September 14, 2019
6,780,590	Gene Identification	August 24, 2004	September 14, 2019
6,785,613	Selection of Sites for Targeting by Zinc Finger Proteins and Methods of Designing Zinc Finger Proteins to Bind to Preselected Sites	August 31, 2004	January 12, 2019
6,794,136	Iterative Optimization in the Design of Binding Proteins	September 21, 2004	November 20, 2020
6,824,978	Regulation of Endogenous Gene Expression in Cells Using Zinc Finger Proteins	November 30, 2004	January 12, 2019
6,866,997	Nucleic Acid Binding Proteins (Design Rules II)	March 15, 2005	May 26, 2018
6,919,204	Modulation of Gene Expression using Localization Domains	July 19, 2005	September 28, 2021
6,933,113	Modulation of Endogenous Gene Expression in Cells	August 23, 2005	January 12, 2019
6,977,154	ZFPs that Bind Modified (Methylated) DNA	December 20, 2005	March 17, 2019
6,979,539	Regulation of Endogenous Gene Expression in Cells Using Zinc Finger Proteins	December 27, 2005	January 12, 2019

Licensed US Patents

Patent No.	Subject	Issue Date	Expiration Date
5,356,802	Functional domains in *Flavobacterium okeanokoites* (*Fok*I) restriction endonuclease	October 18, 1994	October 18, 2011
5,436,150	Functional domains in Flavobacterium okeanokoites (*Fok*I) restriction	July 25, 1995	July 25, 2012

	endonuclease		
5,487,994	Insertion and deletion mutants of *Fok*I restriction endonuclease	January 30, 1996	January 30, 2013
5,789,538	Zinc finger proteins with high affinity new DNA binding specificities	August 4, 1998	February 3, 2015
5,792,640	General method to clone hybrid restriction endonucleases using *lig* gene	August 11, 1998	April 3, 2012
5,916,794	Methods for inactivating target DNA and for detecting conformational change in a nucleic acid	June 29, 1999	April 3, 2012
5,925,523	Interaction trap assay, reagents and uses thereof	July 20, 1999	August 22, 2017
6,140,466	Zinc finger protein derivatives and methods therefor	October 31, 2000	January 18, 2014
6,200,759	Interaction trap assay, reagents and uses thereof	March 13, 2001	August 22, 2017
6,242,568	Zinc finger protein derivatives and methods therefor	June 5, 2001	June 5, 2018

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Patent No.	Subject	Issue Date	Expiration Date
6,265,196	Methods for inactivating target DNA and for detecting conformational change in a nucleic acid	July 24, 2001	April 3, 2012
6,410,248	General Strategy for selecting high-affinity zinc finger proteins for diverse DNA target sites	June 25, 2002	January 29, 2019
6,479,626	Poly-zinc finger proteins with improved linkers.	November 12, 2002	March 1, 2019
6,790,941	Zinc finger protein derivatives and methods therefor	September 14, 2004	January 18, 2014
6,903,185	Poly Zinc Finger Proteins with Improved Linkers	June 7, 2005	March 1, 2019

Technology Licenses

Massachusetts Institute of Technology

The Company entered into a license agreement with the Massachusetts Institute of Technology (MIT) on May 9, 1996, as subsequently amended, whereby the Company was granted 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. The Company pays annual license fees under the agreement and is obligated to make milestone payments upon the issuance of certain patents and upon the initiation of certain phases of clinical development. Since the inception of this agreement, the Company has made a total of $210,000 in milestone payments to MIT. Aggregate potential milestone payments under this agreement are approximately $465,000 through 2007. Additionally, if we sublicense and co-develop products using the MIT technology, we would be required to pay sublicense fees and royalties on product sales during the term of the agreement. The agreement expires upon the expiration of the last patent covered by the agreement. Based on currently issued patents and currently filed patent applications, this agreement will terminate on May 16, 2021.

The Johns Hopkins University

The Company entered into a license agreement with the Johns Hopkins University (JHU) on June 29, 1995, as subsequently amended, whereby the Company was granted a worldwide exclusive license to technology and patents relating to gene targeting technology for all fields of use, including the right to sublicense. Pursuant to the agreement, the Company pays an annual minimum royalty and would pay royalties on product sales. The Company has made a total of $37,500 in milestone payments to date and is not obligated to make any further milestone payments under the agreement. Additionally, if the Company successfully develops a product using the technology licensed to it under this agreement, the Company would be required to pay JHU royalties on product sales during the term of the agreement. The agreement expires upon the expiration of the last patent covered by the agreement. Based on currently issued patents, this agreement will terminate on January 30, 2013.

Johnson & Johnson

The Company entered into a license agreement with Johnson & Johnson (J&J) on May 9, 1996 whereby the Company was granted a worldwide exclusive license to technology and patents for the research, development and commercialization of therapeutic and diagnostic products using engineered ZFPs. Pursuant to the agreement, the

Company paid a license fee and will make future milestone payments and pay royalties on any product sales during the term of the agreement. To date, the Company has not made any milestone payments under the agreement. Aggregate potential milestone payments under this agreement are approximately $125,000. The agreement expires upon the expiration of the last patent covered by the agreement. Based on currently issued patents and currently filed patent applications, this agreement will terminate on June 5, 2018.

The Scripps Research Institute

The Company entered into a license agreement with the Scripps Research Institute (Scripps) on March 14, 2000 whereby the Company was granted 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 engineered ZFPs in plant agriculture, therapeutics and diagnostics. Pursuant to the agreement, the Company must

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pay an annual minimum royalty of $50,000 and royalties on product sales during the term of the agreement, for any products developed under the agreement. No milestone payments are payable under the agreement. Based on currently issued patents and currently filed patent applications, the Scripps agreement will terminate on June 5, 2018.

The California Institute of Technology

The Company entered into a license agreement with the California Institute of Technology (Cal Tech) on November 1, 2003 whereby the Company was granted a worldwide exclusive license to intellectual property covering the use of chimeric nucleases to stimulate gene targeting, in all fields except research tools and diagnostics. In an amendment to this agreement dated February 28, 2005, Sangamo was granted a worldwide exclusive license in all fields of use. Pursuant to the agreement, the Company has paid a license fee of 25,000 shares of unregistered Sangamo common stock, valued at $129,500, which was considered a research and development expense. No costs or expenses have been incurred under this agreement. No royalties or milestone fees are payable under this agreement. Products and services developed under this agreement relate to the use of zinc finger nucleases (ZFNs) for therapeutic gene correction in human healthcare and gene targeting in plant agriculture. The agreement expires upon the expiration of the last patent covered by the agreement. Based on currently filed patent applications, the Cal Tech agreement will terminate on September 5, 2023.

Estimated Licensing Expenses

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

Intellectual Property Related Risks

Although we have filed for patents on some aspects of our technology, we cannot provide assurances that patents will issue as a result of these pending applications or that any patent that has been or may be issued will be upheld. One of our foreign patents, which forms the basis for five European Regional Phase patents, has been revoked as a result of an opposition by a third party . We have appealed the revocation but cannot predict the outcome of our appeal. 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. Despite our efforts to protect our proprietary rights, existing patent, copyright, trademark, and trade secret laws afford only limited protection, and we cannot assure you that our intellectual property rights, if challenged, will be upheld as valid or will be adequate to protect our proprietary technology and information. In addition, the laws of some foreign countries may not protect our proprietary rights to the same extent as do the laws of the United States. Attempts may be made to copy or reverse engineer aspects of our technology or to obtain and use information that we regard as proprietary. Our patent filings may be subject to interferences. Litigation or opposition proceedings may be necessary in the future to enforce or uphold our intellectual property rights, to determine the scope of our licenses, or to determine the validity and scope of the proprietary rights of others. The defense and prosecution of intellectual property lawsuits, United States Patent and Trademark Office interference proceedings, and related legal and administrative proceedings in the United States and internationally involve complex legal and factual questions. As a result, these proceedings would be costly and time consuming to pursue and could result in diversion of financial and management resources without any assurance of success.

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. Any claims,

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with or without merit, could result in costly litigation, divert the efforts of our technical and management personnel, or require us to enter into or modify existing royalty or licensing agreements, any of which could significantly harm our business. Royalty or licensing agreements, if required, may not be available on terms acceptable to us, if at all. 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.

Intellectual Property Related Advantages

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

COMPETITION

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

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

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

existing products that have long histories of safe and effective use.

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

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

Monoclonal antibody companies and product candidates from certain biotechnology firms such as Genentech, Amgen, Medimmune, as well as Abgenix, Medarex, Cambridge Antibody Technology, HGSI and Protein Design Labs.

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

Gene therapy companies who are developing gene-based products in clinical trials. None of these products have yet been approved. Our competitors in this category may include Cell Genesys, which has different versions of the GVAX(R) cancer vaccine in Phase 1, Phase 2 and Phase 3 clinical studies; GenVec, which is working on gene-based therapies such as BIOBYPASS(R) for the treatment of coronary artery disease and a gene therapy approach to AMD; and Valentis, which is conducting pivotal clinical studies of VLTS 934 for the treatment of PAD and which may be competitive with Sangamo s program in this area; and VirxSys , a gene delivery company that is developing a treatment for HIV/AIDS.

Antisense therapeutics and RNA interference technology, or RNAi, which are two 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 numerous biotechnology companies including Isis, Sirna and Alnylam.

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

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

develop proprietary products;

obtain access to gene transfer technology on commercially reasonable terms;

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;

attract and retain scientific and product development personnel;

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

obtain required regulatory approvals; and

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

GOVERNMENT REGULATION

Before commencing clinical investigations in humans, we must submit to, and receive approval from, the U.S. Food and Drug Administration (FDA) of an Investigational New Drug (IND) Application. We filed a Phase 1 clinical protocol for review by the NIH RAC in the fourth quarter of 2004, an IND in January 2005, and intend to file a Phase 2 protocol for review by the FDA in 2006 for our first product candidate, SB-509, for the potential treatment of diabetic neuropathy. Our partner, Edwards Lifesciences, also submitted a Phase 1 clinical protocol for review by the NIH RAC in the fourth quarter of 2003 and filed the first ZFP Therapeutic IND application with the FDA in February 2004. We have not applied for regulatory approvals with respect to any of our other technologies or

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products under development. We anticipate that the research, development, and commercialization of any therapeutic products developed, either alone or with our strategic partners or collaborators, will be subject to extensive regulation in the United States and other countries.

Before marketing in the United States, any therapeutic or pharmaceutical products developed by us must undergo rigorous preclinical testing and clinical trials and an extensive regulatory clearance process implemented by the FDA under the federal Food, Drug and Cosmetic Act. The FDA regulates, among other things, the development, testing, manufacture, safety, efficacy, record keeping, labeling, storage, approval, advertising, promotion, sale, and distribution of biopharmaceutical products. The regulatory review and approval process, which includes preclinical testing and clinical trials of each product candidate, is lengthy, expensive, and uncertain. Securing FDA approval requires the submission of extensive preclinical and clinical data and supporting information 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.

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

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

We have hired personnel with expertise in regulatory affairs to assist us in obtaining appropriate regulatory approvals as required. In 2004 and 2005, we hired employees with experience in preclinical and clinical development of therapeutic programs and products. We also intend to work with our strategic partners and collaborators that have experience in regulatory affairs to assist us in obtaining regulatory approvals for collaborative products. See Risk Factors Our potential therapeutic products are subject to a lengthy and uncertain regulatory process, and if these potential products are not approved, we will not be able to commercialize those products and Regulatory approval, if granted, may be limited to specific uses or geographic areas which could limit our ability to generate revenues.

RESEARCH AND DEVELOPMENT EXPENSES

Over the past three fiscal years, research and development expenses have consisted primarily of salaries and related personnel expenses, laboratory supplies, allocated facilities costs, subcontracted research expenses, and expenses for patent prosecution, trademark registration and technology licenses. Research and development expenses were $11.4 million, $11.0 million and $10.2 million for 2005, 2004 and 2003, respectively. We believe that continued investment in research and development is critical to attaining our strategic objectives. We expect these expenses will increase significantly as we focus increasingly on development of ZFP Therapeutics. Specifically, in order to develop

ZFPs as commercially relevant therapeutics, we expect to expend additional resources for expertise in the manufacturing, regulatory affairs and clinical research aspects of ZFP Therapeutic development.

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EMPLOYEES

As of February 14, 2006, we had 62 full-time employees, all of which are located in Richmond, California. None of our employees are represented by a collective bargaining agreement, nor have we experienced work stoppages. We believe that our relations with our employees are good.

AVAILABLE INFORMATION

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

Item 1A. ***Risk Factors***

We have increased the focus of our research and development programs on human therapeutics, which may increase operating expenditures and the uncertainty of our business. We are increasing the emphasis and focus of our research and development activities on ZFP Therapeutics and have relatively fewer resources invested in our Enabling Technology programs. In the short term, this change in resource allocation may reduce our revenues and increase operating expenditures due to larger financial outlays to fund preclinical studies, manufacturing, and clinical research. The transition will also increase the visibility of our lead therapeutic programs and the potential impact on the stock price of news releases relating to these programs.

We are conducting proprietary research to discover ZFP Therapeutic product candidates. These programs increase our financial risk of product failure, may significantly increase our research expenditures, and may involve conflicts with our collaborators and strategic partners. Our proprietary research programs consist of research which is funded solely by the Company and where the Company retains exclusive rights to therapeutic products generated by the research. This is in contrast to certain of our research programs that may be funded by corporate partners and in which we may share rights to any resulting products. We have conducted proprietary research since inception, however, in the past year, our strategy has shifted toward placing greater emphasis on proprietary research and therapeutic development and we expect this trend will continue in 2006 as we initiate our first Phase 2 clinical trial and bring new ZFP Therapeutics into clinical trials. Conducting proprietary research programs may not generate corresponding revenue and may create conflicts with our collaborators or strategic partners. The implementation of this strategy will involve substantially greater business risks, the expenditure of significantly greater funds than our historic research activities and will require substantial commitments of time from our management and staff.

In addition, disagreements with our collaborators or strategic partners could develop 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 collaboration or strategic partnering agreements and negatively impact our relationship with existing collaborators and strategic partners, which could reduce our revenue and delay or terminate our product development.

We, and our partner, Edwards Lifesciences, have initiated Phase 1 clinical trials in our respective lead ZFP Therapeutic programs, and ZFP Therapeutics have never before been tested in humans. We have completed enrollment and treatment of the patients in the first of these trials of SB-509 for diabetic neuropathy and thus far have not observed any drug-related adverse events. However if our lead ZFP Therapeutic fails its initial safety study, it could reduce our ability to attract new investors and corporate partners. In January 2005, Sangamo filed an IND with the FDA for SB-509, a ZFP TF activator of VEGF-A, for the treatment of mild to moderate diabetic neuropathy. We have completed enrollment and treatment of a Phase 1, single blind, dose-escalation trial to measure the laboratory

and clinical safety of SB-509 and reported that we did not observe dose-limiting toxicity or any severe adverse drug-related events. We expect to present data from this trial in the first half of 2006 and to initiate a Phase 2 clinical trial of SB-509 in the second half of 2006. Edwards Lifesciences also filed an investigational new drug (IND) application with the U.S. Food and Drug Administration (FDA) on February 10, 2004 and initiated a Phase 1 clinical trial in humans in August, 2004 and a second in the first half of 2005. The first Phase 1 studies of a

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ZFP Therapeutic will be a highly visible test of the Company s ZFP Therapeutic approach. Since we have increased our focus on ZFP Therapeutic research and development, investors will increasingly assess the value of the Company s technology based on the continued progress of ZFP Therapeutic products into and through clinical trials. If the initial safety study of our lead therapeutic was halted due to safety concerns, this would negatively affect the value of the Company s stock.

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

We have limited experience in conducting clinical trials, and we may encounter unanticipated toxicity or adverse events or fail to demonstrate the efficacy, causing us to delay, suspend or terminate the development of our ZFP Therapeutics. Our ZFP Therapeutics may fail to show the desired safety and efficacy in initial clinical trials. Even if we successfully complete Phase 1 trials, the FDA will require additional Phase 2 and Phase 3 clinical testing which involves significantly greater resources, commitments and expertise that may require us to enter into a collaborative relationship with a pharmaceutical company that would assume responsibility for late-stage development and commercialization.

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 teminate the the development of a ZFP Therapeutics and if these potential products are not approved, we will not be able to commercialize those products. The FDA must approve any human therapeutic products before they 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 or our commercial partner must submit an Investigational New Drug (IND) application to the FDA. The FDA has 30 days to comment on the IND. If the FDA does not comment on the IND, we or our commercial partner may begin clinical trials.

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

Clinical trials:

- must be conducted in conformance with the FDA s good clinical practices ICH guidelines and other applicable regulations;
- must meet requirements for institutional review board 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 large numbers of test subjects; and

may be suspended by our 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 or the conduct of these trials.

Clinical trials are lengthy and are typically conducted in three sequential phases, but the phases may overlap or be combined. Each trial must be reviewed and approved by an independent ethics committee or institutional review board before it can begin. Phase 1 usually involves the initial introduction of the investigational drug into healthy

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volunteers or patients to evaluate certain factors, including its safety, dosage tolerance and, if possible, to gain an early indication of its effectiveness. 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 preliminarily the 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. Later clinical trials may fail to support the findings of earlier trials, which would delay, limit or prevent regulatory approvals.

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

We may not be able to find acceptable patients or may experience delays in enrolling patients for our clinical trials. The FDA or we may suspend our clinical trials at any time if either believes that we are exposing the subjects participating in these trials to unacceptable health risks. The FDA or institutional review boards and/or institutional biosafety committees at the medical institutions and healthcare facilities where we sponsor clinical trials may suspend any trial indefinitely if they find deficiencies in the conduct of these trials. The FDA and institutional review boards may also require large numbers of patients, and the FDA may require that we repeat a clinical trial.

The results of early Phase 1 trials are based on a small number of patients over a short period of time, and our success may not be indicative of results in a large number of patients or of long-term efficacy. The results in early phases of clinical testing are based upon limited numbers of patients and a limited follow-up period. For example, the results from the Phase 1 clinical trial of our ZFP Therapeutic, SB-509 product, are expected to be available in the first half of 2006. The primary end point of the trial is clinical and laboratory safety, however we expect to be able to collect some preliminary efficacy data. Typically, our Phase 1 clinical trials for indications of safety enroll less than 50 patients. We anticipate that our Phase 2 clinical trials for efficacy would typically enroll approximately 100 patients. Actual results with more data points may not confirm favorable results from our earlier stage 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. In addition, we do not yet know if early results will have a lasting effect. If a larger population of patients does not experience positive results, or if these results do not have a lasting effect, our products may not receive approval from the FDA. Failure to demonstrate the safety and effectiveness of our gene based products in larger patient populations could have a material adverse effect on our business that would cause our stock price to decline significantly.

We cannot predict whether or when we will obtain regulatory approval to commercialize our product candidates, therefore we cannot predict the timing of any future revenue from these product candidates. We cannot commercialize any of our product candidates to generate revenue until the appropriate regulatory authorities have reviewed and approved the applications for the product candidates. We cannot assure you 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.

Our gene regulation and gene modification technology is relatively new, and if we are unable to use this technology in all our intended applications, it would limit our revenue opportunities. Our technology involves a relatively new approach to gene regulation and gene modification. Although we have generated ZFP TFs for hundreds of gene

sequences, we have not created ZFP TFs for all gene sequences and may not be able do so, which could limit the usefulness of our technology. In addition, while we have demonstrated the function of engineered ZFP TFs in mammalian cell culture, yeast, insects, plants, and animals, we have not yet done so in humans, and the failure to do so could restrict our ability to develop commercially viable products. If we, and our collaborators or strategic partners, are unable to extend our results to new commercially important genes, experimental animal

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models, and human clinical studies, we may be unable to use our technology in all its intended applications. Also, delivery of ZFP TFs and ZFNs into cells and organisms, including humans, in these and other environments is limited by a number of technical hurdles, which we may be unable to surmount. This is a particular challenge for therapeutic applications of our technology that will require the use of gene transfer systems that may not be effective for the delivery of our ZFP TFs or ZFNs in a particular therapeutic application.

The expected value and utility of our ZFP TFs and ZFNs is in part based on our belief that the targeted or specific regulation of gene expression and targeted gene modification may enable us to develop a new therapeutic approach as well as to help scientists better understand the role of human, animal, and other genes in disease and to aid their efforts in drug discovery and development. We also believe that the regulation of gene expression and targeted gene insertion will have utility in agricultural applications. There is only a limited understanding of the role of specific genes in all these fields. Life sciences companies have developed or commercialized only a few products in any of these fields based on results from genomic research or the ability to regulate gene expression. We, our collaborators, or our strategic partners may not be able to use our technology to identify and validate drug targets or to develop commercial products in the intended markets.

We are currently engaged in the research and development of a new application of our technology platform: ZFP-mediated gene modification using ZFNs to effect either gene correction or gene disruption. Using this technique, Sangamo scientists have engineered ZFNs to cut DNA at a specific site within a target gene, and to then to either correct the adjacent sequences with newly synthesized DNA copied from an introduced DNA template, gene correction, or to rejoin the two ends of the break which frequently results in the disruption of the gene s function. In so doing, we are attempting to correct an abnormal or disease-related mutation or DNA sequence or to disrupt a gene that is involved in disease pathology. ZFP-mediated gene modification is at an early stage of development. Our scientists have shown ZFP-mediated gene modification to work in isolated cells; however, a significant amount of additional research will be needed before this technique can be evaluated in animals or plants and subsequently tested for applications in human healthcare and plant agriculture.

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

We do not currently have the infrastructure or capability to manufacture therapeutic products on a commercial scale. In order for us to commercialize these products directly, we would need to develop, or obtain through outsourcing arrangements, the capability to execute all of these functions. If we are unable to develop or otherwise obtain the requisite preclinical, clinical, regulatory, manufacturing, marketing, and sales capabilities, we would be unable to directly commercialize our therapeutics products which would limit our future growth.

Even if our technology proves to be effective, it still may not lead to commercially viable products. Even if our collaborators or strategic partners are successful in using our ZFP technology in drug discovery, protein production, therapeutic development, or plant agriculture, they may not be able to commercialize the resulting products or may decide to use other methods competitive with our technology. To date, no company has received marketing approval

or has developed or commercialized any therapeutic or agricultural products based on our technology. The failure of our technology to provide safe, effective, useful, or commercially viable approaches to the discovery and development of these products 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

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and the medical community. A number of additional factors may limit the market acceptance of products including the following:

rate of adoption by healthcare practitioners;

rate of a product s acceptance by the target population;

timing of market entry relative to competitive products;

availability of alternative therapies;

price of our product relative to alternative therapies;

availability of third-party reimbursement;

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

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

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

Our stock price is also influenced by public perception. 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 SCID, or whether the specific company s clinical trials were placed on hold in connection with these events.

Other potential adverse events in the field of gene therapy may occur in the future that could result in greater governmental regulation of our potential products and potential regulatory delays relating to the testing or approval of our potential products.

We are at the development phase of operations and may not succeed or become profitable. We began operations in 1995 and are in the early phases of ZFP Therapeutic product development. We have incurred significant losses and our net losses for the past three fiscal years ended 2005, 2004 and 2003 were $13.3 million, $13.8 million and $10.4 million, respectively. To date, our revenues have been generated from Enabling Technology collaborations, strategic partners, and federal government research grants. In 2005, we have placed more emphasis on higher-value therapeutic product development and related strategic partnerships. This shift in emphasis has the potential to increase the return on investment to our stockholders by allocating capital resources to higher value, therapeutic product development activities. At the same time, it increases our financial risk by increasing expenses associated with product development. In addition, the preclinical or clinical failure of any single product may have a significant effect on the actual or perceived value of our shares. Our business is subject to all of the risks inherent in the development of

a new technology, which include 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;

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

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

Commercialization of our technologies will depend, in part, on strategic partnering with other companies. If we are not able to find strategic partners in the future or our strategic partners do not diligently pursue product development efforts, we may not be able to develop our technologies or products, which could slow our growth and decrease our value. 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 those partners are unable or unwilling to advance our programs, or if they do not diligently pursue product approval, this may slow our progress and defer our revenues. Our partners may sublicense or abandon development programs or we may have disagreements with our partners, which would cause associated product development to slow or cease. There can be no assurance that we will be able to establish additional strategic collaborations for ZFP Therapeutic product development. We may require significant time to secure additional collaborations or strategic partners because we need to effectively market the benefits of our technology to these future collaborators and strategic partners, which use the time and efforts of research and development personnel and our management. Further, each collaboration or strategic partnering arrangement will involve the negotiation of terms that may be unique to each collaborator or strategic partner. These business development efforts may not result in a collaboration or strategic partnership.

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

Our existing strategic partnering agreements are based on the achievement of milestones. Under the strategic partnering agreements, we expect to receive revenue for the research and development of a ZFP Therapeutic product and based on achievement of specific milestones. Achieving these milestones will depend, in part, on the efforts of our strategic partner as well as our own. In contrast, our historic Enabling Technology collaborations only pay us to supply ZFP TFs for the collaborator s independent use, rather than for future results of the collaborator s efforts. If we, or any strategic partner, fail to meet specific milestones, then the strategic partnership may be terminated, which could decrease our revenues.

If our competitors develop, acquire, or market technologies or products that are more effective than ours, this would reduce or eliminate our commercial opportunity. Any products that we or our collaborators or strategic partners develop by using our ZFP technology platform will enter into highly competitive markets. Even if we are able to generate ZFP Therapeutics that are safe and effective for their intended use, competing technologies may prove to be more effective or less expensive, which, to the extent these competing technologies achieve market acceptance, will limit our revenue opportunities. In some cases, competing technologies have proven to be satisfactorily effective and less expensive, as has been the case with technologies competitive with our Enabling Technology(R). The effectiveness of these competing products has reduced the revenues generated by our Enabling Technology. Competing technologies may include other methods of regulating gene expression or modifying genes. ZFP TFs and ZFNs have broad application in the life sciences and compete with a broad array of new technologies and approaches

being applied to genetic research by many companies. Competing proprietary technologies with our product development focus include:

For ZFP Therapeutics:

small molecule drugs;

monoclonal antibodies;

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recombinant proteins;

gene therapy / cDNAs;

antisense; and

siRNA approaches

For our Enabling Technology Applications:

For protein production: gene amplification, meganucleases, insulator technology;

For target validation: antisense, siRNA; and

For plant agriculture: recombination approaches, mutagenesis approaches, meganucleases;

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

substantially greater capital resources than ours;

larger research and development staffs and facilities than ours; and

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

These organizations also compete with us to:

attract qualified personnel;

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

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

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

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, that would delay our ability to test our technology and would delay or terminate the development of potential products based on our ZFP technology. Further, our collaborators and strategic partners may elect not to develop products arising out of our collaborative and strategic partnering arrangements or to devote sufficient resources to the development, manufacturing, marketing, or sale of these products. If any of these events occur, we may not be able to develop our technologies or commercialize our products.

We anticipate continuing to incur operating losses for the next several years. If material losses continue for a significant period, we may be unable to continue our operations. We have generated operating losses since we began operations in 1995. The extent of our future losses and the timing of profitability are uncertain, and we expect to incur losses for the foreseeable future. We have been engaged in developing our ZFP TF technology since inception, which has and will continue to require significant research and development expenditures. In November 2005 we announced that we had completed a registered direct offering to institutional and strategic investors for a total of 5,080,000 shares of common stock at a price of $3.85 per share to the investors, resulting in net proceeds to Sangamo of approximately $18.2 million. To date, we have generated all other revenue from Enabling Technology collaborations, strategic partnering agreements, and federal government research grants. As of December 31, 2005, we had an accumulated deficit of approximately $110.4 million. We expect to incur losses for the foreseeable future. These losses will increase as we expand and extend our research and development activities into human therapeutic product development. If the time required to generate significant product revenues and achieve profitability is longer than we currently anticipate, we may not be able to sustain our operations.

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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 2007, we may seek additional sources of capital through equity or debt financing. In addition, as we focus our efforts on proprietary human therapeutics, we will need to seek FDA approval of potential products, a process that could cost in excess of $100 million per product. We cannot be certain that we will be able to obtain financing on terms acceptable to us, or at all. If adequate funds are not available, our business and our ability to develop our technology and ZFP Therapeutic products would be harmed.

Our stock price has been volatile and may continue to be volatile, which could result in substantial losses for investors. During the past two years, our common stock price has fluctuated significantly, ranging from a low of $3.46 to a high of $6.49 during the year ended December 31, 2005, and a low of $3.00 to a high of $8.02 during the year ended December 31, 2004. 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 the following factors, some of which are beyond our control:

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

Our common stock is thinly traded, which means large transactions in our common stock may be difficult to conduct in a short time frame. We have a low volume of daily trades in our common stock on the Nasdaq National Market. For example, the average daily trading volume in our common stock on the Nasdaq National Market over the ten-day trading period prior to February 1, 2006 was approximately 101,000 shares per day. Any large transactions in our common stock may be difficult to conduct and may cause significant fluctuations in the price of our common stock.

Failure to attract, retain, and motivate skilled personnel and cultivate key academic collaborations will delay our product development programs and our research and development efforts. We are a small company with 62 full-time employees as of February 14, 2006 and our success depends on our continued ability to attract, retain, and motivate highly qualified management and scientific personnel and our ability to develop and maintain important relationships with leading research and academic institutions and scientists. Competition for personnel and academic and other

research collaborations is intense. The success of our technology development programs depends on our ability to attract and retain highly trained personnel and we have experienced a rate of employee turnover that we believe is typical of emerging biotechnology companies. If we lose the services of personnel with the necessary skills, it could significantly impede the achievement of our research and development objectives. We are not presently aware of any plans of specific employees to retire or otherwise leave the company. If we fail to negotiate additional acceptable collaborations with academic and other research institutions and scientists, or if our existing collaborations are unsuccessful, our ZFP Therapeutic development programs may be delayed or may not succeed.

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If conflicts arise between us and our collaborators, strategic partners, scientific advisors, or directors, these parties may act in their self-interest, which may limit our ability to implement our strategies. If conflicts arise between our corporate or academic collaborators, strategic partners, or scientific advisors or directors and us, the other party may act in its self-interest, which may limit our ability to implement our strategies. Our license agreement with Edwards Lifesciences provides Edwards with worldwide, exclusive rights for ZFP Therapeutics for the activation of VEGF and VEGF receptors for the treatment and prevention of ischemic cardiovascular and vascular disease in humans. We have retained all rights to use our technology for all therapeutic applications of VEGF activation outside of the treatment and prevention of ischemic cardiovascular and vascular disease in humans. During the first quarter of 2005, Sangamo commenced a Phase 1 clinical trial for the treatment of diabetic neuropathy using a ZFP Therapeutic for the activation of VEGF. Edwards has stated that its rights include diabetic neuropathy and consequently our activities relating to diabetic neuropathy constitute a breach of the agreement. We strongly disagree with the Edwards assertion because diabetic neuropathy is a neurological disease and not an ischemic vascular disease and therefore is outside the scope of the Edwards license. Sangamo and Edwards are in discussions regarding this issue. Some of our academic collaborators and strategic partners are conducting multiple product development efforts within each area that is the subject of the collaboration with us. Our collaborators or strategic partners, however, may develop, either alone or with others, products in related fields that are competitive with the products or potential products that are the subject of these collaborations. Competing products, either developed by the collaborators or strategic partners or to which the collaborators or strategic partners have rights, may result in the withdrawal of partner support for our product candidates.

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

Because it is difficult and costly to protect our proprietary rights, and third parties have filed patent applications that are similar to ours, we cannot ensure the proprietary protection of our technologies and products. Our commercial success will depend in part on obtaining patent protection of our technology and successfully defending any of our patents which may be challenged. The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and can involve complex legal and factual questions. No consistent policy regarding the breadth of claims allowed in biotechnology patents has emerged to date. Accordingly, we cannot predict the breadth of claims allowed in patents we own or license.

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

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

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

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

- we or our licensors were the first to make the inventions covered by each of our pending patent applications;
- we or our licensors were the first to file patent applications for these inventions;
- the patents of others will not have an adverse effect on our ability to do business;

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others will not independently develop similar or alternative technologies or reverse engineer any of our products, processes or technologies;

any of our pending patent applications will result in issued patents;

any patents issued or licensed to us or our collaborators or strategic partners will provide a basis for commercially viable products or will provide us with any competitive advantages;

any patents issued or licensed to us will not be challenged and invalidated by third parties; or

we will develop additional products, processes or technologies that are patentable.

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

We cannot guarantee that third parties will not challenge our intellectual property. One of our licensed patents, European Patent No. 0 682 699, entitled Functional Domains in *Flavobacterium Okeanokoites* Restriction Endonuclease was granted on May 7, 2003 and forms the basis of Regional Phase patents in France, Germany, Great Britain, Ireland and Switzerland. The granted claims of the patent cover technologies used in our programs in targeted recombination and gene correction. On December 1, 2005 an interlocutory decision revoking this patent was issued by the European Patent Office. We have appealed this decision. If our appeal is ultimately unsuccessful, our ability to exclude potential competitors in the field of targeted recombination and gene correction in Europe may be limited. These developments apply only to Europe and do not affect our ability to practice our targeted recombination and gene correction programs in Europe. Moreover, we also hold licenses to six US patents to the technology covered by the opposed European patent, and hold licenses to related applications pending in Canada and Japan. Accordingly, any effects of the opposition, up to and including invalidation of the European patent, would be restricted to Europe and would have little, if any, material adverse effect on our business.

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.

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

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

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

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

Laws or public sentiment may limit the production of genetically modified agricultural products in the future, and these laws could reduce our partner s ability to sell these products. Genetically modified products are currently subject to public debate and heightened regulatory scrutiny, either of which could prevent or delay production of agricultural products. Effective as of October 1, 2005, we entered into a Research License and Commercial Option Agreement with Dow AgroSciences LLC (DAS), a wholly owned indirect subsidiary of Dow Chemical Corporation. Under this agreement, we will provide DAS with access to our proprietary ZFP technology and the exclusive right to use our ZFP technology to modify the genomes or alter the nucleic acid or protein expression of plant cells, plants, or plant cell cultures. The field-testing, production, and marketing of genetically modified plants and plant products are subject to federal, state, local, and foreign governmental regulation. Regulatory agencies administering existing or future regulations or legislation may not allow production and marketing of our genetically modified products in a timely manner or under technically or commercially feasible conditions. In addition, regulatory action or private litigation could result in expenses, delays, or other impediments to our product development programs or the commercialization of resulting products.

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

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

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

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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.

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, our certificate of incorporation and our bylaws and 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 certificate of incorporation:

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

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

limits who may call a special meeting of stockholders.

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

Insiders have substantial control over Sangamo and could delay or prevent a change in corporate control. The interest of management could conflict with the interest of our other stockholders. Our executive officers and directors beneficially own, in the aggregate, approximately 21% of our outstanding common stock. As a result, these stockholders, if they choose to act together, will be able to have a material impact on all matters requiring stockholder approval, including the election of directors and approval of significant corporate transactions. This could have the effect of delaying or preventing a change of control of Sangamo, which in turn could reduce the market price of our stock.

Item 1B. ***Unresolved Staff Comments***

None.

Item 2. ***Properties***

We currently lease approximately 22,000 square feet of research and office space located at 501 Canal Boulevard in Richmond, California. The lease expires in August of 2014. We believe the facilities we currently lease are sufficient for the foreseeable future.

Item 3. ***Legal Proceedings***

We are not a party to any material litigation.

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Item 4. ***Submission of Matters to a Vote of Security Holders***

Not applicable.

PART II

Item 5. ***Market for the Registrant s Common Stock, Related Stockholder Matters and Issuer Purchases of Equity Securities***

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

Information regarding Sangamo s equity compensation plans is incorporated by reference to Item 12 of this Form 10-K, which incorporates by reference the information set forth in the section entitled Equity Compensation Plans in Sangamo s proxy statement to be filed pursuant to Regulation 14A within 120 days of Sangamo s fiscal year end.

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 National Market were as follows:

Common Stock

	Price	
	High	**Low**
Year ended December 31, 2004		
First Quarter	$ 8.02	$ 5.28
Second Quarter	$ 6.87	$ 5.60
Third Quarter	$ 5.85	$ 3.00
Fourth Quarter	$ 6.00	$ 3.75
Year ended December 31, 2005		
First Quarter	$ 6.49	$ 3.51
Second Quarter	$ 4.20	$ 3.46
Third Quarter	$ 4.95	$ 3.52
Fourth Quarter	$ 4.86	$ 3.71

Holders

As of February 14, 2006 there were approximately 101 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 and other financial institutions.

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

From time to time our directors, executive officers and other insiders may adopt stock trading plans pursuant to Rule 10b5-1 of the Securities Exchange Act of 1934, as amended. These plans are established to allow individuals to diversify their investment portfolio while avoiding conflicts of interest or the appearance of any such conflict that might arise from their positions with the company. Starting in the first quarter of 2002, one of our officers, Edward O. Lanphier II, President and CEO, and one of our directors, have made periodic sales of the Company s stock pursuant to such plans.

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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,				
	2005	2004	2003	2002	2001
	(In thousands, except per share data)				
Statement of Operations Data:					
Total revenues	$ 2,484	$ 1,315	$ 2,579	$ 4,343	$ 4,885
Operating expenses:					
Research and development	11,419	11,046	10,187	12,213	12,952
General and administrative	4,512	4,256	3,594	3,815	3,638
Stock-based compensation(1)	301	663	567	1,499	3,674
Restructuring charge				371	
Goodwill impairment				15,250	
Patent impairment				2,760	
Acquired in-process research and development					13,062
Total operating expenses	16,232	15,965	14,348	35,908	33,326
Loss from operations	(13,748)	(14,650)	(11,769)	(31,565)	(28,441)
Interest income, net	850	620	752	1,366	3,192
Other income/(expense)	(395)	212	584	435	
Net loss	$ (13,293)	$ (13,818)	$ (10,433)	$ (29,764)	$ (25,249)
Basic and diluted net loss per common share	$ (0.51)	$ (0.55)	$ (0.42)	$ (1.22)	$ (1.09)
Shares used in computing basic and diluted net loss per common share	25,855	25,126	24,811	24,493	23,120

	Year Ended December 31,				
	2005	2004	2003	2002	2001
	(In thousands)				
(1) Stock-Based Compensation:					

Research and development stock-based compensation	$ 300	$ 649	$ 451	$ 1,150	$ 2,562
General and administrative stock-based compensation	1	14	116	349	1,112
Total stock-based compensation	$ 301	$ 663	$ 567	$ 1,499	$ 3,674

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	December 31,				
	2005	2004	2003	2002	2001
	(In thousands)				
Balance Sheet Data:					
Cash, cash equivalents, marketable securities, and interest receivable	$ 47,174	$ 33,520	$ 44,343	$ 52,575	$ 62,560
Working capital	41,668	32,028	43,714	52,115	61,102
Total assets	48,983	34,725	46,232	56,227	85,017
Accumulated deficit	(110,408)	(97,115)	(83,297)	(72,864)	(43,100)
Total stockholders equity	37,814	32,377	44,661	54,246	82,349

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Item 7. ***Management s Discussion and Analysis of Financial Condition and***

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 were incorporated in June 1995. From our inception through December 31, 2005, our activities related primarily to establishing and operating a biotechnology research and development organization and developing relationships with our corporate collaborators. Our scientific and business development endeavors currently focus on the engineering of novel zinc finger DNA binding proteins (ZFPs) for the regulation and modification of genes. We have incurred net losses since inception and expect to incur losses in the future as we continue our research and development activities. To date, we have funded our operations primarily through the issuance of equity securities, borrowings, payments from federal government research grants and from corporate collaborators and strategic partners. As of December 31, 2005, we had an accumulated deficit of $110.4 million.

Our revenues have consisted primarily of revenues from our corporate partners for ZFP TFs and ZFNs, contractual payments from strategic partners for research programs and research milestones, and Federal government 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 fundings will continue beyond their initial terms.

In 2005, we have placed more emphasis on higher-value therapeutic product development and related strategic partnerships and less emphasis on our Enabling Technology collaborations. We believe this shift in emphasis has the potential to increase the return on investment to our stockholders by allocating capital resources to higher value, therapeutic product development activities. At the same time, it may reduce our revenues over the next several years and it increases our financial risk by increasing expenses associated with product development. We have filed an Investigational New Drug (IND) application with the U.S. Food and Drug Administration (FDA) and have initiated a Phase 1 clinical trial of a ZFP Therapeutic in patients with diabetic neuropathy during the first quarter of 2005. Development of novel therapeutic products is costly and is subject to a lengthy and uncertain regulatory process by the FDA. Our future products are gene-based therapeutics. Adverse events in both our own clinical program and other programs in gene therapy may have a negative impact on regulatory approval, the willingness of potential commercial partners to enter into agreements and the perception of the public.

Research and development expenses consist primarily of salaries and related personnel expenses, laboratory supplies, allocated facilities costs, subcontracted research expenses, and expenses for patent prosecution, trademark registration and technology licenses. Research and development costs incurred in connection with collaborator-funded activities are expensed as incurred. We believe that continued investment in research and development is critical to attaining our

strategic objectives. We expect these expenses will increase significantly as we focus increasingly on development of ZFP Therapeutics. The Company is also developing zinc finger nucleases (ZFNs) for therapeutic gene correction and therapeutic gene modification as a treatment and possible cure for certain monogenic and infectious diseases. Additionally, in order to develop ZFP TFs and ZFNs as commercially relevant therapeutics, we expect to expend additional resources for expertise in the manufacturing, regulatory affairs and clinical research aspects of biotherapeutic development.

General and administrative expenses consist primarily of salaries and related personnel expenses for executive, finance and administrative personnel, professional fees, allocated facilities costs and other general corporate

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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.

Critical Accounting Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates. Sangamo believes the following critical accounting policies have significant effect in the preparation of our consolidated financial statements.

Revenue Recognition

In accordance with Staff Accounting Bulletin No. 104, Revenue Recognition, revenue from research activities made under strategic partnering agreements is 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 collectibility is reasonably assured. Amounts received under such agreements are deferred until the above criteria are met and the research services are performed. Sangamo s federal government 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 research expenses are incurred. Grant reimbursements are typically received on a quarterly basis and are subject to the issuing agency s right of audit.

Sangamo recognizes revenue from its Enabling Technology collaborations when ZFP-based products are delivered to the collaborators, persuasive evidence of an agreement exists, there are no unfulfilled obligations, the price is fixed and determinable, and collectibility is reasonably assured. Generally, Sangamo receives partial payments from these collaborations prior to the delivery of ZFP-based products and the recognition of these revenues is deferred until the ZFP-based products are delivered, the risk of ownership has passed to the collaborator and all performance obligations have been satisfied. Upfront or signature payments received upon the signing of an Enabling Technology agreement are generally recognized ratably over the applicable period of the agreement or as ZFP-based products are delivered.

Milestone payments under research, partnering, or licensing agreements are recognized as revenue upon the achievement of mutually agreed upon milestones, provided that (i) the milestone event is substantive and its achievement is not reasonably assured at the inception of the agreement, and (ii) there are no further significant performance obligations associated with the milestone payment.

In accordance with Emerging Issues Task Force Issue No. 00-21, Revenue Arrangements with Multiple Deliverables, revenue arrangements entered into after June 15, 2003, that include multiple deliverables, are divided into separate units of accounting if the deliverables meet certain criteria, including whether the fair value of the delivered items can be determined and whether there is evidence of fair value of the undelivered items. In addition, the consideration is allocated among the separate units of accounting based on their fair values, and the applicable revenue recognition criterion is considered separately for each of the separate units of accounting.

Stock-Based Compensation

Sangamo accounts for employee and director stock options using the intrinsic value method in accordance with Accounting Principles Board Opinion No. 25, Accounting for Stock Issued to Employees (APB 25) and has adopted the disclosure-only alternative of Financial Accounting Standards Board Statement No. 123, Accounting for

Stock-Based Compensation (FAS 123). Stock options granted to non-employees, including Scientific Advisory Board Members, are accounted for in accordance with Emerging Issues Task Force Issue No. 96-18, Accounting for Equity Instruments That Are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services, which requires the value of such options to be measured and compensation expense to be recorded as they vest over a performance period. The fair value of such options is determined using

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the Black-Scholes model. Pursuant to FAS 123, as amended by FAS 148, Accounting for Stock-Based Compensation Transition and Disclosure, the effect on net loss and related net loss per share has been calculated, had compensation cost for stock-based compensation plans been determined based upon the fair value method prescribed under FAS 123 (See Note 1 Organization and Summary of Significant Accounting Policies).

Results of Operations

Years Ended December 31, 2005, 2004 and 2003

Total Revenues

	Year Ended December 31,							
	2005	2004	Change	% Change	2004	2003	Change	% Change
	(In thousands, except percentage values)							
Revenues:								
Collaboration agreements	$ 1,832	$ 947	$ 885	93%	$ 947	$ 2,205	$ (1,258)	(57)%
Federal government research grants	652	368	284	77%	368	374	(6)	(2)%
Total revenues	$ 2,484	$ 1,315	$ 1,169	89%	$ 1,315	$ 2,579	$ (1,264)	(49)%

We are increasing the emphasis of our research and development activities on ZFP Therapeutics. Even with this change in resource allocation, we anticipate increasing revenues over the next several years primarily related to our Research License and Commercial Option Agreement with Dow AgroSciences LLC (DAS), a wholly owned indirect subsidiary of Dow Chemical Corporation.

Total revenues consisted of revenues from collaboration agreements, strategic partnerships and federal government research grants. Revenues from our corporate collaboration and strategic partnering agreements were $1.8 million in 2005, compared to $947,000 in 2004, and $2.2 million in 2003. The increase in 2005 from 2004 was principally attributable to increased revenues of approximately $748,000 related to our research collaboration agreement with Pfizer, increased revenues of approximately $677,000 in connection with our Research License and Commercial Option Agreement with DAS, and increased revenues of approximately $280,000 in connection with our collaboration in the field of regenerative medicine with LifeScan. These increases were partially offset by decreased revenues of $615,000 from our therapeutics partnership with Edwards Lifesciences Corporation (Edwards), as well as lower revenues of approximately $100,000 associated with other Enabling Technology collaborations. The decreased revenue from Edwards is due to the submission of the first IND by Edwards for a licensed product under the agreement with Sangamo. The decrease in 2004 from 2003 was principally attributable to decreased revenues of approximately $915,000 from our therapeutics partnership with Edwards, due to completion of our preclinical research and Edwards payments for those activities under the agreement, as well as decreased revenues of $343,000 associated with other Enabling Technology collaborations. Federal government research grant revenues were $652,000 in 2005, $368,000 in 2004, and $374,000 in 2003. The increase in 2005 over 2004 and 2003 was primarily attributable to increased revenue of $352,000 in connection with our Advanced Technology Program grant awarded by the National Institute of Standards and Technology. During the fourth quarter of 2005, the Company concluded that, since the inception, revenues related to this grant had been under-recorded by $254,000. A one-time adjustment for this amount was recorded during the fourth quarter of 2005 and is the primary reason for the increased federal government research grant revenues in 2005 as compared to 2004 and 2003. We plan to continue to apply for federal

government research grants.

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Operating Expenses

	Year Ended December 31,							
	2005	2004	Change	% Change	2004	2003	Change	% Change
	(In thousands, except percentage values)							
Operating expenses:								
Research and development	$ 11,419	$ 11,046	$ (373)	(3)%	$ 11,046	$ 10,187	$ (859)	(8)%
General and administrative	4,512	4,256	(256)	(6)%	4,256	3,594	(662)	(18)%
Stock-based compensation	301	663	362	55%	663	567	(96)	(17)%
Total operating expenses	$ 16,232	$ 15,965	$ (267)	(2)%	$ 15,965	$ 14,348	$ (1,617)	(11)%

Research and development expenses

Over the past three fiscal years, research and development expenses have consisted primarily of salaries and related personnel expenses, laboratory supplies, allocated facilities costs, subcontracted research expenses, and expenses for patent prosecution, trademark registration and technology licenses. 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 ZFP Therapeutic product candidates into clinical trials. To the extent we collaborate with others with respect to clinical trials, increases in research and development expenses may be reduced or avoided.

Research and development expenses were $11.4 million in 2005, compared to $11.0 million in 2004 and $10.2 million in 2003. The increase in 2005 from 2004 was principally due to increased expenses associated with our Phase 1 clinical trial in patients with diabetic neuropathy of approximately $577,000, increased expenses for laboratory supplies of approximately $466,000, increased external research expenses of approximately $406,000 and increased consulting expenses of approximately $209,000. This was partially offset by decreased expenses associated with pre-clinical studies of $915,000 and facilities of approximately $286,000 and $286,000, respectively. The decrease in facility-related expenses was primarily caused by decreased depreciation expense associated with laboratory equipment. The increase of $859,000 in 2004 from 2003 was principally due to pre-clinical studies and manufacturing costs of $1.8 million in connection with our diabetic neuropathy program. This was partially offset by decreased expenses for salaries and related benefits of $687,000, due to lower headcount, and laboratory supplies of $343,000.

Our current research and development programs are focused on the advancement of our ZFP TF technology for several potential applications. Among these are ZFP Therapeutics for cardiovascular disease, neurological disorders, cancer and monogenic diseases, ZFP-engineered cell lines, protein production and ZFP TFs and ZFNs for applications in agricultural biotechnology.

Below is a summary of our programs partially funded by collaborators and the development phase of the leading application:

Program	Collaborator	Stage
ZFP Therapeutics	Edwards	Clinical
	Dow Agrosciences	Research

ZFP technology to modify the genomes or alter the protein expression of plant cells, plants, or plant cell cultures		
ZFP-engineered cell lines for the manufacture of protein pharmaceuticals	Pfizer	Research/Marketing
ZFP TF-engineered cell lines for the treatment of diabetes	LifeScan	Research

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Below is a summary of our programs funded internally and the development stage of the leading application:

Internal Programs

Program	Stage
ZFP Therapeutics	Clinical/Preclinical/ Research
ZFP TF-engineered cell lines for the manufacture of protein pharmaceuticals	Research
Agricultural biotechnology	Research

Due to the early stage of the Company s various internal research and development projects, the Company does not track costs associated with its internal projects on a project-by-project basis. 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 technology is relatively new, and if we are unable to use this technology in all our intended applications, it would limit our revenue opportunities.

General and administrative expenses

General and administrative expenses consist primarily of salaries and related personnel expenses for executive, finance and administrative personnel, professional fees, allocated facilities costs 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 $4.5 million during 2005, $4.3 million in 2004 and $3.6 million in 2003. The increase of $256,000 was principally due to increased salary and benefit expenses of approximately $394,000, partially offset by decreased expenses associated with corporate communications of approximately $108,000. The increase of $662,000 in 2004 from 2003 was principally due to increased expenses in connection with programs for compliance with Section 404 of the Sarbanes-Oxley Act of 2002, the related regulations regarding our required assessment of our internal controls over financial reporting and our external auditors audit of that assessment of approximately $470,000 as well as increased expenses of $110,000 related to corporate communications.

Stock-based compensation

Sangamo accounts for employee and director stock options using the intrinsic value method in accordance with Accounting Principles Board Opinion No. 25, Accounting for Stock Issued to Employees (APB 25) and has adopted the disclosure-only alternative of Financial Accounting Standards Board Statement No. 123, Accounting for Stock-Based Compensation (FAS 123). Stock options granted to non-employees, including Scientific Advisory Board Members, are accounted for in accordance with Emerging Issues Task Force Issue No. 96-18, Accounting for Equity Instruments That Are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services, which requires the value of such options to be measured and compensation expense to be recorded as they vest over a performance period. The fair value of such options is determined using the Black-Scholes model.

Stock-based compensation expenses were $301,000 for 2005, $663,000 for 2004 and $567,000 related to 2003. The decrease in 2005 from 2004 was attributable to lower non-employee stock-based compensation expense. The increase in 2004 from 2003 of $96,000 was attributable to higher non-employee stock-based compensation expense.

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Interest income, net

	Year Ended December 31,							
	2005	2004	Change	% Change	2004	2003	Change	% Change
	(In thousands, except percentage values)							
Interest income, net	$ 850	$ 620	$ 230	37%	$ 620	$ 752	$ (132)	(18)%

Interest income, net

Net interest income was $850,000 in 2005, as compared to $620,000 in 2004, and $752,000 in 2003. The increase in 2005 from 2004 is related to interest earned on higher average cash and investment balances. The decrease in 2004 from 2003 is related to interest earned on lower average cash and investment balances.

Other income/(expense)

	Year Ended December 31,							
	2005	2004	Change	% Change	2004	2003	Change	% Change
	(In thousands, except percentage values)							
Other income/ (expense)	$ (395)	$ 212	$ (607)	(286)%	$ 212	$ 584	$ (372)	(64)%

Other income/(expense)

During 2005, other expense of $395,000 was comprised of a net loss on foreign currency translation of $374,000 and an other than temporary loss on our marketable securities of $21,000. During 2004 other income of $212,000 was comprised of a net gain on foreign currency translation of $261,000 and an insurance settlement of $22,000, partially offset by an other than temporary loss on our marketable securities of $71,000. During 2003, other income of $584,000 was principally comprised of a net gain on foreign currency translation of $298,000, an insurance settlement of $180,000 related to a equipment shipping claim and a research and development credit of $112,000.

We incurred net operating losses in 2005, 2004 and 2003, and consequently did not pay any federal or state income taxes.

Liquidity and Capital Resources

Since inception, we have financed our operations primarily through the sale of equity securities, payments from corporate collaborators, federal government research grants and financing activities such as a bank line of credit. As of December 31, 2005, we had cash, cash equivalents, investments and interest receivable totaling $47.2 million.

Net cash used in operating activities was $4.1 million in 2005, $10.2 million in 2004, and $7.4 million in 2003. In all periods, net cash used in operating activities was primarily due to funding of net operating losses. During 2005, the use of cash related to our net operating loss of $13.3 million and net increases in asset balances of $408,000. This was partially offset by net increases in liability balances of $8.8 million, principally due to an increase in deferred revenue

of $7.2 million, primarily related to the receipt of a license payment of $7.5 million during the fourth quarter of 2005 per the terms of the Research License and Commercial Option Agreement with DAS. Other offsets to our net operating loss were non-cash charges of $536,000 and amortization on investments of $214,000. During 2004, the use of cash related to the net operating loss of $13.8 million, partially offset by non-cash charges and net increases in asset balances of $2.8 million and by amortization on investments of $868,000. During 2003, the use of cash related to the net operating loss of $10.4 million, partially offset by non-cash charges and net increases in asset balances of $1.8 million and by amortization on investments of $1.1 million.

Net cash provided by (used in) investing activities was $(4.4) million in 2005, $8.4 million in 2004 and $(623,000) in 2003. Cash was used during these periods to purchase investments and property and equipment and was offset by the maturities and sale of available-for-sale securities.

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Net cash provided by financing activities $18.4 million in 2005, $553,000 in 2004 and $227,000 in 2003. During 2005, the company completed a registered direct offering to institutional and strategic investors for a total of 5,080,000 shares of common stock at a price of $3.85 per share to the investors, resulting in net proceeds to Sangamo of approximately $18.2 million. All other cash provided by financing activities for 2005, 2004 and 2003 was solely related to proceeds from issuance of common stock related to stock options exercises.

While we expect our rate of cash usage to increase in the future, in particular, in support of our product development endeavors, we believe that the available cash resources, funds received from corporate collaborators, strategic partners and federal government research grants will be sufficient to finance our operations through 2007. We may need to raise additional capital to fund our ZFP Therapeutic development activities. Additional capital may not be available in terms acceptable to us, or at all. If adequate funds are not available, our business and our ability to develop our technology and our ZFP Therapeutic products would be harmed.

There is no provision for income taxes because we have incurred losses. As of December 31, 2005, Sangamo had net operating loss carryforwards for federal income tax purposes of approximately $62.7 million, which expire in the years 2010 through 2025. The Company also has state operating loss carryforwards of approximately $28.3 million, which expire in the years 2006 through 2015. The Company also has federal and state research and development tax credits of $1.8 million and $1.9 million, respectively. The federal research credits will begin to expire in the year 2018 through 2025 and the state research credits have no expiration date. Utilization of the Company s net operating loss may be subject to substantial annual limitation due to the ownership change limitations provided by the Internal Revenue Code and similar state provisions. Such an annual limitation could result in the expiration of the net operating loss before utilization.

Contractual Obligations and Commercial Commitments

As of December 31, 2005 we had contractual obligations and commercial commitments as follows (in thousands):

		Payments Due by Period			
Contractual Obligations	**Total**	**Less than 1 Year**	**1-3 Years**	**3-5 Years**	**More than 5 Years**
Operating leases	$ 4,139	$ 433	$ 1,368	$ 1,473	$ 865
License obligations	1,436	315	1,121		
Total contractual obligations	$ 5,575	$ 748	$ 2,489	$ 1,473	$ 865

Operating leases consist of base rents for facilities we occupy in Richmond, California. License obligations consist of ongoing license maintenance fees, milestones and royalties due from sales of ZFP TFs.

Recent Accounting Pronouncements

In November 2005, the FASB issued FSP FAS 115-1 and FAS 124-1, The Meaning of Other-Than-Temporary Impairment and Its Application to Certain Investments (FSP FAS 115-1), which provides guidance on determining when investments in certain debt and equity securities are considered impaired, whether that impairment is other-than-temporary, and on measuring such impairment loss. FSP FAS 115-1 also includes accounting considerations subsequent to the recognition of an other-than temporary impairment and requires certain disclosures

about unrealized losses that have not been recognized as other-than-temporary impairments. FSP FAS 115-1 is required to be applied to reporting periods beginning after December 15, 2005. We are required to adopt FSP FAS 115-1 in the first quarter of 2006. We do not expect the adoption of this statement will have a material impact on our results of operations or financial condition.

In June 2005, the FASB issued SFAS No. 154, *Accounting Changes and Error Corrections*, a replacement of APB No. 20, *Accounting Changes*, and SFAS No. 3, *Reporting Accounting Changes in Interim Financial Statements.* SFAS No. 154 changes the requirements for accounting for and reporting a change in accounting principle. Previously, most voluntary changes in accounting principles required recognition via a cumulative effect adjustment within the net income of the period of the change. SFAS No. 154 requires retrospective application to prior periods financial statements unless it is impracticable to determine either the period-specific effects or the

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cumulative effect of the change. SFAS No. 154 is effective for accounting changes made in fiscal years beginning after December 15, 2005; however, this statement does not change the transition provisions of any existing accounting pronouncements. The Company does not believe the adoption of SFAS No. 154 will have a material effect on its consolidated financial position, results of operations or cash flows.

In December 2004, the Financial Accounting Standards Board, or FASB, issued a revision of Financial Accounting Standards No. 123, or SFAS 123R, which requires all share-based payments to employees and directors, including grants of employee stock options, to be recognized in the income statement based on their values. We expect to calculate the value of share-based payments under SFAS 123R on a basis substantially consistent with the fair value approach of SFAS 123. We will adopt SFAS 123R in our fiscal quarter beginning January 1, 2006, using the modified prospective method. We expect the adoption of SFAS 123R will have a material impact on our results of operations in that fiscal quarter and in each subsequent quarter, although it will have no impact on our overall liquidity. We cannot reasonably estimate the impact of adoption because it will depend on levels of share-based payments granted in the future as well as certain assumptions that can materially affect the calculation of the value share-based payments to employees and directors. However, had we adopted SFAS 123R in prior periods, the impact of the standard would have approximated the impact of SFAS 123 as described in the disclosure of pro forma net loss and pro forma loss per common share in *Note 1 of Notes to Consolidated Financial Statements* included under Item 8 of this Annual Report on Form 10-K.

Item 7A. ***Quantitative and Qualitative Disclosures about Market Risk***

Our exposure to market risk for changes in interest rates relates primarily to our cash equivalents and investments. The investments are available-for-sale. We do not use derivative financial instruments in our investment portfolio. We attempt to ensure the safety and preservation of our invested funds by limiting default and market risks. Our cash and investments policy emphasizes liquidity and preservation of principal over other portfolio considerations. We select investments that maximize interest income to the extent possible within these guidelines. We invest excess cash in securities with different maturities to match projected cash needs and limit concentration of credit risk by diversifying our investments among a variety of high credit-quality issuers. We mitigate default risk by investing in only investment-grade securities. The portfolio includes marketable securities with active secondary or resale markets to ensure portfolio liquidity. All investments have a fixed interest rate and are carried at market value, which approximates cost. If market interest rates were to increase by one percent from December 31, 2005, the fair value of our portfolio would decline by less than $100,000. The modeling technique used measures the change in fair values arising from an immediate hypothetical shift in market interest rates and assumes ending fair values include principal plus accrued interest. We recognized a loss on foreign currency translation of $374,000 in 2005 and gains on foreign currency translation of $261,000 and $298,000 for 2004 and 2003, respectively.

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Item 8. ***Financial Statements and Supplementary Data***

SANGAMO BIOSCIENCES, INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

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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, 2005 and 2004, and the related consolidated statements of operations, stockholders equity, and cash flows for each of the three years in the period ended December 31, 2005. These financial statements are the responsibility of the Company s management. Our responsibility is to express an opinion on these financial statements based on our audits.

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

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of Sangamo Biosciences, Inc. at December 31, 2005 and 2004, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2005, in conformity with U.S. generally accepted accounting principles.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the effectiveness of Sangamo Biosciences Inc. s internal control over financial reporting as of December 31, 2005, based on the criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated March 13, 2006 expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP

Palo Alto, California
March 13, 2006

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders
Sangamo BioSciences, Inc.

We have audited management s assessment, included in the accompanying Management s Report on Internal Control over Financial Reporting included in Item 9A, that Sangamo BioSciences, Inc. maintained effective internal control over financial reporting as of December 31, 2005, based on criteria established in Internal Control Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (the COSO criteria). The management of Sangamo BioSciences, Inc. is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting. Our responsibility is to express an opinion on management s assessment and an opinion on the effectiveness of 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, evaluating management s assessment, testing and evaluating the design and operating effectiveness of internal control, 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, management s assessment that Sangamo BioSciences, Inc. maintained effective internal control over financial reporting as of December 31, 2005, is fairly stated, in all material respects, based on the COSO criteria. Also, in our opinion, Sangamo BioSciences, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2005, 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, 2005 and 2004, and the related consolidated statements of operations, stockholders equity, and cash flows for each of the three years in the period ended December 31, 2005 and our report dated March 13, 2006 and expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP

Palo Alto, California
March 13, 2006

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SANGAMO BIOSCIENCES, INC.

CONSOLIDATED BALANCE SHEETS

	December 31,	
	2005	2004
	(In thousands, except share and per share amounts)	
ASSETS		
Current assets:		
Cash and cash equivalents	$ 18,507	$ 8,626
Marketable securities	28,449	24,634
Interest receivable	218	260
Accounts receivable, net of allowance for doubtful accounts of $0 and $85,000 for 2005 and 2004, respectively	971	569
Prepaid expenses	317	287
Total current assets	48,462	34,376
Property and equipment, net	472	318
Other assets	49	31
Total assets	$ 48,983	$ 34,725
LIABILITIES AND STOCKHOLDERS EQUITY		
Current liabilities:		
Accounts payable and accrued liabilities	$ 1,534	$ 906
Accrued compensation and employee benefits	933	657
Deferred revenue	4,327	785
Total current liabilities	6,794	2,348
Deferred revenue, non-current portion	4,375	
Total liabilities	11,169	2,348
Commitments and contingencies		
Stockholders equity:		
Common stock, $0.01 par value; 80,000,000 shares authorized, 30,570,912 and 25,271,059 shares issued and outstanding at December 31, 2005 and 2004, respectively	148,162	129,482
Accumulated deficit	(110,408)	(97,115)
Accumulated other comprehensive income	60	10
Total stockholders equity	37,814	32,377
Total liabilities and stockholders equity	$ 48,983	$ 34,725

See accompanying Notes to Consolidated Financial Statements.

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SANGAMO BIOSCIENCES, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS

	Year Ended December 31,		
	2005	2004	2003
	(In thousands, except per share amounts)		
Revenues:			
Collaboration agreements	$ 1,832	$ 947	$ 2,205
Federal government research grants	652	368	374
Total revenues	2,484	1,315	2,579
Operating expenses:			
Research and development (excludes $300, $649 and $451 of stock-based compensation expense for 2005, 2004 and 2003, respectively)	11,419	11,046	10,187
General and administrative (excludes $1, $14 and $116 of stock-based compensation expense for 2005, 2004 and 2003, respectively)	4,512	4,256	3,594
Stock-based compensation	301	663	567
Total operating expenses	16,232	15,965	14,348
Loss from operations	(13,748)	(14,650)	(11,769)
Interest income, net	850	620	752
Other income/(expense)	(395)	212	584
Net loss	$ (13,293)	$ (13,818)	$ (10,433)
Basic and diluted net loss per share	$ (0.51)	$ (0.55)	$ (0.42)
Shares used in computing basic and diluted net loss per share	25,855	25,126	24,811

See accompanying Notes to Consolidated Financial Statements.

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SANGAMO BIOSCIENCES, INC.

CONSOLIDATED STATEMENT OF STOCKHOLDERS EQUITY

	Common Stock		Deferred Stock	Accumulated	Accumulated Other Comprehensive	Total Stockholders
	Shares	Amount	Compensation	Deficit	Income	Equity
Balances at December 31, 2002	24,740,713	$ 127,234	$ (231)	$ (72,864)	$ 107	$ 54,246
Issuance of common stock upon exercise of options, net of repurchases	71,578	14				14
Issuance of common stock in connection with license agreement	25,000	130				130
Issuance of common stock under employee stock purchase plan	116,952	213				213
Amortization of deferred stock compensation			215			215
Vesting of non-qualified stock options		388				388
Reversal of deferred compensation due to employee terminations		(52)	15			(37)
Comprehensive loss:						
Unrealized loss on investments					(81)	(81)
Other than temporary loss					6	6
Net loss				(10,433)		(10,433)
Comprehensive loss						(10,508)
Balances at December 31, 2003	24,954,243	127,927	(1)	83,297	32	44,661
Issuance of common stock upon exercise of options, net of repurchases	120,740	294				294
Issuance of common stock in connection with license agreement	62,500	340				340
Issuance of common stock under employee stock purchase plan	133,576	259				259
			1			1

Amortization of deferred stock compensation						
Vesting of non-qualified stock options		662				662
Comprehensive loss:						
Unrealized loss on investments					(93)	(93)
Other than temporary loss					71	71
Net loss				(13,818)		(13,818)
Comprehensive loss						(13,840)
Balances at December 31, 2004	25,271,059	129,482		(97,115)	10	32,377
Issuance of common stock in connection with registered direct offering and upon exercise of stock options	5,218,239	18,115				18,115
Issuance of common stock under employee stock purchase plan	81,614	264				264
Vesting of non-qualified stock options		301				301
Comprehensive loss:						
Unrealized loss on investments					29	(29)
Other than temporary loss					21	21
Net loss				(13,293)		(13,293)
Comprehensive loss						(13,301)
Balances at December 31, 2005	30,570,912	$ 148,162	$	$ (110,408)	$ 60	$ 37,814

See accompanying Notes to Consolidated Financial Statements.

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SANGAMO BIOSCIENCES, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

	Year Ended December 31,		
	2005	2004	2003
	(In thousands)		
Operating activities:			
Net loss	$ (13,293)	$ (13,818)	$ (10,433)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation	274	611	847
Amortization of premium/discount on investment	214	868	1,145
Net (gain) loss on disposal of property and equipment			(112)
Realized loss on investment	21	71	6
Issuance of common stock in connection with license agreement		340	130
Amortization of deferred stock compensation		1	178
Other stock-based compensation	301	662	389
Forgiveness of notes receivable			188
Changes in operating assets and liabilities:			
Interest receivable	42	228	(56)
Accounts receivable	(402)	89	440
Prepaid expenses and other assets	(48)	7	248
Accounts payable and accrued liabilities	693	91	(122)
Accrued compensation and employee benefits	276	21	(33)
Deferred revenue	7,853	665	(255)
Net cash (used in) operating activities	(4,069)	(10,164)	(7,440)
Investing activities:			
Purchases of investments	(33,518)	(20,702)	(44,803)
Maturities of investments	29,518	29,160	44,028
Proceeds from disposal of property and equipment			216
Purchases of property and equipment	(428)	(24)	(64)
Net cash provided by/(used in) investing activities	(4,428)	8,434	(623)
Financing activities:			
Proceeds from issuance of common stock	18,379	553	227
Net cash provided by financing activities	18,379	553	227
Net increase/(decrease) in cash and cash equivalents	9,882	(1,177)	(7,836)
Cash and cash equivalents, beginning of period	8,626	9,803	17,639
Cash and cash equivalents, end of period	$ 18,507	$ 8,626	$ 9,803

See accompanying Notes to Consolidated Financial Statements.

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SANGAMO BIOSCIENCES, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Organization and Summary of Significant Accounting Policies

Sangamo and Basis of Presentation

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

Sangamo is currently working on a number of long-term development projects that will involve experimental and unproven technology. The projects may require several years and substantial expenditures to complete and ultimately may be unsuccessful. We plan to finance operations with available cash resources, funds received under federal government research grants and Enabling Technology collaborations and strategic partnerships, and from the issuance of equity or debt securities. Sangamo believes that its available cash, cash equivalents and investments as of December 31, 2005, along with expected revenues from Enabling Technology collaborations and strategic partnerships, will be adequate to fund its operations through 2007. Sangamo will need to raise substantial additional capital to fund subsequent operations and complete the development and commercialization of its products either through significant corporate partnerships, sales of zinc finger DNA binding protein transcription factors (ZFP TFs) for government research grants or issuance of equity securities. Sangamo may seek to raise additional capital when conditions permit, however there is no assurance funding will be available on favorable terms, if at all.

The consolidated financial statements include the accounts of Sangamo and its wholly owned subsidiary, Gendaq Limited, after elimination of all intercompany balances and transactions.

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.

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. Sangamo s cash and cash equivalents are maintained with three financial institutions. Cash and cash equivalents of $18.5 million and $8.6 million at December 31, 2005 and 2004, respectively, consist of deposits in money market investment accounts and corporate operating accounts.

Marketable Securities

Sangamo classifies its marketable securities as available-for-sale and records its investments at fair value in accordance with Statement of Financial Accounting Standards (FAS) No. 115, Accounting for Certain Investments in Debt and Equity Securities. Available-for-sale securities are carried at estimated fair value based on quoted market prices. Realized gains and losses and declines in value judged to be other-than-temporary on available-for-sale securities are included in other income / (expense). Unrealized holding gains and losses are included in accumulated

other comprehensive income. Gains and losses on securities classified