

SANGAMO BIOSCIENCES INC

Form 10-K/A

April 01, 2004

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SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K/A

Amendment No. 1

ý **Annual Report Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934**
For the Fiscal Year Ended December 31, 2003

SANGAMO BIOSCIENCES, INC.

(Exact name of registrant as specified in its charter)

Delaware

(State or other jurisdiction
of incorporation or organization)

8731

(Primary Standard Industrial
Identification Number)

**501 Canal Boulevard, Suite A100
Richmond, CA 94804
(510) 970-6000**

(Address, including zip code, and telephone number, including area code,
of the registrant's principal executive offices)

68-0359556

(I.R.S. Employer
Classification Code Number)

Securities registered pursuant to Section 12(b) of the act: **None**

Securities registered pursuant to Section 12(g) of the act:

Common stock \$.01 par value

(Title of Class)

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 ý No o

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (Section 229.405 of this chapter) 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 an accelerated filer (as defined in Exchange Act Rule 12b-2). Yes o No ý

The aggregate market value of the voting stock held by non-affiliates of the Registrant on June 30, 2003, based on the closing sale price as reported by the Nasdaq National Market of the Company's Common Stock, was approximately \$50,955,969.

The total number of shares outstanding of the Registrant's Common Stock was 24,975,003 as of February 18, 2004.

DOCUMENTS INCORPORATED BY REFERENCE

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Portions of the Registrant's Proxy Statement for its 2004 Annual Meeting of Stockholders (the "2004 Proxy Statement") are incorporated by reference into Part III of this Form 10-K.

TABLE OF CONTENTS

	Page
PART I	
Item 1. Business	3
Item 2. Properties	29
Item 3. Legal Proceedings	29
Item 4. Submission of Matters to a Vote of Security Holders	29
PART II	
Item 5. Market for the Registrant's Common Stock and Related Stockholder Matters	30
Item 6. Selected Consolidated Financial Data	32
Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations	33
Item 7A. Quantitative and Qualitative Disclosures About Market Risk	41
Item 8. Financial Statements and Supplementary Data	42
Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure	66
Item 9A. Controls and Procedures	66
PART III	
Item 10. Directors and Executive Officers of the Registrant	67
Item 11. Executive Compensation	67
Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters	67
Item 13. Certain Relationships and Related Transactions	67
Item 14. Principal Accountant Fees and Services	67
PART IV	
Item 15. Exhibits, Financial Statement Schedules and Report on Form 8-K	68

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Some statements contained in this report are forward-looking with respect to our operations, economic performance 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;

sufficiency of our cash resources;

product development;

revenues from existing and new collaborations;

our research and development and other expenses;

our operational and legal risks; and

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

Various terms and expressions similar to them are intended to identify these cautionary statements. These terms include: "anticipates," "believes," "continues," "could," "estimates," "expects," "intends," "may," "plans," "seeks," "should" and "will." Actual results may differ materially from 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.

2

PART I

Item 1. Business

Company Overview and Business Strategy

Background

Sangamo is the worldwide leader in the research, development, and commercialization of DNA binding proteins for the therapeutic regulation and repair of disease-associated 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 TFs, which are proteins that bind to DNA and are able to turn genes on or off (see Figure A). Alternatively, ZFPs may be engineered to create zinc finger nucleases (ZFNs). Engineered ZFNs can precisely cut genomic DNA at a preselected location, facilitating the transfer of "corrected" or "donor" genetic information into the site and may thus allow the repair or correction of genes which carry disease-causing mutations.

Pharmaceutical companies have spent billions of dollars to successfully discover and validate new genomic targets over the last several years, yet they have failed, in many cases, to identify small-molecule drugs which can therapeutically modulate these targets in man. We believe that our ZFP technology platform constitutes a novel therapeutic approach enabling the regulation of validated drug targets which have proven intractable to conventional methods of drug discovery. Sangamo, by offering ZFP TF regulation or correction of such targets at the DNA level, is poised to address such high-value targets by providing a unique and proprietary approach to the therapeutic regulation or correction of disease-associated genes. Our corporate partner, Edwards Lifesciences (Edwards), has filed an investigational new drug (IND) application to initiate a Phase I/III clinical study, which is intended to evaluate the safety and preliminary efficacy of a proprietary Sangamo ZFP Therapeutic for the treatment of peripheral artery disease (PAD). We have also initiated preclinical animal studies of ZFP Therapeutics in diabetic neuropathy and congestive heart failure and have research-stage programs in neuropathic pain, cancer immunotherapy, X-linked severe combined immunodeficiency (X-linked SCID), and sickle cell anemia.

Going forward, we intend to invest the majority of our financial and scientific resources in therapeutic applications of our ZFP technology. Notwithstanding our therapeutic focus, we believe the potential commercial applications of ZFP TFs are broad-based and range from human therapeutics and drug discovery to protein pharmaceutical production and the precision engineering of commercial crop plants. Our business model permits us to capitalize on the ZFP platform by permitting the sale or licensing of ZFP TFs or ZFNs to companies working in any of these fields. For instance, Sangamo has supplied its pharmaceutical partners with ZFP TFs for the engineering of human cells to enable their use in compound screening against cell surface receptors that are high-value drug targets. In addition, we are supplying Medarex, Inc. with ZFP-engineered cells for the enhanced production and yield of therapeutic antibodies, an advance which could substantially increase the efficiency of Medarex's pharmaceutical antibody production. Finally, while Sangamo is not currently investing in plant agriculture projects, our ZFP technology has been demonstrated to enable precise changes in the genomes of crop plants for commercially desirable traits.

We have amassed a substantial proprietary position in the design, selection, composition, and use of engineered ZFPs to support all of these commercial products. We either own outright or have licensed the commercial rights to approximately 45 patents issued in the United States and

foreign national jurisdictions, and we have over 150 patent applications pending worldwide. We continue to license and file new patent applications that strengthen our core and accessory patent portfolio. We

believe that our proprietary position will protect our ability to research, develop, and commercialize products and services based on ZFP technology across all of our chosen applications.

Over the last 18 months, we have increasingly focused our company on ZFP Therapeutic product development and recruited experienced scientists and managers with substantial product development experience. Working with the Edwards Lifesciences development team, we have played an integral role in the filing of the IND application. We are also building our capabilities in preclinical development, regulatory affairs, manufacturing, and clinical research and are applying these capabilities across our product development programs in cardiovascular disease, neurological disorders, cancer immunotherapy, and the treatment of monogenic diseases, including X-linked SCID and sickle cell anemia.

DNA, Genes, and Transcription Factors

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

The human body is composed of specialized cells that perform different functions and are thus organized into tissues and organs. All 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 activated or repressed in response to a wide variety of stimuli (external factors) and developmental signals (internal factors). 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 genes and regulate their 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.

The Two Domain Structure of a ZFP Therapeutic

Figure A

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 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 preselected DNA sequences within genes of commercial interest.

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 expressed in a cell transiently or continuously. 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 inhibit gene expression and, in some cases, even silence their target genes.

To date, we have designed, engineered, and assembled several thousand ZFPs and have thoroughly tested the majority 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 standardized 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,

5

pigs, plants, fruit flies, worms, and yeast. Sangamo scientists have published extensively, 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 Correction

The ZFP DNA binding domain may also be coupled to a cleavage domain of a restriction endonuclease – an enzyme that cuts DNA at a precise location – creating a zinc finger nuclease or ZFN. Using the DNA binding domain of an engineered ZFP, we can design a ZFN to generate a physical break at a defined position in the DNA sequence of a target gene that carries a disease-causing mutation. This targeted break in the

DNA facilitates the replacement of the disease-causing mutation or DNA sequence with the "normal" or "corrected" DNA sequence. We believe that ZFN-mediated gene correction will allow the corrected gene to be expressed in its natural chromosomal context and may provide a safe and effective approach to the precise repair of DNA sequence mutations responsible for monogenic diseases such as X-linked SCID and sickle cell anemia.

A Novel Class of Human Therapeutics

With our ability to deliver gene-specific ZFP TFs and ZFNs for the activation, repression, silencing, or repair of target genes and DNA sequences, we are poised to develop a novel 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.

Following the genomics revolution of the 1990s, the sequencing and publication of the human genome, and the industrialization of genomics-based drug discovery in this decade, 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 to clinical trials. There are thousands of potential drug targets which, although they have a clear role in disease processes, cannot be bound or modulated 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 of disease-associated genes with engineered ZFP transcription factors.

ZFP Therapeutics provide a unique approach to non-druggable targets. ZFP TFs act through a mechanism that is unique among biological drugs: direct modulation of the "disease" gene as opposed to the protein target encoded by that gene. Thus, a protein target which may be intractable to compound screening can instead be "turned on" or "turned off" at the DNA level. Engineered ZFP TFs are the only class of therapeutic molecules which act directly through the regulation of gene expression. This mode of action is not available to conventional small molecules, antibodies, or other protein pharmaceuticals.

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 gene expression, allowing direct modulation of the gene or target;

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 the expression of all variant proteins encoded by a particular gene;

6

ZFP TFs may themselves be expressed either transiently, for acute indications, or longer term, for chronic conditions;

ZFP TFs may ultimately be controllable by orally available small molecules for finer control of the intended gene target.

ZFP Therapeutic Gene Correction of Monogenic Disease

Genetic diseases such as X-linked SCID, sickle cell anemia, and Gaucher's disease 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 by its replacement with the "correct" DNA sequence, restoring normal gene function. As mentioned above, 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, facilitating the incorporation of the corrected DNA sequence into the chromosomal location where the disease-related mutation previously existed.

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While gene correction has been pursued in academic research laboratories for over a decade, its clinical application has been prevented by the low efficiency of homologous recombination (HR), the biological process of gene replacement. Unaided by an engineered ZFN, HR will only occur at a rate of approximately once in every one million cells; this rate is too low to be of clinical use. However, we and our collaborators have shown that the use of an engineered ZFN to cleave the target gene near the defective sequence can increase the efficiency of targeted HR by several thousand-fold. ZFP Therapeutic gene correction is a revolutionary technical approach to gene repair because ZFNs, like all ZFPs, 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 and sickle cell anemia.

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 an optimal level of affinity and specificity and can regulate 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 some of these data in peer-reviewed journals, and our partner, Edwards Lifesciences, submitted these data to the United States Food & Drug Administration (FDA) along with preclinical toxicology and biodistribution data as part of an IND application. This IND application was filed on February 10, 2004 to support a Phase I/II clinical study to investigate the safety and preliminary efficacy of ZFP TFs designed to up-regulate the expression of vascular endothelial growth factor A (VEGF-A) in patients with PAD. The study will be conducted under the supervision of Robert J. Lederman, M.D. of the National Heart, Lung and Blood Institute, National Institutes of Health (NIH). We intend to develop the necessary preclinical data to support the filing of additional INDs for the clinical testing of ZFP Therapeutics in patients with cardiovascular disease, neurological disorders, cancer, and monogenic diseases including X-linked SCID and sickle cell anemia.

Product Development Programs

In addition to the IND application to initiate the Phase I/II PAD clinical trial, we currently have three preclinical-stage programs (i.e., lead ZFP TF molecules in animal efficacy studies) and five

7

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
Peripheral artery disease (PAD)	IND (February 2004)	ZFP TF 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, or poor leg function due to PAD
Diabetic neuropathy	Preclinical (animal efficacy)	ZFP TF up-regulation of VEGF-A to induce growth of neuronal cells	Evidence from animal models of diabetic neuropathy suggests that up-regulation of endogenous VEGF-A may induce the growth and repair of neuronal cells
Congestive heart failure (CHF)	Preclinical (animal efficacy)	ZFP TF down-regulation of phospholamban (PLN) to increase the contractility of heart muscle	Currently evaluating the preclinical efficacy of PLN repression to increase the contractility of heart muscle in a rat model of congestive heart failure
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 to induce angiogenesis in a porcine model of blood flow restriction
X-linked severe combined immunodeficiency (X-linked)	Research (cell-based studies)	ZFN-mediated correction of IL2R γ mutations in stem cells	X-linked SCID is caused by loss-of-function mutations in the IL2R γ gene

Clinical Indication	Development Stage	Therapeutic Approach	Comments
SCID)		from patients with X-linked SCID	
Neuropathic pain	Research (cell-based studies)	ZFP TF down-regulation of cell surface receptors involved in pain signaling	Sangamo scientists evaluating various ZFP TFs for the down-regulation of cell surface receptors VR1, TrkA, and PN3 to choose the optimal ZFP TF and target receptor
Sickle cell anemia (SCA)	Research (cell-based studies)	ZFN-mediated correction of the β -globin mutation in stem cells from patients with SCA	Bone marrow transplantation is the only efficacious therapy available for SCA patients; however, most patients lack matched donors
Cancer	Research (cell-based studies)	ZFP TF up-regulation of GM-CSF, delivered via oncolytic virus, a virus that can kill tumor cells, to induce a systemic antitumor immune response	Sangamo scientists evaluating the combination of ZFP TFs and an Onyx oncolytic virus as a means to kill tumor cells near the injection site and stimulate a systemic, cell-mediated, antitumor response
Amyotrophic lateral sclerosis (ALS)	Research (cell-based studies)	ZFP TF up-regulation of insulin-like growth factor I (IGF-I) to slow the degeneration of motor neurons	Evidence from clinical studies of recombinant IGF-I in ALS patients suggests that up-regulation of IGF-I could be a viable approach to ALS treatment

Table 1. Clinical indications currently targeted by Sangamo's clinical, preclinical, and research-stage product development programs.

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 pain in the absence of exercise; and finally leading to tissue damage and severely impaired mobility. While the condition affects 8-12 million people in the United States, 80% of these patients have intermittent claudication and do not progress to resting pain or critical limb ischemia. This program is funded and managed by our development partner, Edwards Lifesciences, who filed an IND application in February 2004 to initiate a Phase I/II clinical trial in PAD.

Diabetic Neuropathy

Diabetic neuropathy is a frequent complication of diabetes. Left unchecked, diabetic neuropathy can lead to impaired sensation in the feet, which can result in undiscovered soft tissue damage, infection, and, ultimately, amputation of the lower extremity. The most common form of diabetic neuropathy affects approximately 50% of patients with diabetes, or roughly six million people in the United States. In 2001, there were approximately 82,000 non-traumatic lower-limb amputations performed on diabetics in the United States. There are no pharmaceutical therapies approved by the FDA for the treatment of diabetic neuropathy. 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 initiated preclinical studies of VEGF-A activation in similar preclinical models to confirm and extend these findings by using our ZFP Therapeutic to up-regulate the chromosomal VEGF-A gene.

Congestive Heart Failure (CHF)

CHF is a gradual and long-term loss of pumping capacity by the heart that results in the "backing up" 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 at an alarming rate, 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 now strong scientific evidence to suggest that down-regulation of the gene encoding phospholamban (PLN) can improve the contractility of heart muscle in

mammalian animal models of CHF. We have identified a lead ZFP TF inhibitor of PLN for the CHF program and have initiated preclinical studies in a rodent model of CHF.

Ischemic Heart Disease (IHD)

Ischemic heart disease 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; however, patients with downstream blood flow restrictions are not addressed by these interventions. Patients who are poor candidates for a revascularization procedure may be candidates for a biological drug designed to up-regulate the expression of VEGF-A. There are approximately 1.1 million revascularization procedures in the United States each year, and we believe that a significant fraction of these patients could potentially benefit from a less invasive, therapeutic angiogenesis product. Our IHD program is funded and managed by our partner, Edwards Lifesciences, and utilizes the same VEGF-targeted ZFP TF as the PAD program.

9

X-linked Severe Combined Immunodeficiency (X-linked SCID)

X-linked severe combined immunodeficiency is a rare, inherited genetic disease leading to severe T-cell and B-cell dysfunction, severe infection, and death by the age of 2 years. Approximately 50% of these patients harbor a defined mutation in the gene encoding the gamma chain of the interleukin-2 receptor (IL2R γ). Sangamo scientists are using ZFN-mediated gene correction in an effort to repair this genetic lesion in hematopoietic stem cells.

Neuropathic Pain

Neuropathic pain comprises a set of chronic pain disorders that cannot be connected to previous or underlying trauma as is the case with acute pain. There are several million patients with neuropathic pain in the United States, and the few drugs available show marginal efficacy and many 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 three of these pain targets in cell-based models. We are incorporating these ZFP TFs into gene transfer vectors for testing in pain models during 2004.

Sickle Cell Anemia

Sickle cell anemia is caused by a mutation in the human β -globin gene that alters the solubility of hemoglobin under certain physiological conditions. The ensuing disease is characterized by chronic hemolytic anemia with episodes of severe pain and tissue damage often resulting in kidney failure, liver disease, stroke, and other complications. According to the National Heart, Lung and Blood Institute of the NIH, approximately 72,000 people in the U.S. have sickle cell disease. Moreover, approximately 2.5 million Americans carry the sickle cell trait. Although there is still no adequate long-term treatment or cure, some patients may benefit from bone marrow transplantation. However, very few patients have matched donors, and the risks of infection and toxicity are quite high. Sangamo scientists and collaborators are developing methods for ZFN-mediated correction of the β -globin gene mutation that causes sickle cell anemia. We are collaborating on this program with the Childrens Hospital Research Institute of Oakland.

Cancer

The American Cancer Society estimates that the incidence of new cancer cases will be approximately 1.3 million in 2004, with 565,500 cancer deaths, accounting for 1 of every 4 deaths in the United States overall. 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 TF technology has potential applications in cancer therapy, both in regulating endogenous genes and in activating the body's natural mechanisms for fighting disease. In December 2003, we exclusively licensed the oncolytic adenovirus technology of Onyx Pharmaceuticals for therapeutic applications of ZFP TFs (Armed Therapeutic Viruses or ATV) in cancer. Sangamo scientists are engineering the ATV to deliver a ZFP TF that up-regulates granulocyte macrophage colony-stimulating factor (GM-CSF). GM-CSF is a powerful immunostimulator and has been shown to augment anti-tumor immune responses. We believe that the Armed Therapeutic Virus generated by combining these two technologies may have advantages over other cancer immunotherapies in development and may be used to treat cancer both at the tumor site and systemically.

Amyotrophic Lateral Sclerosis (ALS)

Amyotrophic lateral sclerosis (ALS), also called Lou Gehrig's disease, is a progressive, fatal neurological disease affecting as many as 20,000 Americans, with 5,000 new cases occurring in the United States each year. The disease belongs to a class of disorders known as motor neuron diseases. ALS occurs when specific nerve cells in the brain and spinal cord that control voluntary movement gradually degenerate. The loss of these motor neurons causes the muscles under their control to weaken and waste away, leading to paralysis. Evidence from preclinical and clinical studies using recombinant insulin-like growth factor I (IGF-I) suggests that the targeted up-regulation of IGF-I could be a viable approach to the treatment of ALS. This program is in the cell-based testing stage for selection of a lead ZFP TF molecule.

Product Development Resources and Infrastructure

As Sangamo makes its transition to a development-stage biotechnology company, we are building our capabilities in regulatory affairs, quality assurance, manufacturing, and clinical research. Our current plan is to establish these capabilities internally, while relying on third-party contract research organizations and contract manufacturers of ZFP Therapeutic products for toxicology and Phase I/II studies. This will serve to minimize our investment in fixed capital while maximizing our flexibility in our selection of gene transfer systems for the delivery of ZFP TF genes. Our manufacturing and quality assurance personnel will 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 the products provide ourselves and our strategic partners and collaborators with 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.

We believe the advancement of our first ZFP Therapeutic into a clinical trial in 2004 comes at a timely point in the evolution of the worldwide pharmaceutical industry. Large pharmaceutical companies face revenue growth challenges that may compel them to in-license or acquire emerging therapeutic technologies. Our success in advancing the VEGF program into Phase I/II clinical trials may bring attention to the potential of ZFP Therapeutics to address the non-druggable, yet high-value 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 diseases. 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 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 initial public offering at the IPO price. Through 2001, we received \$2 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. We have retained all rights to use our technology for therapeutic applications of VEGF activation outside of ischemic cardiovascular and vascular diseases, including use in wound healing and neurological disorders. Revenues attributable to milestone achievement and collaborative research and development performed under the Edwards agreement were \$1.5 million, \$2.0 million and \$2.5 million for 2003, 2002 and 2001, respectively. The remainder of funding relates to two milestones, one each in the VEGF and phospholamban programs. In the future, Sangamo may receive option fees, milestone payments, royalties and additional research funding from this agreement. During each of 2003, 2002 and 2001, the revenues attributable to milestone achievement and collaborative research and development performed under the Edwards agreement comprised over 10%

of total revenues earned by Sangamo.

Under the Sangamo-Edwards agreement, we have been 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 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 has granted Edwards a right of first refusal to Sangamo's ZFP TFs for the regulation of PLN. This right of first refusal terminates 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.

Exclusive License to Oncolytic Vector Technology from Onyx Pharmaceuticals, Inc.

In April 2001, we announced a strategic collaboration with Onyx Pharmaceuticals, Inc. to jointly research and develop novel cancer therapeutics by using our ZFP TF technology platform and Onyx's oncolytic adenovirus technology. Under the terms of the agreement, the two companies were to conduct studies on an Armed Therapeutic Virus (ATV) modified to express a ZFP TF, equally share preclinical and clinical development costs, and jointly commercialize products resulting from the alliance. As a result of a change in their strategic direction, Onyx terminated its internal research activities relating to the adenovirus technology and decided not to continue co-development of product candidates under the initial Sangamo-Onyx agreement.

In December 2003, we announced that Sangamo has exclusively licensed rights to Onyx's oncolytic adenovirus vector technology to independently develop ATV products that encode ZFP TFs. In the initial therapeutic application, we will engineer the ATV to express ZFP TFs designed to up-regulate the expression of human granulocyte macrophage colony-stimulating factor (GM-CSF), a powerful activator of the immune system known to augment anti-tumor immune responses. The license agreement provides us with exclusive worldwide rights for all therapeutic uses of ATVs encoding ZFP TFs that regulate the expression of any target gene. Under the terms of the agreement, Sangamo will have full responsibility for research and commercial development of the ZFP TF ATV. Onyx will

12

receive milestone payments as products advance into and through clinical testing and will receive a royalty on product sales. The status of our initial program is reviewed above under "Therapeutic Product Development."

Research Collaboration with Avigen, Inc.

In October 2002, we announced a collaborative research agreement with Avigen, Inc. to evaluate potential therapies for intractable neuropathic pain based on the combination of Sangamo's ZFP TFs and Avigen's adeno-associated viral vector (AAV) gene delivery technology. Under the terms of the agreements, each company will bear its own expenses and will share any data generated during the term of the agreement. The status of this program is reviewed under "Therapeutic Product Development."

Enabling Technologies for Drug Discovery

We began marketing our Enabling Technologies to the pharmaceutical and biotechnology industry in 1998. Our Enabling Technology Agreements are based upon the delivery of an engineered ZFP TF which is capable of regulating the expression of a gene for which it is specifically designed and targeted. These agreements typically involve non-exclusive rights to use one or more ZFP TFs for internal research purposes and provide no commercial rights to our core ZFP technology.

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 toward these critical areas. Specifically, we are supplying our partners with ZFP-engineered cells which over-express a drug target of interest for use in high-throughput compound screening. Typically, pharmaceutical company researchers will use a cDNA encoding the drug target of interest to create these cell-based drug screens. However, if the patent covering such a cDNA is held by a third party, the pharmaceutical company might be prevented from using the cDNA for this purpose. The ZFP-engineered cell-based system allows our pharmaceutical partners to screen against drug targets whose gene sequence is

covered by competitor intellectual property.

Enabling Technology Agreements for Pharmaceutical Protein Production

Protein pharmaceuticals manufactured with genetically modified cells accounted for more than \$13.3 billion in annual worldwide sales in 2001. Of this total, monoclonal antibodies accounted for approximately \$2.6 billion. Industry experts believe that the introduction of new protein pharmaceuticals may lead to a significant shortfall in production capacity over the next several years.

Sangamo scientists have demonstrated that ZFP-engineered mammalian cells may be used to increase the yield of bulk pharmaceutical protein from systems used for pharmaceutical antibody production. In January 2002, we announced an agreement with Medarex, Inc. to develop these cell lines to enhance the production yields of monoclonal antibodies. Under this agreement, Medarex provided Sangamo with research funding in 2002 and 2003, and Sangamo will be entitled to milestone payments and, potentially, royalties on sales of Medarex antibodies manufactured with our ZFP TF technology. Medarex will receive a non-exclusive license to the resulting technology, and Sangamo will have the ability to utilize the technology in collaborations with other partners. Revenues attributable to collaborative research and development performed under the Medarex agreements were \$600,000 for both 2003 and 2002 and none for 2001. During both 2003 and 2002, the revenues attributable to collaborative research and development performed under the Medarex agreements comprised over 10% of total revenues earned by Sangamo.

13

Plant Agriculture

Sangamo scientists and collaborators have also shown that ZFP TFs can be used to regulate the expression of endogenous genes in plants with similar efficacy as has been repeatedly shown in various mammalian cells and animals. The ability to identify and subsequently 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. To commercialize ZFP TFs in agricultural biotechnology, we intend to seek strategic relationships with corporate partners having capabilities in the research, development, and commercialization of agricultural products.

In January 2001, we announced our first plant agriculture collaboration with Renessen LLC, a joint venture between Cargill and Monsanto Company. Under the terms of the agreement, Sangamo received research funding and milestone payments in 2001 and 2002. Sangamo and Renessen scientists expect to report on the optimization of α -tocopherol levels in the seed oil of *Arabidopsis* by using ZFP TFs in 2004.

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 and licensing agreements, to establish and protect our proprietary rights.

We have licensed intellectual property directed to the design, selection, and use of ZFPs and ZFP TFs for gene regulation from the Massachusetts Institute of Technology, Johnson and Johnson, The Scripps Research Institute, Johns Hopkins University, California Institute of Technology, and Harvard University. These licenses grant us rights to make, use, and sell ZFPs and ZFP TFs under nine families of patent filings. All of these patent families have been filed in the United States, and four have been filed internationally in selected countries. As of January 1, 2004, these patent filings have resulted in 13 issued U.S. patents and 7 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 March 16, 2004, we had 52 families of Sangamo-owned patent filings, including 11 issued U.S. patents and 14 granted foreign patents, 73 pending U.S. patent applications and 95 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. 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 \$2.0 million. For risks associated with our intellectual property, see "Risks Related to Our Business 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.

Although we have filed for patents on some aspects of our technology, we cannot assure you 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 opposed by a third party, and we cannot predict the outcome of these opposition proceedings. 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.

However, 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, 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 "Risks Related to Our Business 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 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 which 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 "Risks Related to Our Business 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 the worldwide leader in the research, development, and commercialization of DNA binding proteins for the regulation of gene expression and gene correction. We are aware of many 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 correction 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.

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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 the Gendaq acquisition and our strong presence in the field of ZFP technology and intellectual property, any products that we develop with our ZFP TF technology will participate in highly competitive markets. Many of our potential competitors in these markets, either alone or with their collaborative partners, may have substantially greater financial, technical, and personnel resources than we do, and they may succeed in developing technologies and products that would render our technology obsolete or non-competitive. In addition, many of those competitors may have significantly greater experience than we do in their respective fields.

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.

Competition may arise from other drug development technologies and therapeutic approaches such as small-molecules, monoclonal antibodies or other pharmaceutical proteins, gene therapy, and other nucleic acid technologies such as antisense RNA and siRNA. Furthermore, there are alternative approaches to gene correction that could prove technically superior to our gene correction technology or be commercialized more rapidly.

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

16

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 FDA of an Investigational New Drug (IND) application. Our partner, Edwards Lifesciences, submitted a Phase I/II clinical protocol for review by the Recombinant DNA Advisory Committee (RAC) of the NIH 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 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.

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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 before it can begin. Phase I usually involves the initial introduction of the investigational drug into healthy volunteers or patients to evaluate certain factors, including its safety, dosage tolerance and, if possible, to gain an early indication of its effectiveness. Phase II 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 III 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.

Outside the United States, our ability to market a product is contingent upon receiving a 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 begun to hire personnel with expertise in regulatory affairs to assist us in obtaining appropriate regulatory approvals as required. In 2003, 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

17

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 \$10.2 million, \$12.2 million and \$13.0 million for 2003, 2002 and 2001, respectively. Research and development costs incurred in connection with company 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 (ZFN) for therapeutic gene correction as a treatment and possible cure for certain monogenic diseases. Additionally, in order to develop ZFP TFs as commercially relevant therapeutics, we expect to expend additional resources for expertise in the manufacturing, regulatory affairs and clinical research aspects of biotherapeutic development.

EMPLOYEES

As of February 18, 2004, we had 57 full-time employees, all of which are located in Richmond, California. None of our employees is 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> and <http://www.expressinglife.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.

RISKS RELATED TO OUR BUSINESS

We are increasing 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 are moving away from our historic emphasis on Enabling Technology agreements. In the short term, this change in resource allocation will 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.

Our partner, Edwards Lifesciences, is planning to initiate Phase I/II clinical testing in our lead ZFP Therapeutic program, and ZFP Therapeutics have never before been tested in humans. If our lead ZFP Therapeutic fails its initial safety study, it could damage our ability to attract new investors and corporate partners. Edwards Lifesciences filed an investigational new drug (IND) application with the U.S. Food and Drug Administration (FDA) on February 10, 2004. Under the FDA's review process, the FDA has 30 days to comment on an IND filing. The IND application has completed the 30 day review period and is now active. We expect the principal investigator to begin enrolling patients into the Phase I/II clinical trial in the second quarter of 2004. The Phase I/II study of our lead therapeutic

18

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.

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 we expect this trend will continue in 2004. 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.

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. 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 and:

must be conducted in conformance with the FDA's good clinical practices and other applicable regulations;

must meet requirements for institutional review board oversight;

must meet requirements for informed consent;

are subject to continuing FDA oversight;

may require large numbers of test subjects; and

may be suspended by us, our commercial partner, or the FDA 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 I usually involves the initial

19

introduction of the investigational drug into healthy volunteers or patients to evaluate certain factors, including its safety, dosage tolerance and, if possible, to gain an early indication of its effectiveness. Phase II 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 III 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 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.

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.

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. Our technology involves a relatively new approach to gene regulation. 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 to 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 models, and human clinical studies, we may be unable to use our technology in all its intended applications. Also, delivery of ZFP TFs into cells and organisms, including humans, in these and other environments is limited by a number of technical challenges, 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 in a particular therapeutic application.

The expected value and utility of our ZFP TFs is in part based on our belief that the targeted or specific regulation of gene expression and targeted gene repair 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 correction. Using this technique, Sangamo scientists have engineered gene-specific ZFPs to cut DNA at a specific site within a target gene, and to then replace the adjacent sequences with new DNA. In so doing, we are attempting to "repair" or "correct" an abnormal or disease-related mutation or DNA sequence. ZFP-mediated gene correction is at an early stage of development. Our scientists have shown ZFP-mediated gene correction 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 must be efficiently delivered to the cell. We have licensed certain gene transfer technologies for use with our Enabling Technologies, which are ZFP TFs 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 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.

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. Recent reports of serious adverse events in a retroviral gene transfer trial for infants with severe combined immunodeficiency (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 put 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 2003, 2002 and 2001 were \$10.4 million, \$29.8 million and \$25.2 million, respectively. To date, our revenues have been generated from

Enabling Technology agreements, strategic partners, and federal government research grants. In 2003, we have placed more emphasis on higher-value therapeutic product development and related strategic partnerships and less emphasis on our Universal GeneTools® collaborations. 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;

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, 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, and we would expect any future arrangement to be, 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 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 agreements 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 TF 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

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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 Universal Gene Tools®. The effectiveness of these competing products has reduced the revenues generated by our Universal Gene Tools®. Competing technologies may include other methods of regulating gene expression. ZFP TFs 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. Competitive technologies include those used to analyze the expression of genes in cells or tissues, determine gene function, discover new genes, analyze genetic information, and regulate genes. Competing proprietary technologies with our product development focus include:

For ZFP Therapeutics: small molecule drugs, monoclonal antibodies, recombinant proteins, antisense and siRNA approaches

For our Enabling Technology Applications:

Universal GeneTools®: antisense, siRNA

high throughput screening: cDNA, naturally occurring cell lines

protein production: gene amplification

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;

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

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.

Early commercial application in drug discovery research of our engineered ZFP TFs delivered to our Universal GeneTools® collaborators have not produced useful results in every case. In the past, some of our Universal GeneTools® collaborators were unable to substantiate the effects of our gene regulation technology. Generally, failures were re-evaluated at Sangamo by using our most current approach. In some cases, additional ZFP TFs were designed and tested for these targets, and data were generated at Sangamo, or by our partners, confirming the ability to regulate these targets. However, there can be no assurance that we will be able to regulate all gene targets. Although we have been able to achieve targeted activation or repression of numerous genes, the degree of activation or repression is not always sufficient to allow our collaborators to realize their objectives. If we are unsuccessful in engineering ZFP TFs that achieve positive results for our collaborators or strategic partners, this would significantly harm our business by reducing our revenues.

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. To date, we have generated our revenues from Universal GeneTools® collaboration agreements, strategic partnering agreements, and federal government research grants. As of December 31, 2003, we had an accumulated deficit of approximately \$83.3 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.

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 2005, 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 \$2.60 to a high of \$5.50 during the year ended December 31, 2003, and a low of \$1.30 to a high of \$10.25 during the year ended December 31, 2002. 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:

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;

announcements by us or our partners providing updates on the progress or development status of ZFP Therapeutics; and

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.

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 57 full-time employees as of February 18, 2004, 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.

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

25

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 generally do not control the prosecution of patent applications that we license from third parties; therefore, the patent applications may not be prosecuted in a timely manner.

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

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we or our licensors were the first to make the inventions covered by each of our pending patent applications;

we or our licensors were the first to file patent applications for these inventions;

the patents of others will not have an adverse effect on our ability to do business;

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

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

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

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

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

Others have filed and in the future are likely to file patent applications that are similar to ours. We are aware that there are academic groups and other companies that are attempting to develop technology which 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

26

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 our intellectual property will not be challenged by third parties. One of our licensed foreign patents, which forms the basis of five European Regional Phase patents, has been opposed by a third party. We cannot predict the outcome of these opposition proceedings. We cannot guarantee that the patent will not be invalidated or that granted claims will not have to be narrowed to overcome the opposition.

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.

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

27

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 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. We may develop genetically modified agricultural products for ourselves or with our strategic partners. 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 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 of 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, 28% 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 2. Properties

We currently lease approximately 22,000 square feet of research and office space located at 501 Canal Boulevard in Richmond, California. The leases expire in August of 2004. We have efforts underway to arrange for facilities after the termination of this lease and believe sufficient space is available locally for the next 24-36 months.

Item 3. Legal Proceedings

We are not a party to any material litigation.

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

Not applicable.

PART II**Item 5. Market for the Registrant's Common Stock and Related Stockholder Matters**

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 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, of which is incorporated herein by reference.

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, 2002		
First Quarter	\$ 10.25	\$ 7.57
Second Quarter	\$ 9.20	\$ 3.99
Third Quarter	\$ 6.24	\$ 1.65
Fourth Quarter	\$ 4.95	\$ 1.30
Year ended December 31, 2003		
First Quarter	\$ 4.99	\$ 2.60
Second Quarter	\$ 5.35	\$ 2.45
Third Quarter	\$ 4.09	\$ 2.60
Fourth Quarter	\$ 5.50	\$ 4.05

Holdings

As of February 18, 2004 there were approximately 97 stockholders of record of Sangamo's common stock.

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, two officers, Edward O. Lanphier II, President and CEO, and Peter Bluford, Vice President of Corporate Development, have made periodic sales of the Company's stock pursuant to such plans.

Use of Proceeds from the Sale of Registered Securities

Sangamo's Registration Statement on Form S-1 with respect to our initial public offering was declared effective on April 6, 2000. In a public offering managed by Lehman Brothers, Chase H&Q (now JP Morgan H&Q), ING Barings (now ABN AMRO), and William Blair & Company, Sangamo

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registered and sold an aggregate of 3.5 million shares of our common stock at a public offering price of \$15.00 per share for an aggregate offering of \$52.5 million.

Sangamo received net proceeds of approximately \$47.4 million, after deducting offering expenses of \$5.1 million. Offering expenses included underwriting discounts and commissions of \$3.7 million and other offering expenses of \$1.4 million. None of the offering expenses represented direct or indirect payments to directors, officers or general partners of Sangamo or their associates, to persons owning 10 percent or more of any class of equity securities of Sangamo or to affiliates of Sangamo.

As of February 18, 2004, Sangamo has used the net proceeds from its public offering of common stock to invest in short-term and long-term, interest bearing, investment grade securities, to purchase capital equipment and to fund the general operations of the company. Sangamo intends to use the net proceeds of the offering for research and development and general corporate purposes. A portion of the net proceeds may also be used to acquire or invest in complementary businesses or products or to obtain the right to use complementary technologies. Sangamo has no agreements or commitments with respect to any such acquisition or investments and Sangamo is not currently engaged in any material negotiations with respect to any such transaction. None of the net proceeds of the offering is expected to be paid directly or indirectly to directors or officers of the Company or their associates, to persons owning 10 percent or more of any class of equity securities of the Company or to affiliates of the Company.

Recent Sales of Unregistered Securities

Pursuant to a license agreement between the California Institute of Technology (Caltech) and us entered into in November 2003, we issued 25,000 shares of our common stock with a market value of \$129,500 to Caltech as partial consideration in return for license rights. Based in part upon the representations of Caltech, we issued these shares pursuant to the exemption from registration provided by Section 4(2) of the Securities Act of 1933, as amended.

31

Item 6. Selected Consolidated 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,				
	2003	2002	2001	2000	1999
	(in thousands, except per share data)				
Statement of Operations Data:					
Total revenues	\$ 2,579	\$ 4,343	\$ 4,885	\$ 3,433	\$ 2,182
Operating expenses:					
Research and development	10,187	12,213	12,952	8,462	3,991
General and administrative	3,594	3,815	3,638	2,602	1,578
Stock-based compensation	567	1,499	3,674	4,852	519
Restructuring charge(1)		371			
Goodwill impairment(2)		15,250			
Patent impairment(2)		2,760			
Acquired in-process research and development			13,062		

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Year Ended December 31,

Total operating expenses	14,348	35,908	33,326	15,916	6,088
Loss from operations	(11,769)	(31,565)	(28,441)	(12,483)	(3,906)
Interest income, net	752	1,366	3,192	3,417	131
Other income	584	435			
Net loss	(10,433)	(29,764)	(25,249)	(9,066)	(3,775)
Deemed dividend upon issuance of convertible preferred stock				(1,500)	(4,500)
Net loss attributable to common stockholders	\$ (10,433)	\$ (29,764)	\$ (25,249)	\$ (10,566)	\$ (8,275)
Basic and diluted net loss per common share	\$ (0.42)	\$ (1.22)	\$ (1.09)	\$ (0.61)	\$ (1.38)
Shares used in computing basic and diluted net loss per common share	24,811	24,493	23,120	17,383	5,991

(1) See Note 3 in the footnotes to consolidated financial statements

(2) See Notes 1, 4 and 5 in the footnotes to consolidated financial statements

Year Ended December 31,

	2003	2002	2001	2000	1999
	(in thousands)				
Stock-Based Compensation:					
Research and development stock-based compensation	\$ 451	\$ 1,150	\$ 2,562	\$ 2,885	\$ 275
General and administrative stock-based compensation	116	349	1,112	1,967	244
Total stock-based compensation	\$ 567	\$ 1,499	\$ 3,674	\$ 4,852	\$ 519

32

December 31,

	2003	2002	2001	2000	1999
	(in thousands)				
Balance Sheet Data:					
Cash, cash equivalents, marketable securities, and interest receivable	\$ 44,343	\$ 52,575	\$ 62,560	\$ 64,681	\$ 7,503
Working capital	43,714	52,115	61,102	64,477	7,206
Total assets	46,232	56,227	85,017	68,925	9,162

December 31,

Long-term debt					250
Accumulated deficit	(83,297)	(72,864)	(43,100)	(17,851)	(8,785)
Total stockholders' equity	44,661	54,246	82,349	66,890	7,882

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

The discussion in "Management's Discussion and Analysis of Financial Condition and Results of Operations" contains trend analysis, estimates and other forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. These forward-looking statements include, without limitation, statements containing the words "believes," "anticipates," "expects," "continue," and other words of similar import or the negative of those terms or expressions. Such forward-looking statements are subject to known and unknown risks, uncertainties, estimates and other factors that may cause the actual results, performance or achievements of the Company, or industry results, to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements. Actual results could differ materially from those set forth in such forward-looking statements as a result of, but not limited to, the "Risk Factors" described in Part I, Item 1. 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, 2003, 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 novel transcription factors for the regulation of gene expression. 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, 2003, we had an accumulated deficit of \$83.3 million.

Our revenues have consisted primarily of revenues from our corporate partners for ZFP TFs, 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 2003, we have placed more emphasis on higher-value therapeutic product development and related strategic partnerships and less emphasis on our Universal GeneTools® 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 increases our financial risk by increasing expenses associated with product development.

33

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 (ZFN) for therapeutic gene correction as a treatment and possible cure for certain monogenic diseases. Additionally, in order to develop ZFP TFs 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 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 generally recognized on a ratable basis 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 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 Universal GeneTools® agreements when ZFP Transcription Factors ("ZFP TFs") are delivered to the Universal GeneTools® 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 TFs and the recognition of these revenues is deferred until the ZFP TFs 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 a Universal GeneTools® agreement are generally recognized ratably over the applicable period of the agreement or as ZFP TFs 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.

34

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 criteria 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 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).

Goodwill and Patents Impairment

In connection with our acquisition of Gendaq Limited, in accordance with an independent valuation, we allocated \$15.3 million to goodwill and \$3.4 million to patents with estimated useful lives of 7 years, the term of expected benefit. The valuation in connection with the initial purchase price allocation and the ongoing evaluation for impairment of goodwill and intangible assets requires significant management estimates and judgment. The purchase price allocation process requires management estimates and judgment as to expectations for various products and business strategies. If any of the significant assumptions differ from the estimates and judgments used in the purchase price allocation, this could result in different valuations for goodwill and intangible assets. Once the purchase price allocation is established, we must test goodwill annually for impairment using a two-step process as required by FAS No. 142 "Goodwill and Other Intangible Assets." In addition, in certain circumstances, we must assess if goodwill should be tested for impairment between annual tests. Intangible assets with definite useful lives must be tested for impairment in accordance with FAS No. 144 "Accounting for the Impairment or Disposal of Long-Lived Assets." When we

conduct our impairment tests for goodwill and intangibles, factors that are considered important in determining whether impairment might exist include significant continued under-performance compared to peers, significant changes in our underlying business and products, or other factors specific to each asset being evaluated. Any changes in key assumptions about the business and its prospects, or changes in market conditions or other externalities, could result in an impairment charge and such a charge could have a material adverse effect on our consolidated results of operations. We performed the first of the required annual impairment tests for goodwill as of September 30, 2002, which resulted in a one-time charge being taken for the entire balance of goodwill of \$15.3 million. Given that goodwill was determined to be impaired, we also assessed our long-lived assets for impairment at that time, resulting in an additional one-time charge of \$2.8 million being taken for the entire unamortized balance of patents.

Acquisition of Gendaq

On July 4, 2001, we completed our acquisition of Gendaq Limited, a privately held biotechnology company located in the United Kingdom. We issued 2,124,638 shares of common stock in exchange for 100% of the outstanding shares of Gendaq's common stock. We also reserved a total of 125,366 shares for issuance upon exercise of outstanding Gendaq stock options, which were assumed in the transaction. Gendaq had a research and development organization with a focus and research activities similar to ours. In February 2002, we made the decision to begin consolidation of our Gendaq operations from the United Kingdom to our Richmond, California headquarters. The decision followed a post-acquisition review that was initiated in October 2001 where we evaluated technology, personnel, costs, and various alternatives to maximize the synergy between Sangamo and Gendaq. As this review was initiated after the acquisition was completed, and the final decision to consolidate was not made until February 2002, the decision had no impact on our accounting for the acquisition reported in 2001. The Gendaq facility was closed September 30, 2002.

Results of Operations

Years Ended December 31, 2003, 2002 and 2001

Total revenues

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 \$2.2 million in 2003, compared to \$4.1 million in 2002, and \$4.7 million in 2001. The decrease in 2003 from 2002 was principally attributable to lower year-over-year revenues of \$1.5 million associated with Universal GeneTools® agreements as well as lower year-over-year revenues of \$425,000 recognized from a therapeutics partnership with Edwards Lifesciences Corporation ("Edwards"). Revenues associated with Universal GeneTools® agreements have declined by \$1.5 million as competing technology has been commoditized and our emphasis has shifted to therapeutic product development. Total revenues decreased by \$542,000 from 2001 to 2002 principally due to lower year-over-year revenues of \$425,000 recognized from with Edwards. The decrease in revenues under the agreement with Edwards is due to the maturation of the agreement which provided for research funding and certain initial milestones earlier in the agreement. Revenues attributable to milestone achievement and collaborative research and development performed under the Edwards agreement were \$1.5 million, \$2.0 million and \$2.5 million for 2003, 2002 and 2001, respectively. Federal government research grant revenues were \$374,000 in 2003, \$237,000 in 2002, and \$155,000 in 2001. The increase in 2003 represented the continuation of two grants, one of which began in 2002 and the other in 2001. We plan to continue to apply for federal government research grants.

Research and development expenses

Research and development expenses were \$10.2 million in 2003, compared to \$12.2 million in 2002 and \$13.0 million in 2001. The decrease of \$2.0 million from 2002 to 2003 was principally due to the consolidation of the research activities at Gendaq, our wholly owned U.K. subsidiary, into our Richmond operations during the third quarter of 2002. Specifically, decreased year-over-year expenses were salary and benefits of \$897,000, lab supplies of \$705,000 and facility-related costs of \$390,000. The decrease of \$800,000 from 2001 to 2002 was also principally due to the consolidation of the research activities at Gendaq, our wholly owned U.K. subsidiary, into our Richmond operations during the third quarter of 2002. Specifically, decreased year-over-year expenses were salary and benefits of \$310,000, lab supplies of \$274,000 and facility-related costs of \$190,000. 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 product candidates

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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.

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 TF-engineered cell lines for drug screening and protein production, ZFP TFs for the discovery and validation of genes and drug targets, and ZFP TFs for applications in agricultural biotechnology.

Below is a summary of our programs and the development phase of the leading application:

PROGRAM	PHASE
ZFP-Therapeutics	Preclinical
Gene correction	Research
ZFP TF-engineered cell lines for small molecule drug discovery	Research/Marketing
ZFP TF-engineered cell lines for the manufacturing of protein pharmaceuticals	Research/Marketing
Discovery and validation of gene targets	Marketing
Agricultural biotechnology	Research

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. See Risks Related to Our Business "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 were \$3.6 million during 2003, \$3.8 million in 2002 and \$3.6 million in 2001. General and administrative expenses were consistent over this three-year period. We expect that general and administrative expenses will increase in the future to support continued growth of our research and development efforts.

Restructuring charge

Restructuring charges of \$371,000 related to the closure of the Gendaq facility were recorded in 2002. These expenses primarily represent incremental employee restructuring costs and a loss on disposal of fixed assets of \$74,000.

Impairment charges

During 2002, in accordance with FAS No. 142, the Company performed the required two-step annual impairment test of goodwill. In the first step of the analysis, we compared the carrying value of the Company to its fair value and determined that goodwill was impaired. The fair value of the Company was determined using the income approach. The income approach focuses on the income-producing capability of an asset, measuring the current value of the asset by calculating the present value of its future economic benefits such as cash earnings, cost savings, tax benefits and proceeds from disposition incorporating current equity market conditions in the United States, industry-specific volatility factors, general equity market forecasts, the risk-free rate for the use of funds and the

expected rate of inflation. The Company recognized an impairment charge of \$15.3 million, representing the entire capitalized balance of goodwill at the time of the test.

FAS 142 requires that if an impairment test of goodwill and any other asset is required at the same time, impairment tests of all other assets should be completed and reflected in the carrying value of the Company prior to the completion of the goodwill impairment test. If it is determined that an asset is not recoverable, FAS 144 directs that an impairment loss should be recognized based on the excess of its carrying value over its fair value. Impairment tests of the Company's long-lived assets were conducted in accordance with FAS 144. Based upon the results of this review, we concluded that the carrying amount of patents was not recoverable. The Company recognized an impairment loss of \$2.8 million, representing the entire unamortized balance of patents. Management assessed all other assets as being recoverable.

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In-process research and development expenses

As a part of Sangamo's \$36.7 million cost to acquire Gendaq, \$13.1 million was expensed as research and development in the third quarter of 2001. In-process research and development represents that portion of the purchase price of the acquisition related to the research and development activities which: (i) have not demonstrated their technological feasibility, and (ii) have no alternative future uses. Sangamo recognized an expense of \$13.1 million upon consummation of the transaction.

The amount of in-process research and development was determined based on an analysis using the risk-adjusted cash flows expected to be generated by the products that result from the in-process projects. The analysis included forecasted future cash flows that were expected to result from the progress made on each of the in-process projects prior to the purchase dates. These cash flows were estimated by first forecasting, on a product-by-product basis, total revenues expected from sales of the first generation of each in-process product, as well as expected expenses to complete in process research and development for each project. Appropriate operating expenses and cash flow adjustments were deducted from the forecast to establish projected net cash flows for the in process technology. Finally, these net returns were discounted to a present value at discount rates that incorporate both the weighted average cost of capital (relative to the biotechnology industry and the Company) as well as the product-specific risk associated with the purchased in-process research and development products. The product-specific risk factors included each product in each phase of development, type of molecule under development, likelihood of regulatory approval, manufacturing process capability, scientific rationale, pre-clinical safety and efficacy data, target product profile and development plan. The overall discount rate used for the purchase valuation ranged from 35% to 50% depending upon the stage of completion of each product and the risks associated with each, which represents a significant risk premium to our weighted average cost of capital.

The forecast data in the analysis was based on internal product level forecast information maintained by management in the ordinary course of managing the business. The inputs used in analyzing in-process research and development were based on assumptions, which management believed to be reasonable but which are inherently uncertain and unpredictable. These assumptions may be incomplete or inaccurate, and no assurance can be given that unanticipated events and circumstances will not occur.

A brief description of projects that were included in the in-process research and development charge is set forth below. Projects subsequently added to the research and development pipeline are not included. Since the acquisition date, there has been no significant progress in the development of the projects listed. At the time of the acquisition, management estimated that research and

38

development expenditures of at least \$30.0 to \$35.0 million will be required to complete the in-process projects.

Project	Description / Indication	Phase of Development	Estimated Substantial Completion Date	Fair Value (in millions)
HIV	Therapeutic product candidate	Pre-clinical	2008	\$ 1.9
Anti-Inflammatory	Therapeutic product candidate	Pre-clinical	2007	3.4
EPO	Therapeutic product candidate	Pre-clinical	2007	0.9
Insulin	Therapeutic product candidate	Pre-clinical	2009	1.2
Functional Genomics	Gene regulation product	Pre-marketing	2002	3.2
Agriculture	Gene regulation product	Pre-marketing	2005	2.5
				\$ 13.1

Interest income, net

Net interest income was \$752,000 in 2003, as compared to \$1.4 million in 2002, and \$3.2 million in 2001. The year-over-year decline over the three-year period reflects lower average cash and investment balances (due to the utilization of cash to fund operations).

Other income

During 2003, other income of \$584,000 was principally comprised of a 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. During 2002, we recognized a

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net gain of \$435,000 on foreign currency translations. Of that gain, \$367,000 represents cumulative currency translation recognized as a result of the closure of our Gendaq facility in the U.K. Prior to the closure of our Gendaq facility during 2002, currency translation gains or losses were reported as a component of equity.

We incurred net operating losses in 2003, 2002, and 2001, and consequently we did not pay any federal, state or foreign 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, 2003, we had cash, cash equivalents, investments and interest receivable totaling \$44.3 million.

Net cash used in operating activities was \$7.4 million in 2003, \$8.9 million in 2002, and \$5.9 million in 2001. In all periods, net cash used in operating activities was primarily due to funding of net operating losses. During 2003, the use of cash related to the net operating loss of \$10.4 million was partially offset by non-cash charges and net increases in asset balances of \$1.8 million and by amortization on investments of \$1.2 million. During 2002, the use of cash related to the net operating loss of \$29.8 million was partially offset by goodwill and patent impairment charges of \$15.3 million and \$2.8 million, respectively, as well as other non-cash charges and net increases in asset balances of \$2.8 million. During 2001, the use of cash related to the net operating loss of \$25.2 million was partially offset by acquired in-process research and development expenses recognized related to the Gendaq acquisition of \$13.1 million, non-cash charges and net increases in asset balances of \$3.2 million as well as amortization of deferred stock compensation expenses of \$3.1 million.

39

Net cash provided by (used in) investing activities was \$(623,000) in 2003, \$18.9 million in 2002, and \$2.6 million in 2001. Included in 2001 was \$4.7 million of net cash acquired in the Gendaq acquisition. 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.

Net cash provided by financing activities was \$227,000 in 2003, solely related to proceeds from issuance of common stock. Net cash provided by financing activities in 2002 and 2001 of \$183,000 and \$662,000, respectively, was related to proceeds from issuance of common stock, partially offset by payments made for an equipment loan.

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 2005.

As of December 31, 2003, Sangamo had net operating loss carryforwards for federal income tax purposes of approximately \$35.0 million, which expire in the years 2010 through 2023. The Company also has state operating loss carryforwards of approximately \$4.3 million, which expire in the years 2004 through 2014. The Company also has federal and state research credits of \$970,000 and \$945,000, respectively. The federal research credits will begin to expire in the year 2018 through 2023 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, 2003 we had contractual obligations and commercial commitments as follows (in thousands):

Contractual Obligations	Payments Due by Period				
	Total	Less than 1 year	1-3 years	3-5 years	More than 5 years
Operating leases	\$ 416	\$ 416	\$	\$	\$
License obligations	1,134	378	756		
Total contractual obligations	\$ 1,550	\$ 794	\$ 756		

Payments Due by Period

Operating leases consist of base rents for facilities we occupy in Richmond, California.

License obligations consist of ongoing license maintenance fees and royalties due from sales of ZFP TFs.

Recent Accounting Pronouncements

In January 2003, the FASB issued FASB Interpretation No. 46, "Consolidation of Variable Interest Entities, an Interpretation of ARB No. 51". The Interpretation establishes accounting guidance for consolidation of variable interest entities that function to support the activities of the primary beneficiary. Interpretation 46 applies to any business enterprise, both public and private, that has a controlling interest, contractual relationship or other business relationship with a variable interest entity. The provisions of Interpretation No. 46 are effective immediately for all variable interests in variable interest entities created before February 1, 2003 and no later than the first fiscal period beginning after June 15, 2003 for all variable interests in variable interest entities created before February 1, 2003. The adoption of Interpretation 46 did not have a material impact on our consolidated financial position, results of operations or cash flows

40

In March 2003, the EITF reached a consensus on Issue No. 00-21, "Revenue Arrangements with Multiple Deliverables", which provides guidance on accounting for arrangements involving the delivery or performance of multiple products, services and/or rights to use assets. Specifically, EITF 00-21 addresses: (1) how to determine whether an arrangement with multiple deliverables contains more than one unit of accounting, and (2) how the arrangement consideration should be measured and allocated among the separate units of accounting. The provisions of Issue 00-21 are effective for revenue arrangements entered into in fiscal periods beginning after June 15, 2003. We believe that the adoption of EITF 00-21 did not have a material impact on our results of operations or financial position.

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 satisfy liquidity requirements by investing 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, 2003, the fair value of our portfolio would decline by less than \$200,000. 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 gain on foreign currency translation of \$298,000 and \$435,000 for 2003 and 2002, respectively. No foreign currency translation gains were recorded during 2001.

41

Item 8. Financial Statements and Supplementary Data

SANGAMO BIOSCIENCES, INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

	Page
Report of Ernst & Young LLP, Independent Auditors	43
Consolidated Balance Sheets	44
Consolidated Statements of Operations	45
Consolidated Statement of Stockholders' Equity	46
Consolidated Statements of Cash Flows	47
Notes to Consolidated Financial Statements	48

REPORT OF ERNST & YOUNG LLP, INDEPENDENT AUDITORS

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, 2003 and 2002, and the related consolidated statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2003. 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 auditing standards generally accepted in the United States. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Sangamo BioSciences, Inc. at December 31, 2003 and 2002, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2003, in conformity with accounting principles generally accepted in the United States.

/s/ Ernst & Young LLP

Palo Alto, California
January 30, 2004

SANGAMO BIOSCIENCES, INC.

CONSOLIDATED BALANCE SHEETS

(In thousands, except share and per share amounts)

	December 31,	
	2003	2002
Assets		
Current assets:		
Cash and cash equivalents	\$ 9,803	\$ 17,639
Marketable securities	34,052	34,504
Interest receivable	488	432
Accounts receivable	658	1,098

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	December 31,	
	2003	2002
Prepaid expenses	284	423
Total current assets	45,285	54,096
Property and equipment, net	906	1,793
Other assets	41	338
Total assets	\$ 46,232	\$ 56,227

Liabilities and stockholders' equity

Current liabilities:

Accounts payable and accrued liabilities	\$ 815	\$ 937
Accrued compensation and employee benefits	636	669
Deferred revenue	120	375
Total liabilities	1,571	1,981

Commitments and contingencies (See Note 7 in Notes to Consolidated Financial Statements)

Stockholders' equity:

Common stock, \$0.01 par value; 80,000,000 shares authorized, 24,954,243 and 24,740,713 shares issued and outstanding at December 31, 2003 and 2002, respectively	127,927	127,234
Deferred stock compensation	(1)	(231)
Accumulated deficit	(83,297)	(72,864)
Accumulated other comprehensive income	32	107
Total stockholders' equity	44,661	54,246
Total liabilities and stockholders' equity	\$ 46,232	\$ 56,227

See accompanying Notes to Consolidated Financial Statements.

SANGAMO BIOSCIENCES, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS

(In thousands, except per share amounts)

	Year ended December 31,		
	2003	2002	2001
Revenues:			
Collaboration agreements	\$ 2,205	\$ 4,106	\$ 4,730
Federal government research grants	374	237	155

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	Year ended December 31,		
	2003	2002	2001
Total revenues	2,579	4,343	4,885
Operating expenses:			
Research and development (excludes \$451, \$1,150 and \$2,562 of stock-based compensation expense for 2003, 2002 and 2001, respectively)	10,187	12,213	12,952
General and administrative (excludes \$116, \$349 and \$1,112 of stock-based compensation expense for 2003, 2002 and 2001, respectively)	3,594	3,815	3,638
Restructuring charge		371	
Stock-based compensation	567	1,499	3,674
Goodwill impairment		15,250	
Patent impairment		2,760	
Acquired in-process research and development			13,062
Total operating expenses	14,348	35,908	33,326
Loss from operations	(11,769)	(31,565)	(28,441)
Interest income, net	752	1,366	3,192
Other income	584	435	
Net loss	\$ (10,433)	\$ (29,764)	\$ (25,249)
Basic and diluted net loss per share	\$ (0.42)	\$ (1.22)	\$ (1.09)
Shares used in computing basic and diluted net loss per share	24,811	24,493	23,120

See accompanying Notes to Consolidated Financial Statements.

SANGAMO BIOSCIENCES, INC.

CONSOLIDATED STATEMENT OF STOCKHOLDERS' EQUITY

(In thousands, except share amounts)

	Common Stock		Note Receivable from Stockholder	Deferred Stock Compensation	Accumulated Deficit	Accumulated Other Comprehensive Income	Total Stockholders' Equity
	Shares	Amount					
Balances at December 31, 2000	22,147,391	\$ 89,764	\$ (463)	\$ (4,697)	\$ (17,851)	\$ 137	\$ 66,890
Issuance of common stock upon exercise of options and warrants, net of repurchases	195,842	369					369
Issuance of common stock under employee stock purchase plan	35,679	321					321
Issuance of common stock for purchase of Gendaq	2,124,638	34,874					34,874
Assumption of Gendaq common stock options, less intrinsic value of unvested options		1,734		(684)			1,050
Repayment of note receivable from stockholder	(17,900)	(267)	267				
Repayment of note receivable from employee	(3,600)	(53)					(53)
Forgiveness of notes receivable from stockholder			196				196
		596		3,079			3,675

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	Common Stock		Note		Accumulated		
			Receivable		Other		
			from		Comprehensive		
			Stockholder		Income		
Amortization of deferred stock compensation and vesting of non-qualified stock options							
Reversal of deferred compensation due to employee terminations		(177)		177			
Comprehensive loss:							
Unrealized gain on investments					129		129
Translation adjustment					147		147
Net loss					(25,249)		(25,249)
Comprehensive loss							(24,973)
Balances at December 31, 2001	24,482,050	127,161		(2,125)	(43,100)	413	82,349
Issuance of common stock upon exercise of options and warrants, net of repurchases	176,566	216					216
Issuance of common stock under employee stock purchase plan	82,097	252					252
Deferred stock compensation		232		(232)			
Amortization of deferred stock compensation and vesting of non-qualified stock options		489		1,342			1,831
Reversal of deferred compensation due to employee terminations		(1,116)		784			(332)
Comprehensive loss:							
Unrealized loss on investments					(158)		(158)
Translation adjustment					(148)		(148)
Net loss					(29,764)		(29,764)
Comprehensive loss							(30,070)
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

See accompanying Notes to Consolidated Financial Statements.

SANGAMO BIOSCIENCES, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

Year ended December 31,

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	2003	2002	2001
Operating activities:			
Net loss	\$ (10,433)	\$ (29,764)	\$ (25,249)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation	847	955	992
Amortization of patents		360	239
Amortization of premium / discount on investment	1,146	796	185
Net (gain) loss on disposal of property and equipment	(112)	74	
Realized loss on investment	6		
Issuance of common stock in connection with license agreement	130		
Gain on currency translation		(367)	
Goodwill impairment		15,250	
Patent impairment		2,760	
Amortization of deferred stock compensation	178	1,198	3,079
Other stock-based compensation	388	301	596
Forgiveness of notes receivable	188		196
Acquired in-process research and development			13,062
Changes in operating assets and liabilities:			
Interest receivable	(56)	534	205
Accounts receivable	440	(335)	789
Prepaid expenses and other assets	248	(236)	201
Accounts payable and accrued liabilities	(122)	(324)	73
Accrued compensation and employee benefits	(33)	(2)	(25)
Deferred revenue	(255)	(76)	(265)
Net cash used in operating activities	(7,440)	(8,876)	(5,922)
Investing activities:			
Purchases of investments	(44,803)	(36,289)	(55,538)
Maturities of investments	44,028	50,687	54,891
Sales of investments		4,467	
Proceeds from disposal of property and equipment	216	79	
Purchases of property and equipment	(64)	(69)	(1,403)
Net cash acquired in Gendaq acquisition			4,656
Net cash provided by (used in) investing activities	(623)	18,875	2,606
Financing activities:			
Proceeds from issuance of common stock	227	468	690
Payments on equipment loan		(285)	(28)
Net cash provided by financing activities	227	183	662
Effect of exchange rate changes on cash		(187)	147
Net increase (decrease) in cash and cash equivalents	(7,836)	9,995	(2,507)
Cash and cash equivalents, beginning of period	17,639	7,644	10,151
Cash and cash equivalents, end of period	\$ 9,803	\$ 17,639	\$ 7,644
Noncash investing and financing activities:			
Deferred compensation related to stock options	\$	\$ 232	\$ 684

	Year ended December 31,		
	2003	2002	2001
Shares tendered as repayment of note receivable from shareholder	\$	\$	\$ 320
Supplemental disclosures:			
Cash paid for interest	\$	\$ 3	\$
Non-cash disclosure related to the acquisition of Gendaq:			
Tangible assets acquired	\$	\$	\$ 475
Acquired in-process technology			13,062
Goodwill and other intangible assets acquired			18,609
Liabilities assumed			(878)
Deferred stock compensation			684
Common stock and options issued			(36,608)
Cash received in acquisition, net of \$781 transaction costs paid	\$	\$	\$ (4,656)

See accompanying Notes to Consolidated Financial Statements.

47

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 the regulation of gene expression. Our gene regulation technology platform is enabled by the engineering of a class of transcription factors known as zinc finger DNA binding proteins ("ZFPs"). Potential applications of Sangamo's technology include pharmaceutical discovery, development of human therapeutics and plant agriculture. 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 Universal GeneTools® 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, 2003, along with expected revenues from Universal GeneTools® collaborations and strategic partnerships, will be adequate to fund its operations through 2005. 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 pharmaceutical discovery, 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 material 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 equivalents of \$9.8 million and \$17.6 million at December 31, 2003 and 2002, 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. Debt securities are held at amortized cost and the discount / premium is accounted for using the straight-line method. Realized gains and losses and declines in value judged to be other-than-temporary on available-for-sale securities are included in interest income. Unrealized holding gains and losses are included in accumulated other comprehensive

48

income. Interest on securities classified as available-for-sale is also included in interest income, which is determined using the specific identification method. Through December 31, 2003, Sangamo has recorded \$6,000 in other than temporary losses on its investments.

The table below summarizes our available-for-sale securities (in thousands):

	<u>Amortized Cost</u>	<u>Gross Unrealized Gains</u>	<u>Estimated Fair Value</u>
December 31, 2003			
US government investments:			
Maturing within 1 year	\$ 7,578	\$ 8	\$ 7,586
Maturing between 1 and 2 years	6,251	19	6,270
Total government investments	13,829	27	13,856
Corporate debt investments:			
Maturing within 1 year	14,175	2	14,177
Maturing between 1 and 2 years	6,022	(3)	6,019
Total corporate investments	20,197	(1)	20,196
Total available-for-sale investments	\$ 34,026	\$ 26	\$ 34,052
December 31, 2002			
US government investments:			
Maturing within 1 year	\$ 11,658	\$ 35	\$ 11,693
Maturing between 1 and 2 years	1,812	13	1,825
Total government investments	13,470	48	13,518
Corporate debt investments:			
Maturing within 1 year	19,894	52	19,946
Maturing between 1 and 2 years	1,035	5	1,040
Total corporate investments	20,929	57	20,986

	Amortized Cost	Gross Unrealized Gains	Estimated Fair Value
Total available-for-sale investments	\$ 34,399	\$ 105	\$ 34,504

Gross unrealized losses on available-for-sale securities at December 31, 2003 and 2002 were not material.

Property and Equipment

Property and equipment are stated at cost, less accumulated depreciation and amortization. Depreciation is calculated using the straight-line method based on the estimated useful lives of the related assets (generally three to five years). For leasehold improvements, amortization is calculated using the straight-line method based on the shorter of the useful life or the lease term.

Impairment of Long-Lived Assets

Effective January 1, 2002, the Company adopted FAS No. 144 "Accounting for the Impairment or Disposal of Long-Lived Assets" ("FAS 144"). FAS No. 144 addresses the financial accounting and reporting for the impairment or disposal of long-lived assets and supercedes FAS No. 121 "Accounting

49

for the Impairment of Long-Lived Assets and Long-Lived Assets to Be Disposed Of." The primary objectives of FAS No. 144 are to develop one accounting model based on the framework established in FAS No. 121 for long-lived assets to be disposed of by sale, and to address significant implementation issues. The adoption of FAS No. 144 did not have an impact on the Company's consolidated financial statements.

Goodwill and Other Intangible Assets

Goodwill represents the difference between the purchase price and the fair value of the net assets acquired in connection with our Gendaq acquisition on July 4, 2001. In June, July, and August 2001, respectively, the Financial Accounting Standards Board issued FAS No. 141, ("FAS 141"), "Business Combinations," FAS No. 142, "Goodwill and Other Intangible Assets" and FAS No. 144, "Accounting for the Impairment or Disposal of Long-Lived Assets." FAS No. 141 prohibits the use of the pooling-of-interests method for business combinations initiated after June 30, 2001, and includes criteria for the recognition of intangible assets separately from goodwill. FAS No. 142 is effective for fiscal years beginning after December 15, 2001, and includes requirements to test goodwill and indefinite lived intangible assets for impairment, rather than amortizing them. Accordingly, goodwill was not amortized and was reviewed for impairment in accordance with FAS No. 142 as of January 1, 2002 for the transitional impairment test and September 30, 2002 for the annual impairment test. The entire balance of goodwill was written off in September of 2002 as an impairment charge as a result of the annual impairment test (See Note 4 in Notes to Consolidated Financial Statements).

Other intangible assets represents the fair value of patents purchased in connection with the Gendaq acquisition. In accordance with FAS 142, patents were being amortized on a straight-line basis over the estimated useful life of seven years, and were also reviewed for impairment as of September 30, 2002, in accordance with FAS 144. As a result, the unamortized balance of patents was written off in September of 2002 as an impairment charge (See Note 5 in Notes to Consolidated Financial Statements).

Reclassifications

Certain reclassifications of prior years balances have been made to conform to the current year presentation. These reclassifications had no effect on prior years net loss or stockholders equity.

Foreign Currency Translation

Sangamo translates the assets and liabilities of its foreign subsidiary stated in local functional currencies to U.S. dollars at the rates of exchange in effect at the end of the period. Revenues and expenses are translated using rates of exchange in effect during the period. Gains and losses from translation of financial statements denominated in foreign currencies, if material, were included as a separate component of other comprehensive income (loss) in the statement of stockholders' equity until closure of the Gendaq facility in September 2002. Subsequently, gains and losses from translation of Gendaq's financial statements are recorded as other income.

The Company records foreign currency transactions at the exchange rate prevailing at the date of the transaction. Monetary assets and liabilities denominated in foreign currency are retranslated at the exchange rates in effect at the balance sheet date. Foreign currency transaction gains and losses are

recorded through profit and loss and gains of \$298,000 and \$435,000 were recorded during 2003 and 2002, respectively. No foreign currency translation gains were recorded during 2001.

Comprehensive Loss

Comprehensive loss is comprised of net loss and other comprehensive income (loss). Comprehensive loss for the years ended December 31, 2003, 2002 and 2001 is included in the statement of stockholders' equity. Comprehensive loss includes all changes in equity during a period from non-owner sources. These items include unrealized gains / (losses) on investments and foreign currency translation adjustments.

Revenue Recognition

Sangamo recognizes revenue from its Universal GeneTools® agreements when ZFP Transcription Factors ("ZFP TFs") are delivered to the Universal GeneTools® 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 TFs and the recognition of these revenues is deferred until the ZFP TFs are delivered. The risk of ownership has passed to the collaborator and all performance obligations have been satisfied at the time revenue is recognized.

In accordance with Staff Accounting Bulletin No. 104, "Revenue Recognition," revenue from research activities made under strategic partnering agreements is generally recognized on a ratable basis, 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 in advance under such agreements are deferred until 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 qualified research expenses are incurred. Grant reimbursements are received on a quarterly or monthly basis and are subject to the issuing agency's right of audit.

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 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 criteria are considered separately for each of the separate units of accounting.

Research and Development Expenses

Research and development expenses consist of costs incurred for Company-sponsored as well as collaborative research and development activities. These costs include direct and research-related overhead expenses, which include salaries and other personnel-related expenses, facility costs, supplies and depreciation of facilities and laboratory equipment, as well as the cost of funding research at universities and other research institutions, and are expensed as incurred. Costs to acquire technologies that are utilized in research and development and that have no alternative future use are expensed as incurred.

Stock-Based Compensation

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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 FAS No. 123, "Accounting for Stock-Based Compensation." 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 expenses to be recorded as they vest over a performance period. The fair value of such options is determined using the Black-Scholes model. The following table illustrates, pursuant to FAS No. 123, as amended by FAS No. 148, "Accounting for Stock-Based Compensation Transition and Disclosure," the effect on net loss and related net loss per share had compensation cost for stock-based compensation plans been determined based upon the fair value method prescribed under FAS No. 123:

	Year ended December 31,		
	2003	2002	2001
	(in thousands, except per share data)		
Net loss:			
As reported	\$ (10,433)	\$ (29,764)	\$ (25,249)
Add: stock-based employee compensation expense included in reported net loss	567	1,499	3,674
Less: stock-based employee compensation expense determined under the fair value based method	(2,515)	(2,909)	(8,370)
	Pro forma net loss	\$ (12,381)	\$ (31,174)
	\$ (12,381)	\$ (31,174)	\$ (29,945)
Basic and diluted net loss per share:			
As reported	\$ (0.42)	\$ (1.22)	\$ (1.09)
	Pro forma	\$ (0.50)	\$ (1.27)
	\$ (0.50)	\$ (1.27)	\$ (1.30)

The above pro forma effect may not be representative of that to be expected in future years, due to subsequent years including additional grants and related vesting. The fair value for all options granted in 2003, 2002, and 2001 was estimated at the date of grant using the Black-Scholes method

52

following the Company's initial public offering and using the minimum value method for periods prior to the initial public offering with the following weighted-average assumptions:

	Year ended December 31,		
	2003	2002	2001
Risk-free interest rate	3.1%	3.8%	5.0%
Expected life of option	5 yrs	5 yrs	5 yrs
Expected dividend yield of stock	0%	0%	0%
Expected volatility	1.08	1.0	0.8

The Company amortizes deferred compensation pertaining to employee stock options over the respective employees' vesting period using the graded vesting method.

Income Taxes

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Sangamo accounts for income taxes as required by FAS No. 109, "Accounting for Income Taxes." Under this method, deferred tax assets and liabilities are determined based on differences between financial reporting and tax bases of assets and liabilities. Deferred tax assets and liabilities are measured using enacted tax rates and laws that will be in effect when the differences are expected to reverse. Deferred tax assets are reduced by a valuation allowance when, in the opinion of management, it is more likely than not that some or all of the deferred tax assets may not be realized.

Net Loss Per Share

Basic and diluted net loss per share information for all periods is presented under the requirements of FAS No. 128, "Earnings per Share." Basic net loss per share has been computed using the weighted-average number of shares of common stock outstanding during the period, less shares subject to repurchase. The following table presents the calculation of historical basic and diluted net loss per common share (in thousands, except per share data):

	Year ended December 31,		
	2003	2002	2001
Net loss	\$ (10,433)	\$ (29,764)	\$ (25,249)
Basic and diluted:			
Weighted-average shares of common stock outstanding	24,816	24,577	23,342
Less: weighted-average shares subject to repurchase	(5)	(84)	(222)
Shares used in computing basic and diluted net loss per share	24,811	24,493	23,120
Basic and diluted net loss per share	\$ (0.42)	\$ (1.22)	\$ (1.09)

53

Recent Accounting Pronouncements

In January 2003, the FASB issued FASB Interpretation No. 46, "Consolidation of Variable Interest Entities, an Interpretation of ARB No. 51". The Interpretation establishes accounting guidance for consolidation of variable interest entities that function to support the activities of the primary beneficiary. Interpretation 46 applies to any business enterprise, both public and private, that has a controlling interest, contractual relationship or other business relationship with a variable interest entity. The provisions of Interpretation No. 46 are effective immediately for all variable interests in variable interest entities created before February 1, 2003 and no later than the first fiscal period beginning after June 15, 2003 for all variable interests in variable interest entities created before February 1, 2003. The adoption of Interpretation 46 did not have a material impact on our consolidated financial position, results of operations or cash flows.

In March 2003, the EITF reached a consensus on Issue No. 00-21, "Revenue Arrangements with Multiple Deliverables", which provides guidance on accounting for arrangements involving the delivery or performance of multiple products, services and/or rights to use assets. Specifically, EITF 00-21 addresses: (1) how to determine whether an arrangement with multiple deliverables contains more than one unit of accounting, and (2) how the arrangement consideration should be measured and allocated among the separate units of accounting. The provisions of Issue 00-21 are effective for revenue arrangements entered into in fiscal periods beginning after June 15, 2003. The adoption of EITF 00-21 did not have a material impact on our results of operations or financial position.

2. Major Customers, Partnerships and Strategic Alliances

In January 2000, we announced a therapeutic product development collaboration with Edwards Lifesciences Corporation ("Edwards"). 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 diseases. Edwards purchased a \$5 million note that converted, together with accrued

interest, into common stock at the time of our initial public offering 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 terminated in March 2003. Together with accrued interest, this note converted into common stock at the time of our initial public offering at the IPO price. Through 2001, we received \$2 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. Under the Edwards agreement, Sangamo recognized \$500,000 related to the achievement of research-related milestones in the fourth quarter of 2003. We have retained all rights to use our technology for therapeutic applications of VEGF activation outside of ischemic cardiovascular and vascular diseases, including use in wound healing and neurological disorders. Revenues attributable to milestone achievement and collaborative research and development performed under the Edwards agreement were \$1.5 million, \$2.0 million and \$2.5 million for 2003, 2002 and 2001, respectively. The remainder of funding relates to two milestones, one each in the VEGF and phospholamban programs. In the future, Sangamo may receive option fees, milestone payments, royalties and additional research funding from this agreement. During each of 2003, 2002 and 2001, the

revenues attributable to milestone achievement and collaborative research and development performed under the Edwards agreement comprised over 10% of total revenues earned by Sangamo.

Under the Sangamo-Edwards agreement, we have been 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 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 has granted Edwards a right of first refusal to Sangamo's ZFP TFs for the regulation of PLN. This right of first refusal terminates 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.

In January 2002, Sangamo signed a non-exclusive research and license agreement with Medarex, Inc. ("Medarex") to use ZFP TF gene regulation technology to increase the expression of antibodies in mammalian cell lines. Under the agreement, Medarex provided research funding in 2003 and 2002 and Sangamo will be entitled to milestone payments and, potentially, royalties on sales of Medarex antibodies manufactured using Sangamo technology. In June 2001, we signed a collaboration agreement with Medarex to develop fully human antibody therapeutics for certain cell surface receptors. Revenues attributable to collaborative research and development performed under the Medarex agreements were \$600,000 for both 2003 and 2002 and none for 2001. During both 2003 and 2002, the revenues attributable to collaborative research and development performed under the Medarex agreements comprised over 10% of total revenues earned by Sangamo.

In April 2001, we announced a strategic collaboration with Onyx Pharmaceuticals, Inc. to jointly research and develop novel cancer therapeutics by using our ZFP TF technology platform and Onyx's oncolytic adenovirus technology. Under the terms of the agreement, the two companies were to conduct studies on an Armed Therapeutic Virus (ATV) modified to express a ZFP TF, equally share preclinical and clinical development costs, and jointly commercialize products resulting from the alliance. As a result of a change in their strategic direction, Onyx terminated its internal research activities relating to the adenovirus technology and decided not to continue co-development of product candidates under the initial Sangamo-Onyx agreement.

In December 2003, we announced that Sangamo has exclusively licensed rights to Onyx's oncolytic adenovirus vector technology to independently develop ATV products that encode ZFP TFs. In the initial therapeutic application, we will engineer the ATV to express ZFP TFs designed to up-regulate the expression of human granulocyte macrophage colony-stimulating factor (GM-CSF), a powerful activator of the immune system known to augment anti-tumor immune responses. The license agreement provides us with exclusive worldwide rights for all therapeutic uses of ATVs encoding ZFP

TFs that regulate the expression of any target gene. Under the terms of the agreement, Sangamo will have full responsibility for research and commercial development of the ZFP TF ATV. Onyx will receive milestone payments as products advance into and through clinical testing and will receive a royalty on product sales. The status of our initial program is reviewed above under "Therapeutic Product Development."

At December 31, 2003, receivables from one company equaled 76% of total accounts receivable. As of December 31, 2002 and 2001, receivables from one company equaled 75% and 92%, respectively, of total accounts receivable.

3. Acquisition of Gendaq Limited

On July 4, 2001, Sangamo completed the acquisition of the outstanding shares of Gendaq Limited, a privately held biotechnology company located in the United Kingdom, in a purchase transaction. Sangamo issued 2,124,638 shares of common stock in exchange for 100% of the outstanding shares of Gendaq's common stock. Sangamo also reserved a total of 125,366 shares for issuance upon exercise of outstanding Gendaq stock options, which were assumed in the transaction. Gendaq is a research and development organization focused on regulating genes through the engineering of transcription factors known as zinc finger DNA binding proteins (ZFPs).

Sangamo's total cost to acquire Gendaq was approximately \$36.7 million based on the fair market value of \$16.41 per share of Sangamo's common stock. The stock price used to value the securities issued was based on an average price during the few days before and after May 30, 2001, the day Sangamo and Gendaq announced an agreement under which Sangamo received an option to purchase all of the outstanding stock of Gendaq. The purchase price also included the assumption of certain stock options and transaction costs.

The cost to acquire Gendaq was allocated to the assets acquired and liabilities assumed according to their respective fair values, with the excess purchase price being allocated to goodwill. The allocation of the aggregate purchase price was based in part on an independent valuation analysis, which was obtained for purposes of assisting management with the allocation of the purchase price to the fair value of purchased assets and assumed liabilities.

The purchase cost of Gendaq is as follows (in thousands):

Value of securities issued	\$ 34,874
Assumption of Gendaq's common stock options	1,734
Less intrinsic value of unvested options	(684)
Transaction costs and expenses	781
	<u> </u>
Total	<u>\$ 36,705</u>

56

The purchase price allocation is as follows (in thousands):

	Amount	Useful Life (In years)	Annual Amortization of Intangibles
	<u> </u>	<u> </u>	<u> </u>
Net tangible assets of Gendaq	\$ 5,034		
Intangible assets acquired:			
Patents	3,359	7	\$ 480
In-process research and development	13,062		
Goodwill	15,250		
	<u> </u>		<u> </u>
Total purchase price allocation	<u>\$ 36,705</u>		<u>\$ 480</u>

In-process research and development represents that portion of the purchase price related to the research and development activities which: (i) had not demonstrated their technological feasibility, and (ii) had no alternative future uses. Sangamo recognized an expense of \$13.1 million upon consummation of the transaction.

The amount of in-process research and development was determined based on an analysis using the risk-adjusted cash flows expected to be generated by the products that result from the in-process projects. The analysis included forecasted future cash flows that were expected to result

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from the progress made on each of the in-process projects prior to the purchase dates. These cash flows were estimated by first forecasting, on a product-by-product basis, total revenues expected from sales of the first generation of each in-process product, as well as expected expenses to complete in process research and development for each project. Appropriate operating expenses and cash flow adjustments were deducted from the forecast to establish projected net cash flows for the in process technology. Finally, these net returns were discounted to a present value at discount rates that incorporate both the weighted average cost of capital (relative to the biotechnology industry and the Company) as well as the product-specific risk associated with the purchased in-process research and development products. The product-specific risk factors included each product in each phase of development, type of molecule under development, likelihood of regulatory approval, manufacturing process capability, scientific rationale, pre-clinical safety and efficacy data, target product profile and development plan. The discount rates used to determine the fair value of the in-process projects ranged from 35% to 50%, depending upon the stage of completion of each product and the risks associated with each, which represents a significant risk premium to our weighted average cost of capital.

The forecast data in the analysis was based on internal product level forecast information maintained by management in the ordinary course of managing the business. The inputs used in analyzing in-process research and development was based on assumptions, which management believed to be reasonable but which were inherently uncertain and unpredictable. These assumptions may be incomplete or inaccurate, and no assurance can be given that unanticipated events and circumstances will not occur.

A brief description of projects that were included in the in-process research and development charge is set forth below. Projects subsequently added to the research and development pipeline are not included. Since the acquisition date, there has been no significant progress in the development of

57

the projects listed below. Management estimated that research and development expenditures of at least \$30.0 to \$35.0 million will be required to complete the in-process projects.

Project	Description/Indication	Phase of Development	Estimated Substantial Completion Date	Estimated Fair Value (in millions)
HIV	Therapeutic product candidate	Pre-clinical	2008	\$ 1.9
Anti-Inflammatory	Therapeutic product candidate	Pre-clinical	2007	3.4
EPO	Therapeutic product candidate	Pre-clinical	2007	0.9
Insulin	Therapeutic product candidate	Pre-clinical	2009	1.2
Functional Genomics	Gene regulation product	Pre-marketing	2002	3.2
Agriculture	Gene regulation product	Pre-marketing	2005	2.5
				\$ 13.1

The following table represents unaudited pro forma condensed combined financial results of operations as if the Gendaq acquisition had occurred as of January 1, 2001.

The unaudited pro forma condensed combined financial information is presented for illustrative purposes only and is not necessarily indicative of the operating results or financial positions that would have occurred if the transaction had been consummated at the dates indicated, nor is it necessarily indicative of future operating results or financial position of the combined companies and should not be construed as representative of these amounts for any future dates or periods. In the opinion of management, this information is presented in conformity with accounting standards generally accepted in the United States. Loss from operations and net loss include amortization of acquired deferred compensation and intellectual property. The pro forma financial information excludes in-process research and development expense, due to its non-recurring nature, and excludes amortization of goodwill (in thousands, except per share amounts):

Year Ended December 31, 2001 (pro-forma)	
Total revenues	\$ 5,040
Loss from operations	\$ (30,043)
Net loss	\$ (26,893)
Basic and diluted net loss per share	\$ (1.11)
Shares used to compute basic and diluted net loss per share	24,191

In February 2002, Sangamo made the decision to begin consolidation of certain Gendaq operations from the United Kingdom to its Richmond, California headquarters. The decision followed a post-acquisition review that was initiated in October 2001 where Sangamo evaluated technology, personnel, costs, and various alternatives to maximize the synergy between Sangamo and Gendaq. As this review was initiated after the acquisition was completed, and the final decision to consolidate was not made until February 2002, the decision had no impact on accounting for the acquisition reported in 2001. The final decision made in February 2002 related to the rationalization of positions in the United Kingdom; at that time there were 15 employees at Gendaq. In the first quarter of 2002, Sangamo recorded restructuring expense of \$190,000 related to this rationalization in accordance with EITF 94-3, "Liability Recognition for Certain Employee Termination Benefits and Other Costs to Exit an Activity (Including Certain Costs Incurred in a Restructuring)." The workforce reduction charge included

58

incremental restructuring charges for the employees. These employees primarily worked on research and development and administrative activities to be continued by employees at the Company's headquarters. As of September 30, 2002, the facility in the United Kingdom was closed and all of the employees were terminated. Fixed assets at the U.K. facility were either disposed of or returned to the Richmond facility. Loss on sale of property and equipment of \$74,000 resulted from the disposition of U.K. assets. Restructuring costs in the third quarter of this year included additional employee retention costs of \$107,000 reflecting unexpectedly high participation in the employee retention program. From the date of the acquisition until the closure of the Gendaq facility, cumulative gains of \$367,000 were reported as a component of consolidated stockholders' equity. At the time of the closure, the entire balance of cumulative gain on foreign currency translation was reclassified out of stockholders' equity and included in other income. All restructuring expenses were during the year ended December 31, 2002.

4. Goodwill

During the year ended December 31, 2002, in accordance with the provisions of FAS No. 142 (see Note 1), the Company performed the required two-step annual impairment test of goodwill. In the first step of the analysis, after comparing the carrying value of the Company to its fair value, it was determined that goodwill recorded by the Company was impaired. After the second step of comparing the implied fair value of the goodwill to its carrying value, the Company recognized an impairment loss of \$15.3 million, representing the entire capitalized balance of goodwill in the third quarter of 2002.

The fair value of the Company was determined using the income approach. The income approach focuses on the income-producing capability of an asset, measuring the current value of the asset by calculating the present value of its future economic benefits such as cash earnings, cost savings, tax deductions, and proceeds from disposition. Value indications are developed by discounting expected cash flows to their present value at a rate of return that incorporates the risk-free rate for the use of funds, the expected rate of inflation, current equity market conditions in the United States, increased biotechnology sector volatility, general equity market forecasts and business and operational assumptions specific to Sangamo.

5. Intangible Assets

Statement No. 142 requires that if an impairment test of goodwill is required, the fair values of all assets and liabilities should be reflected in the carrying value of the company prior to the completion of the goodwill impairment test. In determining these fair values, the Company's long-lived assets were reviewed for impairment in accordance with FAS No. 144 by comparing the undiscounted cash flows associated with the intangible assets to their carrying value to indicate whether such assets are recoverable. If it is determined that an asset is not recoverable, FAS No. 144 directs that an impairment loss should be recognized based on the excess of its carrying value over its fair value. Based upon the results of this review, management has concluded that operational adjustments, including, but not limited to, the post-acquisition review and rationalization of Gendaq, has rendered the carrying amount of patents to be not recoverable. After comparing the carrying value of patents to their fair

59

value, the Company recognized an impairment loss of \$2.8 million representing the entire unamortized balance of patents. Management assessed all other assets as being recoverable.

December 31, 2002

Impairment

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December 31, 2002

	Gross Carrying Value	Accumulated Amortization	Net Carrying Value
Patents	\$ 3,359	\$ 599	\$ (2,760)

6. Property and Equipment

Property and equipment consist of the following:

	December 31,	
	2003	2002
	(in thousands)	
Laboratory equipment	\$ 1,714	\$ 1,787
Furniture and fixtures	716	705
Leasehold improvements	1,658	1,658
	4,088	4,150
Less accumulated depreciation	(3,182)	(2,357)
	\$ 906	\$ 1,793

7. Commitments

Sangamo occupies office and laboratory space under operating leases in Richmond, California that expire in 2004. License obligations consist of ongoing license maintenance fees and royalties due from sales of ZFP TFs. Consolidated rent expense for 2003, 2002 and 2001 was \$620,000, \$615,000, and \$633,000, respectively. Future minimum payments under contractual obligations and commercial commitments at December 31, 2003 consist of the following (in thousands):

Contractual Obligations	Payments Due by Period				
	Total	Less than 1 year	1-3 years	3-5 years	More than 5 years
Operating leases	\$ 416	\$ 416	\$	\$	\$
License obligations	1,134	378	756		
Total contractual obligations	\$ 1,550	\$ 794	\$ 756	\$	\$

8. Stockholders' Equity

Convertible Preferred Stock

All outstanding convertible preferred stock converted into common stock upon consummation of the Company's initial public offering in April 2000. The Company has 5,000,000 preferred shares authorized, which may be issued at the Board's discretion.

Common Stock

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At December 31, 2003, the Company had no outstanding common stock subject to the company's contractual right of repurchase.

Warrants

Warrants to purchase 74,570 shares of common stock were outstanding at an exercise price of \$1.50 per share, and were exercisable through October 2002. The warrants to purchase common stock were issued in connection with a 1997 bridge loan transaction. Sangamo had reserved common stock for issuance upon exercise of the warrants. 50,728 of the warrants were exercised before expiration in 2002. As of December 31, 2003, there were no warrants outstanding.

Stock Option Plan

Sangamo's 2000 Stock Option Plan (the "2000 Option Plan"), which supersedes the 1995 Stock Option Plan, provides for the issuance of common stock and grants of options for common stock to employees, officers, directors and consultants. The exercise price per share will be no less than 85 percent of the fair value per share of common stock on the option grant date, and the option term will not exceed ten years. If the person to whom the option is granted is a 10 percent stockholder, then the exercise price per share will not be less than 110 percent of the fair value per share of common stock on the option grant date, and the option term will not exceed five years. Options granted under the 2000 Option Plan generally vest over four years at a rate of 25 percent one year from the grant date and one thirty-sixth per month thereafter and expire ten years after the grant, or earlier upon employment termination. Options granted pursuant to the 2000 Option Plan may be exercised prior to vesting, with the related shares subject to Sangamo's right to repurchase the shares that have not vested at the issue price if the option holder terminates employment. The right of repurchase lapses over the original option vesting period, as described above. A total of 5.8 million shares are reserved for issuance pursuant to the 2000 Option Plan. The number of shares authorized for issuance automatically increases on the first trading day of the fiscal year by an amount equal to 3.5 percent of the total number of shares of our common stock outstanding on the last trading day of the preceding fiscal year.

As a part of Sangamo's acquisition of Gendaq, outstanding Gendaq stock options were replaced by options to purchase a designated number of shares of Sangamo Stock. The share reserve for replacement of Gendaq options was 125,366 shares, with the number of shares and exercise price per share adjusted to reflect application of the exchange ratio of the acquisition. Due to the termination of the Gendaq employees in 2002, there were no Gendaq options outstanding as of December 31, 2003.

61

A summary of Sangamo's stock option activity follows:

	Shares available for grant of options	Options Outstanding	
		Number of shares	Weighted-average exercise per share price
Balance at December 31, 2000	1,635,767	1,890,283	\$ 4.86
Additional shares authorized	775,158		
Options granted	(718,000)	718,000	\$ 10.20
Options exercised		(109,197)	\$ 12.85
Shares repurchased	10,767		\$ 0.20
Options canceled	124,603	(124,603)	\$ 9.34
Balance at December 31, 2001	1,828,295	2,374,483	\$ 6.33
Additional shares authorized	856,872		
Options granted	(535,750)	535,750	\$ 6.31
Options exercised		(95,946)	\$ 0.31
Options canceled	253,554	(253,554)	\$ 9.14
Balance at December 31, 2002	2,402,971	2,560,733	\$ 6.26
Additional shares authorized	865,925		

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		Options Outstanding	
Options granted	(652,700)	652,700	\$ 4.05
Options exercised		(72,495)	\$ 0.19
Shares repurchased	917		\$ 0.23
Options canceled	179,686	(179,686)	\$ 7.99
Balance at December 31, 2003		2,796,799	2,961,252 \$ 5.81

There were no shares subject to Sangamo's right of repurchase as of December 31, 2003. The weighted-average fair value per share of options granted during 2003, 2002, and 2001 was \$3.52, \$7.55, and \$10.20, respectively.

The following table summarizes information with respect to stock options outstanding at December 31, 2003:

Options Outstanding and Exercisable		
Range of Exercise Price	Number of Shares	Weighted Average Remaining Contractual Life (In Years)
\$ 0.05-\$ 0.17	635,083	4.30
\$ 0.23-\$ 3.81	519,394	8.11
\$ 3.99-\$ 6.06	501,625	9.47
\$ 6.94-\$ 7.49	501,500	7.55
\$ 7.57-\$11.44	495,900	7.26
\$ 11.75-\$38.00	307,750	6.20
	2,961,252	7.09

62

As permitted by FAS No. 123, Sangamo accounts for its stock option and stock incentive plans in accordance with APB 25 and recognizes no stock compensation expense for options granted with exercise prices equal to the fair market value of Sangamo's common stock at the date of grant. In 2000 and 1999, Sangamo granted options to employees with exercise prices below the fair value of Sangamo's common stock. Accordingly, the Company recognized deferred stock compensation of \$6.8 million in 2000. Deferred stock compensation is being amortized to expense over the vesting term of the option using the graded vesting method.

In 2003, 2002 and 2001, respectively, Sangamo granted 10,000, 6,000, and 32,500 nonqualified common stock options to consultants at exercise prices that range from \$2.42 to \$7.57 per share for services rendered. Such options are included in the option tables disclosed above. The options generally vest over four years at a rate of 25 percent one year from the grant date and one thirty-sixth per month thereafter and expire ten years after the grant date. Total nonqualified stock-based compensation expense was \$388,000, \$301,000 and \$596,000 in 2003, 2002 and 2001, respectively. The fair value of these options was determined using the Black-Scholes model and periodic adjustments as the options vest.

Employee Stock Purchase Plan

The Board of Directors adopted the 2000 Employee Stock Purchase Plan in February 2000, effective upon the completion of Sangamo's initial public offering of its common stock. Sangamo reserved a total of 400,000 shares of common stock for issuance under the plan. Eligible employees may purchase common stock at 85 percent of the lesser of the fair market value of Sangamo's common stock on the first day of the applicable two-year offering period or the last day of the applicable six-month purchase period. The reserve for shares available under the plan will automatically increase on the first trading day of the second fiscal quarter each year, beginning in 2001, by an amount equal to 1 percent of the total number of outstanding shares of our common stock on the last trading day of the immediately preceding first fiscal quarter.

Common Stock

At December 31, 2003, the Company has reserved shares of common stock for future issuance as follows:

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2000 Stock Option Plan	5,758,051
2000 Employee Stock Purchase Plan	870,687
	6,628,738

63

9. Comprehensive Loss

For the years ended December 31, 2003, 2002 and 2001, comprehensive loss was as follows (in thousands):

	Year ended December 31,		
	2003	2002	2001
Net loss	\$ (10,433)	\$ (29,764)	\$ (25,249)
Unrealized gain/(loss) on investments	(81)	(158)	129
Change in foreign currency translation adjustment		219	147
Other than temporary loss	6		
Reclassification of loss on foreign currency translation adjustment		(367)	
Comprehensive loss	\$ (10,508)	\$ (30,070)	\$ (24,973)

10. Loans to Officers

On May 10, 2002, Sangamo advanced its former Chief Scientific Officer a \$250,000 housing loan under a Secured Promissory Note. The note bore interest at six percent per annum and was being forgiven 25 percent annually beginning in 2003. The entire amount of the housing loan and accrued interest was forgiven and a related charge of \$263,000 was recorded during 2003.

11. Income Taxes

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

Deferred tax assets:

	December 31,	
	2003	2002
Deferred tax assets:		
Net operating loss carryforwards	\$ 12,161	\$ 9,600
Research and development credit carryforwards	1,697	700
Capitalized research	1,767	1,130
Other reserves and accruals	581	220
	16,206	11,650
Valuation allowance	(16,206)	(11,650)
Net deferred tax assets	\$	\$

Realization of deferred tax assets is dependent upon future earnings, if any, the timing and amount of which are uncertain. Accordingly, the net deferred tax assets have been fully offset by a valuation allowance. The valuation allowance increased by \$5,000 and \$2,000 for the periods

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ended December 31, 2003 and 2002, respectively. As of December 31, 2003, Sangamo had net operating loss carryforwards for federal income tax purposes of approximately \$36.0 million which expire in the years 2010 through 2023. The Company also has state operating loss carryforwards of approximately \$4.0 million which

64

expire in the years 2004 through 2014. The Company also has federal and state research credits of \$970,000 and 945,000, respectively. The federal research credits will begin to expire in the year 2018 through 2023 and the state research credits have no expiration date. Use of the 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. The annual limitation could result in the expiration of the net operating loss before use. However, management has not determined if the use of the net operating loss carryforwards will be limited.

12. Accounts Payable and Accrued Liabilities

Accounts payable and accrued liabilities consist of the following:

	December 31,	
	2003	2002
Accounts payable	\$ 139	\$ 283
Accrued professional fees	318	271
Accrued research and collaboration expense	154	298
Accrued severance	153	
Other	51	85
Net deferred tax assets	\$ 815	\$ 937

13. Quarterly Financial Data (Unaudited)

The following table sets forth certain unaudited quarterly financial data for the eight quarters ended December 31, 2003. The unaudited information set forth below has been prepared on the same basis as the audited information and includes all adjustments necessary to present fairly the information set forth herein. The operating results for any quarter are not indicative of results for any future period. All data is in thousands except per common share data.

	Fiscal Year 2003				Fiscal Year 2002			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Revenues	\$ 551	\$ 518	\$ 507	\$ 1,003	\$ 501	\$ 366	\$ 1,012	\$ 2,464
Expenses	\$ 3,622	\$ 4,221	\$ 3,473	\$ 3,032	\$ 5,452	\$ 4,343	\$ 22,614(2)	\$ 3,499
Net loss	\$ (2,895)	\$ (3,274)	\$ (2,584)	\$ (1,680)	\$ (4,487)	\$ (3,631)	\$ (20,940)	\$ (706)
Net loss per share(1)	\$ (0.12)	\$ (0.13)	\$ (0.10)	\$ (0.07)	\$ (0.18)	\$ (0.15)	\$ (0.85)	\$ (0.03)

(1) Net loss per share is calculated based on the weighted average number of common shares outstanding during the quarter.

(2) Q3 2002 expenses include the write-down of patents and goodwill of \$18.0 million.

65

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

(a) Evaluation of Disclosure Controls and Procedures

The Company's management, with the participation of the Company's Chief Executive Officer and Principal Financial Officer, evaluated the effectiveness of the Company's disclosure controls and procedures as of the end of the period covered by this report. Based on that evaluation, the Chief Executive Officer and Principal Financial Officer concluded that the Company's disclosure controls and procedures as of the end of the period covered by this report have been designed and are functioning effectively to provide reasonable assurance that the information required to be disclosed by the Company in reports filed under the Securities Exchange Act of 1934 is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms.

(b) Change in Internal Control over Financial Reporting

No change in the Company's internal control over financial reporting occurred during the Company's most recent fiscal year that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting.

(c) Limitations on the Effectiveness of Internal Controls

The Company believes that a controls system, no matter how well designed and operated, cannot provide absolute assurance that the objectives of the controls system are met, and no evaluation of controls can provide absolute assurance that all control issues within a company have been detected.

66

PART III

Certain information required by Part III is omitted from this Report on Form 10-K since we intend to file our definitive Proxy Statement for our next Annual Meeting of Stockholders, pursuant to Regulation 14A of the Securities Exchange Act of 1934, as amended (the "2004 Proxy Statement"), no later than April 29, 2004, and certain information to be included in the Proxy Statement is incorporated herein by reference.

Item 10. Directors and Executive Officers of the Registrant

The information required by this item concerning our directors, executive officers, Section 16 compliance and code of ethics is incorporated by reference to the information set forth in the sections titled "Election of Directors," "Executive Officers of the Company," "Section 16(a) Beneficial Ownership Reporting Compliance" and "Code of Ethics" in our 2004 Proxy Statement.

Item 11. Executive Compensation

The information required by this item regarding executive compensation is incorporated by reference to the information set forth in the sections titled "Executive Compensation" in our 2004 Proxy Statement.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this item regarding security ownership of certain beneficial owners and management is incorporated by reference to the information set forth in the section titled "Security Ownership of Certain Beneficial Owners and Management" and "Equity Compensation Plans" in our 2004 Proxy Statement.

Item 13. Certain Relationships and Related Transactions

The information required by this item regarding certain relationships and related transactions is incorporated by reference to the information set forth in the section titled "Certain Relationships and Related Transactions" in our 2004 Proxy Statement.

Item 14. Principal Accountant Fees and Services

The information required by this item regarding principal auditor fees and services is incorporated by reference to the information set forth in the section titled "Principal Auditor Fees and Services" in our 2004 Proxy Statement.

67

PART IV

Item 15. Exhibits, Financial Statement Schedules and Reports on Form 8-K

(a) The following documents are filed as part of this report:

1. Financial Statements See Index to Consolidated Financial Statements in Item 8 of the report.
2. Financial Statement Schedules None.
3. See Index to Exhibits.

(b) Reports on Form 8-K and form 8-K/A:

On October 28, 2003 we furnished a Current Report on Form 8-K containing a copy of our earnings release for the period ended September 30, 2003 pursuant to Item 12 (Results of Operations and Financial Condition). On November 5, 2003, we filed a Form 8-K/A to correct a clerical error.

(c) See the Index of Exhibits

(d) See the Financial Statements beginning on page 42 of this Form 10-K

68

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this amendment to be signed on its behalf by the undersigned, thereunto duly authorized, on March 31, 2004.

SANGAMO BIOSCIENCES, INC.

By: /s/ EDWARD O. LANPHIER II

Edward O. Lanphier II
President, Chief Executive Officer and Director

Index to Exhibits

Exhibit Number	Description of Document
2.1*	Agreement for the Sale and Purchase of all the Issued Share Capital of Gendaq Limited between Sangamo and Certain Shareholders of Gendaq Limited, dated June 28, 2001.
3.1	Amended and Restated Certificate of Incorporation.
3.2	Amended and Restated Bylaws.
4.1	Form of Specimen Common Stock Certificate.
10.1 ^	2000 Stock Incentive Plan.
10.2 ^	2000 Employee Stock Purchase Plan.
10.3	[Intentionally left blank]
10.4	Form of Indemnification Agreement entered into between Sangamo and each of its directors and executive officers.
10.5	Triple Net Laboratory Lease, between Sangamo and Point Richmond R&D Associates II, LLC, dated May 23, 1997.
10.6	Form of collaboration agreement.
10.7	License Agreement, between Sangamo and Baxter Healthcare Corporation, dated January 11, 2000.
10.8	Sublicense Agreement, by and between Sangamo and Johnson & Johnson, dated May 9, 1996.
10.9 ++	Second Amendment to License Agreement between Sangamo and Edwards Lifesciences LLC (formerly Baxter Healthcare Corporation), dated November 14, 2002.
10.10	Financial Assistance Award from U.S. Department of Commerce, dated March 31, 1997.
10.11	Notice of Grant Award from National Institute of Allergy and Infectious Diseases, dated August 9, 1999.
10.12	Patent License Agreement between Sangamo and Massachusetts Institute of Technology dated May 9, 1996, as amended.
10.13	License Agreement between Sangamo and the Johns Hopkins University dated July 16, 1998, as amended.
10.14 ++	First Amendment to Research Funding Agreement between Sangamo and Edwards Lifesciences LLC (formerly Baxter Healthcare Corporation), dated November 14, 2002.
10.15 ^	Employment Agreement, between Sangamo and Edward O. Lanphier II, dated June 1, 1997.
10.16 ^	1995 Stock Option Plan.

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Exhibit Number	Description of Document
10.17	Research Funding Agreement, by and between Sangamo and Edwards Lifesciences LLC (formerly Baxter Healthcare Corporation), dated January 11, 2000.
10.18 ^	Employment Agreement, between Sangamo and Alan Wolffe, Ph.D., dated March 17, 2000.
10.19	License Agreement by and between The Scripps Research Institute and Sangamo, dated March 14, 2000.

70

10.20+^	Employment Agreement between Sangamo and Carl Pabo, Ph.D., dated September 12, 2001.
10.21	Third Amendment to Research Funding Agreement between Sangamo and Edwards Lifesciences LLC (formerly Baxter Healthcare Corporation), dated August 14, 2003.
21.1++	Subsidiaries of the Company.
23.1	Consent of Ernst & Young LLP, Independent Auditors.
31.1	Rule 13a-14(a) Certification of Chief Executive Officer.
31.2	Rule 13a-14(a) Certification of Principal Financial Officer.
32.1	Certification Pursuant to 18 U.S.C. Section 1350.

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

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

^

Indicates management contract or compensatory plan or arrangement.

Incorporated by reference to Sangamo's Registration Statement on Form S-1 (Reg. No. 333-30314), as amended.

*

Incorporated by reference to Sangamo's Current Report on Form 8-K dated July 4, 2001.

+

Incorporated by reference to Sangamo's Annual Report on Form 10-K, filed March 29, 2002.

++

Incorporated by reference to Sangamo's Annual Report on Form 10-K, filed March 27, 2003.

71

QuickLinks

TABLE OF CONTENTS

PART I

Item 1. Business

Item 2. Properties

Item 3. Legal Proceedings

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

PART II

Item 5. Market for the Registrant's Common Stock and Related Stockholder Matters

Item 6. Selected Consolidated Financial Data

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

Item 8. Financial Statements and Supplementary Data

REPORT OF ERNST & YOUNG LLP, INDEPENDENT AUDITORS

SANGAMO BIOSCIENCES, INC. CONSOLIDATED BALANCE SHEETS (In thousands, except share and per share amounts)

SANGAMO BIOSCIENCES, INC. CONSOLIDATED STATEMENTS OF OPERATIONS (In thousands, except per share amounts)

SANGAMO BIOSCIENCES, INC. CONSOLIDATED STATEMENT OF STOCKHOLDERS' EQUITY (In thousands, except share amounts)

SANGAMO BIOSCIENCES, INC. CONSOLIDATED STATEMENTS OF CASH FLOWS (In thousands)

SANGAMO BIOSCIENCES, INC. NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

Item 9A. Controls and Procedures

PART III

Item 10. Directors and Executive Officers of the Registrant

Item 11. Executive Compensation

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

Item 13. Certain Relationships and Related Transactions

Item 14. Principal Accountant Fees and Services

PART IV

Item 15. Exhibits, Financial Statement Schedules and Reports on Form 8-K

SIGNATURES

Index to Exhibits