SANGAMO BIOSCIENCES INC
Form 10-K405
March 29, 2002

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SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

ý **Annual Report Pursuant to Section 13 or 15 (d) of the Securities Exchange Act of 1934**
For the Fiscal Year Ended December 31, 2001

SANGAMO BIOSCIENCES, INC.

(Exact name of registrant as specified in its charter)

Delaware	**8731**	**68-0359556**
(State or other jurisdiction of incorporation or organization)	(Primary Standard Industrial Identification Number)	(I.R.S. Employer Classification Code 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)

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. ý

The aggregate market value of the voting stock held by non-affiliates of the Registrant of the Common Stock listed on the NASDAQ Stock Market was $142,773,135 based on a closing stock price of $9.24 per share on March 15, 2002.

The total number of shares outstanding of the Registrant's Common Stock was 24,489,140 as of March 15, 2002.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of Registrant's Definitive Proxy Statement filed with the Commission pursuant to Regulation 14A in connection with the Annual Meeting are incorporated herein by reference into Part III of this Report.

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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;

revenues from existing and new collaborations;

product development;

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.

BUSINESS

Overview

Sangamo is the worldwide leader in the research, development and commercialization of engineered transcription factors for the regulation of gene expression. We are developing a proprietary technology platform based on the engineering of a naturally occurring class of transcription factors referred to as zinc finger DNA-binding proteins, or ZFPs. We believe that ZFP transcription factors, or ZFP TFs, represent a fundamentally enabling technology capable of activating or repressing a targeted gene that may be widely applicable to pharmaceutical discovery, development of human therapeutics, plant agriculture, industrial biotechnology and clinical diagnostics. We intend to commercialize our technology broadly over its many applications.

Background

Genes and Gene Expression. Deoxyribonucleic acid, or DNA, is present in all cells and is responsible for determining the inherited characteristics of all living organisms. DNA is arranged on chromosomes in individual units called genes. Genes encode proteins, which are assembled through the processes of transcription, whereby DNA is transcribed into ribonucleic acid, or RNA, and translation, whereby RNA is translated into protein. DNA, RNA, and proteins represent many of the molecular targets for pharmaceutical drug discovery and therapeutic intervention.

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 turned on or turned off (activated or repressed) in response to a wide variety of stimuli and developmental signals. Different sets of genes are expressed in distinct types of cells. 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. Regulation of gene expression is controlled by proteins, called transcription factors, which bind to DNA. A transcription factor regulates gene expression by recognizing and binding to a specific DNA sequence associated with a particular gene and causing that gene to be activated or repressed. In higher organisms, transcription factors typically consist of two principal components: the first is a DNA-binding element, or domain, that recognizes a specific DNA sequence and thereby directs the transcription factor to the proper chromosomal location; the second is a functional domain that determines whether the gene at that location is activated or repressed.

Chromatin Architecture. In order to efficiently organize the massive amounts of genetic information present in every cell, DNA is packaged within a structure known as chromatin, which renders certain areas of DNA less accessible than others. One way that cells are able to control chromatin structure, and make certain DNA sequences accessible, is through the action of specific enzymes that target regulatory regions within chromatin. It is through the action of these enzymes that the chromatin structure within the nucleus is altered, and DNA is made more or less accessible to transcriptional machinery. Our process for the identification of ZFP TFs that regulate a target gene frequently involves examining the chromatin structure of the gene to identify regions that are accessible for binding to ZFP TFs.

The Genomics Revolution. Genomics refers to the sequencing and functional analysis of the complete set of genes of diverse organisms throughout the animal, plant, and microbial world. Enormous scientific and financial resources have been dedicated to the sequencing of all human genes, including the Human Genome Project and other publicly and privately funded genomics initiatives. The sequence of a large percentage of the human genome was published in 2001.

Over the past decade, genomics research has produced a significant quantity of information on the location, sequence and structure of thousands of genes. The number of genes in the human genome is currently believed to be approximately 30,000 to 40,000 unique genes. A challenge facing the pharmaceutical and other life science industries lies in deriving medically and commercially valuable knowledge about the function of these genes from this large accumulation of new genomic sequence information.

Genome-Based Drug Discovery and Other Applications. The completion of the sequence of the human genome, with its bounty of new genes and potential drug discovery targets, simultaneously poses a competitive challenge and offers a significant commercial opportunity for every pharmaceutical company to:

accelerate the identification of drug targets from thousands of newly discovered genes whose functions are unknown or poorly understood;

sort through the hundreds of potential drug targets to confirm those for which proprietary drugs may be successfully developed;

increase the accuracy and efficiency of the process by which pharmaceutical researchers screen large libraries of chemical compounds to identify those which may have therapeutic activity, known as compound screening; and

discover and develop new therapeutics that can control disease through the regulation of genes.

The genomics revolution is also providing the sequences of plant genomes. Likewise, this poses a similar set of challenges and opportunities to agricultural biotechnology researchers, including identification of agriculturally important genes, the assessment of which genes may provide commercially important traits, and the development of improved agrochemicals and crops. In yet another application of genomics research, bacteria, yeast and plants may be engineered and used for the biological production of industrial chemicals.

Our ZFP TF technology, which enables the design of transcription factors to regulate genes, could have significant commercial utility in each of the applications listed above.

Sangamo's Technology Platform

The Sangamo technology platform combines our ability to engineer ZFP TFs with our knowledge of the chromatin structure of individual target genes. ZFP TFs have two distinct elements, or domains: a DNA-recognition domain that directs the transcription factor to the proper chromosomal location by recognizing a specific DNA sequence, and a functional domain that causes the gene to be activated or repressed. This two-component structure of our engineered ZFP TFs is modeled on the structure of naturally occurring transcription factors in higher organisms.

Consistent with this two-domain structure, we take a modular approach to the design of engineered ZFP TFs. The recognition domain is composed of one or more zinc fingers. Each finger recognizes and binds to a three base pair sequence of DNA. Multiple fingers can be linked together to recognize longer stretches of DNA. By modifying those portions of a ZFP that interact with DNA, we believe that we can create novel ZFPs capable of recognizing DNA sequences in genes whose sequence is known.

The ZFP DNA recognition domain is coupled to a functional domain, creating a ZFP TF capable of controlling or regulating the target gene in a 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. It is also possible to use a ZFP TF in a way that temporarily activates or represses a gene. This conditional regulation of a gene allows the effects of gene expression to be controlled in a reversible fashion.

An important variable influencing the expression of a specific gene in an individual cell is the surrounding chromosomal environment. Though every gene exists within every cell in the human body, only a fraction of our genes are activated in any given cell. To manage this

genetic information efficiently, nature has evolved a sophisticated system that facilitates access to specific genes. This system relies on a DNA-protein complex called chromatin to efficiently package the genetic information that exists within each cell, thereby making certain genes in certain cells more readily accessible to transcription factors. By evaluating the chromatin structure of a target gene, Sangamo scientists have been able to more effectively access and regulate specific genes. Complementing this understanding of chromosomal architecture is a growing appreciation of the role that regulatory DNA sequences play in gene regulation. Regulatory DNA determines when and how a gene is regulated. By applying our knowledge of this specialized regulatory machinery, we believe we can more efficiently and predictably control gene function.

In order to regulate a gene, the ZFP TF must be delivered to a cell, typically in the form of a gene encoding the ZFP TF. We have licensed gene transfer technology from Targeted Genetics, Inc. for use with our ZFP TFs in pharmaceutical discovery. We are evaluating this gene transfer technology and other technologies for the delivery of ZFP TFs into cells for *in vitro* and *in vivo* applications.

To date, we have generated thousands of ZFPs and have tested 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. We have linked these ZFPs to functional domains to create ZFP TFs and have demonstrated the ability of these ZFP TFs to regulate several hundred genes many of which may be commercially important. We have also shown that engineered ZFPs can detect single nucleotide polymorphisms, or SNPs, in medically important genes, and have demonstrated that our methods of manipulating chromatin structure can reveal medically important changes in regulatory DNA.

The Sangamo Advantage

We believe that the features of our ZFP TF technology platform will result in certain technical advantages as compared to other technologies. Among the advantages of our ZFP TF-based approach to gene regulation are:

ZFPs normally and naturally regulate genes in all higher organisms;

ZFPs can be designed to recognize unique DNA sequences;

ZFP TFs can activate or repress genes, enhancing their versatility;

ZFP TFs can be used to regulate the genes of humans, animals, plants, microbes and viruses; and

ZFP TFs can themselves be regulated, allowing conditional and reversible regulation of a gene.

We believe that the technical advantages of ZFP TFs create leverage across multiple applications, products, markets and commercial partners. While there are multiple market opportunities for our technology, we are concentrating our internal resources on human therapeutics and pharmaceutical discovery research. While we also intend to leverage our technology in the areas of plant agriculture, diagnostics and industrial biotechnology, we plan to pursue these applications in conjunction with corporate partners who have an established commercial focus in those areas.

Human Therapeutics

ZFP-Therapeutics . ZFP TFs have the potential to be developed as pharmaceutical products to treat a broad spectrum of diseases through the regulation of disease-related genes in patients.

Drug Screening and Antibody Development. The targeted regulation of genes with ZFP TFs may be an effective approach to engineering proprietary cell lines for screening and identification of new small molecule drug candidates and for the generation of human monoclonal antibodies.

Manufacturing of Protein Pharmaceuticals. ZFP TF-engineered cell lines can be developed to enhance production yields of protein pharmaceuticals and monoclonal antibodies.

Pharmaceutical Discovery Research

Validation of Gene Targets. ZFP TFs can be engineered to target a specific gene which is important to researchers trying to confirm the validity of gene targets in genomics-based drug discovery.

Discovery of New Genes and Targets. ZFP TFs can be used to change patterns of gene expression in cells to determine the consequences associated with these changes, and to thereby discover gene function and identify new targets for drug discovery.

Agricultural and Industrial Biotechnology

Agricultural Biotechnology. ZFP TFs can be used to regulate genes in plants, leading to potential applications in the identification of plant genes, agrochemical discovery, and the development of new crops with enhanced nutritional properties.

Industrial Biotechnology. ZFP TFs may be used to regulate genes in yeast, other microorganisms and plants which may permit the expanded use of engineered organisms for the manufacture of industrial chemicals.

Clinical Diagnostics

Regulatory DNA. Our ability to identify regulatory DNA, and changes in regulatory DNA associated with diseases, may provide the basis for novel approaches to genome-based clinical diagnosis.

SNP Detection. The specificity of ZFPs permits the detection of single base pair differences in DNA, also known as single nucleotide polymorphisms, or SNPs. We believe SNPs are likely to become increasingly important in clinical diagnosis to determine an individual's susceptibility to disease or probable response to drug therapy.

Commercial Applications

We are actively pursuing commercial applications of our ZFP TF technology in human therapeutics, pharmaceutical discovery and plant agriculture, and may, in the future, pursue applications in industrial biotechnology and clinical diagnostics.

Sangamo's Business Platform

Human Therapeutics

We believe our ZFP TF technology has applicability in the treatment of human diseases both through the development of ZFP TF-based therapeutics and through the use of our technology to identify new small molecule drugs and human monoclonal antibodies. In addition, we are applying our platform to the development of methods to enhance the production yield of protein pharmaceuticals.

ZFP-Therapeutics

The promise of genome-based drug discovery includes expansion of the supply of new drug targets, some of which are not amenable to current drug development approaches. ZFP TFs may offer a highly specific approach to regulation of disease-related genes. Due to alternative gene splicing, human genes make many more and different proteins per gene than lower organisms. Because our ZFP TFs act directly on an endogenous gene, they potentially allow us to control this important variable. In addition, the regulatory patterns governing human genes are more complex than those for lower organisms. Understanding this regulatory DNA is potentially important, and Sangamo has developed

methods to analyze and utilize the regulatory genome. We are developing ZFP-Therapeutics for the treatment of human diseases including cardiovascular diseases and cancer.

Cardiovascular Disease. Cardiovascular disease is the leading cause of death in the United States with nearly one million deaths annually. Approximately 700,000 Americans undergo angioplasty (a procedure designed to open coronary blood vessels) each year due to cardiovascular disease. Approximately 35% of these patients suffer from restenosis, or partial reclosing of treated blood vessels, and require a second procedure or more invasive surgery such as coronary bypass.

There is increasing interest in the development of therapeutic approaches to cardiovascular disease that might stimulate the human body's natural ability to form new blood vessels. This natural process is called angiogenesis. We have developed ZFP TFs designed to activate the expression of angiogenic factors called VEGFs for this purpose.

We believe an advantage of the ZFP-Therapeutic approach is the ability to activate therapeutically relevant endogenous genes with their natural variants. If successful, this may provide a more effective biological stimulation of angiogenesis compared to other approaches in which only a single form of VEGF is administered. This is a critical difference as VEGF, in its natural state, has multiple splice variants that are involved in the normal physiologic response.

To date we have seen initial preclinical results demonstrating that our ZFP TFs can induce the growth of blood vessels in rodent models. Other studies further demonstrated that ZFP TFs stimulated the production of all the major VEGF splice variants in the same proportion normally observed when tissues are oxygen-deprived. These results were presented at the annual meeting of the American Society of Gene Therapy in May 2001 by Frank Giordano, M.D., assistant professor of internal medicine and cardiology at Yale University School of Medicine, who directed many of these experiments.

We have a collaborative agreement with Edwards Lifesciences Corporation for the exclusive worldwide development of ZFP TFs for the activation of VEGF and VEGF receptors in cardiovascular and peripheral vascular disease. We are responsible for advancing product candidates into preclinical animal testing. Edwards will be responsible for preclinical development, regulatory affairs, clinical development and the sales and marketing of ZFP-Therapeutic products covered under the agreement. In October 2001, we received a $1.4 million milestone payment from Edwards following the delivery of a lead ZFP TF VEGF product candidate. We have retained rights to use our technology for other applications in VEGF activation and repression, including wound healing, ophthalmic indications and cancer.

Cancer. Through the mapping of the human genome, 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.

Through a strategic alliance with Onyx Pharmaceuticals, Inc., we are jointly developing novel cancer therapeutics using our ZFP TFs and Onyx's selectively replicating adenovirus technology, known as Therapeutic Viruses. Onyx is testing Therapeutic Viruses capable of delivering a therapeutic payload,

such as an engineered ZFP TF, into cells. Under this agreement, Onyx's Therapeutic Virus will be engineered to deliver a ZFP TF whose protein product has been shown to augment anti-tumor immune responses, thereby creating an Armed Therapeutic Virus that may treat cancer both at the tumor site and systemically. When product candidates meet certain mutually determined criteria, the companies will equally share research and clinical development costs and jointly commercialize products resulting from the alliance.

Commercialization of ZFP-Therapeutics . We plan to develop and commercialize ZFP-Therapeutics in partnership with pharmaceutical and biotechnology companies. For certain ZFP-Therapeutics we intend to negotiate partnerships with terms that will provide partners with exclusive rights to the regulation of specific genes for certain clinical indications and geographic areas covered under the agreement. For other ZFP-Therapeutics , we intend to retain commercial product rights or outlicense such products after substantial internal development.

Drug Screening and Antibody Development

Through several collaborations, we are applying our ZFP technology to assist in the identification of new small molecule drugs active against genomics-based targets and to develop fully human monoclonal antibodies.

ZFP-Engineered Cell Lines for Identification of Small Molecule Drug Candidates

We are incorporating ZFP TFs into appropriate cell lines for the purpose of screening chemical compounds for drug discovery. In particular, we are engineering cell lines that permit the regulation of validated gene targets. Activating a gene may allow pharmaceutical researchers to increase the sensitivity, or responsiveness, to a given concentration of test compound in an assay. In addition, if a response is observed when the gene is both activated and repressed, it can be concluded that the test compound is not acting through the protein encoded by that gene and may be showing a false positive result. To date, we have entered into agreements with the R.W. Johnson Pharmaceutical Research Institute and Pharmacia Corporation to create engineered cell lines for high-throughput small molecule screening.

Human Antibody Development

We have a collaboration with Medarex, Inc., a developer of human monoclonal antibodies, to use our ZFP TF technology to create cell lines that overexpress selected G-protein coupled receptors, or GPCRs. The GPCRs are a family of cell surface receptors that are critical to intercellular communication. Many current treatments for diseases of the cardiovascular, respiratory, gastrointestinal, neurologic and other physiologic systems act by influencing GPCR signaling pathways. However, since a number of GPCRs have yet to be identified, a significant amount of drug discovery research is focused on increasing the understanding of these important proteins. Under the terms of the agreement, we will work exclusively with Medarex on human antibodies developed using our technology and will share costs and commercialization rights to such products.

ZFP-Engineered Cell Lines for the Production of Pharmaceuticals

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 and growth in demand for current protein pharmaceuticals could lead to a significant shortfall in capacity over the next five years. We are actively engaged in the research and development of ZFP TF-engineered mammalian cells for the enhanced production of pharmaceutical proteins.

In collaboration with Medarex, Inc. we are developing ZFP TF-engineered cell lines to enhance the production yields of monoclonal antibodies. Under this agreement, Medarex is providing research funding to us and we will be entitled to milestone payments and, potentially, royalties on sales of Medarex antibodies manufactured using our technology.

Universal GeneTools for Pharmaceutical Discovery

We are applying Universal GeneTools to assist pharmaceutical researchers in their efforts to capitalize on the large accumulation of new genetic information being generated by the genomics revolution. Among the challenges that researchers must address are identifying disease-related genes, and confirming the validity of these genes and their protein products as appropriate targets for drug discovery by determining the function and suitability of targets for therapeutic intervention. We believe our Universal GeneTools can accelerate the pace and quality of genome-based drug discovery at these critical steps.

To date, we have entered into Universal GeneTools agreements with more than 20 leading pharmaceutical and biotechnology companies or their subsidiaries. These collaborators have used our ZFP TFs to validate gene targets from several organisms for drug discovery. ZFP TFs are being incorporated into both cells and animals for this purpose.

In Vivo Research Models

A key attribute of our ZFP TF technology is its potential applicability in multiple species. To leverage this attribute, we have entered into a technology partnership agreement with Charles River Laboratories, Inc. to apply our ZFP TF technology to the creation of a novel rat model for use in developing new drugs and therapies for cancer. Rats may offer practical advantages over mouse models, principally due to their physiology and larger size. Under this agreement, Charles River is funding the development at Sangamo of ZFP TFs for novel transgenic, or gene-altered, rat models in exchange for a royalty-bearing license to breed and sell these new models. We will also be entitled to milestone payments based on the progress of the collaboration.

ZFP Transcription Factors for Plant Agriculture

The multibillion-dollar agrochemical industry is undergoing a transition to genome-based product discovery that is parallel to that of the worldwide pharmaceutical industry. In a relatively recent development, the genomics revolution has been applied to the sequencing of plant genes from some of the world's largest commercial crops. We believe that the genomes of most commercially important plants will be sequenced over the next several years. Similar to trends in pharmaceutical research, discovery of thousands of plant genes is creating enormous

demand for technologies that can help ascertain gene function, identify important gene and agrochemical targets and regulate those genes through improved transgenic plants.

Natural ZFP TFs also regulate genes in plants. The ability to identify and subsequently regulate the expression of genes with ZFP TFs could lead to the creation of new plants that may increase crop yields, lower production costs, resist herbicides, pesticides and plant pathogens, and permit the development of branded agricultural products with unique nutritional and processing characteristics. In addition, ZFP TFs may be used to confirm the role of newly discovered genes in plant growth, metabolism and resistance to pathogens.

In January 2001, we signed our first partnership in the area of plant agriculture with Renessen LLC, a joint venture between Monsanto Corporation and Cargill. Sangamo and Renessen scientists have achieved significant results in the first year of this collaboration, including the regulation of a gene target in model systems and a commercial crop.

ZFPs for Pharmacogenomics and Clinical Diagnostics

Single nucleotide polymorphisms, or SNPs, are DNA sequence variations at specific chromosomal sites. SNPs have been the subject of increasing research in recent years. Some SNPs are strongly associated with some disease states, providing indicators of disease susceptibility and how individual patients might respond to a particular drug therapy. The pharmaceutical industry is investing in technology to monitor and record patient SNPs in clinical trials and to correlate clinical outcomes with SNP status.

We have shown that our proprietary methods for probing chromosomal structure can be applied to the large-scale identification of regulatory DNA short DNA sequences that are interspersed throughout the genome and which provide the binding sites for endogenous transcription factors. We believe that these regulatory DNA sequences may be a key to understanding the role of "non-coding" SNPs, which are those SNPs that fall outside the structural region of genes that may play a critical role in the disease-related misregulation of certain genes.

In addition, we believe that changes in regulatory DNA can be correlated with the onset of disease, and therefore potentially used as a molecular diagnostic tool in the clinic. Finally, regulatory DNA sequences may be a valuable addition to the human genome database.

We intend to commercialize ZFPs for SNP detection and DNA diagnostics in conjunction with partners engaged in the development of SNP diagnostic technology or the manufacturing and marketing of clinical diagnostics.

ZFPs for Industrial Biotechnology

The U.S. chemical industry is undertaking a major strategic initiative to develop bacterial, fungal, and plant biological systems for the production of industrial chemicals. This initiative is motivated by considerations of product performance, capital costs, environmental impact, and dependence on fossil fuels to provide the raw materials for the production of many chemical intermediates in the United States and around the world. A principal challenge in harnessing biological systems for this purpose is engineering bacterial and fungal cells and plants to achieve predictable and specific regulation of multiple genes. ZFP TFs may be applicable for this task.

ZFP TFs may prove to be a commercially feasible approach for the engineering of cells and plants for the biological production of industrial chemicals and food additives. We intend to seek strategic relationships with corporate partners in the chemical and food processing industries to develop and commercialize applications of ZFP TFs in industrial biotechnology.

Gendaq Acquisition

In July 2001, we acquired Gendaq Limited, a privately held biotechnology company located in London, U.K. Among its scientific founders is Professor Sir Aaron Klug, O.M., P.R.S., recipient of the Nobel Prize for Chemistry. The acquisition provided us with new intellectual property in the field of ZFP and ZFP TFs, as well as the expertise of the Gendaq scientific group. In connection with the acquisition, we issued approximately 2.1 million shares of Sangamo stock in exchange for all of the outstanding Gendaq shares, and have reserved approximately 125,000 shares of our common stock for options granted to former Gendaq employees that we assumed in the acquisition. In addition, Stephen Reeders, M.D., Chief Executive Officer at MVM Limited, a venture capital firm, was appointed to our Board of Directors.

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, and we recorded no restructuring liability during 2001. We anticipate the consolidation will take approximately eight months to complete, and the associated costs which will all be incurred during 2002, will be minimal (see "Part II, 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).

Corporate Collaborations

We intend to apply our ZFP TF technology platform in several commercial applications where the products provide ourselves and our strategic partners and collaborators with technical and economic advantages. We have established and will continue to pursue strategic partnerships and Universal GeneTools collaborations with selected pharmaceutical and biotechnology companies to fund internal research and development activities and to assist in product commercialization.

Edwards Lifesciences Strategic Partnership

In January 2000, we announced the initiation of 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 cardiovascular and peripheral 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. We have 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 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. Together with accrued interest, this note converted into common stock at the time of our initial public offering at the IPO price. We will be responsible for advancing product candidates into preclinical animal testing. Edwards will be responsible for preclinical development, regulatory affairs, clinical development and the sales and marketing of the ZFP-Therapeutic products. In the future, we may receive up to $26 million in milestone payments in connection with the development and commercialization of the first product under this agreement. Sangamo will also receive royalties on product sales. There is no assurance that the companies will achieve our development and commercialization milestones. 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.

Universal GeneTools Collaborations

We began marketing our Universal GeneTools products to the pharmaceutical and biotechnology industry in 1998. Our Universal GeneTools business is 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. Since 1998, we have entered into Universal GeneTools collaborations with more than 20 leading pharmaceutical or biotechnology companies or their subsidiaries.

Our Universal GeneTools agreements generally contain the following terms:

- collaborators provide us with the gene target they wish to study and we design and deliver ZFP TFs designed specifically for that collaborator's gene target;
- collaborators retain all their rights in confidential gene targets and any data they generate with our ZFP TFs;
- collaborators must provide us with the DNA sequence for the genes they wish to regulate;

- in most agreements, we retain the rights to make, use, develop, and sell any product or service utilizing the ZFP TFs we provide to our collaborators. In the other agreements, however, our rights are limited, but we do not regard these limitations as material to our business;

many of our agreements provide that collaborators make a partial payment for ZFP TFs during the design stage, and complete their payment after receipt of the ZFP TFs. The agreements generally do not provide for milestone or royalty payments.

To date, we have not licensed any intellectual property rights to our current Universal GeneTools collaborators that we believe are material to our business. Our Universal GeneTools collaborators are under no obligation to pursue product development programs with us, to use our technology, or to purchase any additional product from us. We have recently begun shifting our commercial development focus from Universal GeneTools collaborations to higher value strategic partnerships with selected pharmaceutical and biotechnology companies. See "Risk Factors Commercialization of our technologies depends on strategic partnering with other companies, and if we are not able to find strategic partners in the future, we may not be able to develop our technologies or products which could slow our growth and decrease our revenues," and " Initial evaluations of our engineered ZFP TFs delivered to our Universal GeneTools collaborators have produced mixed results."

Plant Agriculture Collaboration

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 has received certain payments, including research funding and milestone payments, and will receive royalties on product sales. In return, Renessen will receive the right to commercialize ZFP-engineered seeds for specific applications in the animal feed and processing industries.

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, 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. These patent filings have resulted in eleven issued U.S. patents to date. We believe these licensed patents and patent applications include several of the early and important patent filings directed to design, selection and use of ZFPs and ZFP TFs.

We have forty families of U.S. patent filings, including two U.S. and seven foreign issued patents, based on Sangamo and Gendaq internal research. Thirty-six of these have been filed internationally in selected countries to date. These patent filings are directed to improvements in the design and use of ZFPs and ZFP TFs. 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 protect the commercial development of ZFPs and ZFP TFs. 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 should not exceed $1 million. For risks associated with our intellectual property, see "Risk Factors Because it is difficult and costly to protect our proprietary rights, and third parties have filed patent applications that are similar to ours, we cannot ensure the proprietary protection of our technologies and products." We plan to continue to license and to internally generate intellectual property covering the design, selection, generation and composition of ZFPs, the genes encoding these proteins and the application of ZFPs and ZFP TFs in pharmaceutical discovery, therapeutics for the treatment of human diseases, clinical diagnostics, and agricultural and industrial biotechnology applications.

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 or may be issued will be upheld. 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 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 result in diversion of resources. The outcome of these proceedings is uncertain and could significantly harm our business.

We have received unsolicited invitations to license existing patented technology from a number of third parties, at least one of which contained an allegation of infringement. No litigation is being threatened and no license fees have been proposed. Upon careful analysis of each of these technologies, we have determined that we already own rights to these technologies or that our scientific and commercial interests would not benefit from the acquisition of rights to these technologies. Further, we believe that the making, using or selling of our products and processes need not infringe any claims in the proffered patents. Accordingly, we have declined to enter into license negotiations with these parties. We cannot assure you, however, that these parties will not bring future actions against us, our collaborators or strategic partners alleging infringement of their patents. As detailed above, the outcome of any litigation, particularly lawsuits involving biotechnology patents, is difficult to predict and likely to be costly regardless of the outcome. In these circumstances, i.e. litigation, the risks of a negative impact on our business can neither be clearly defined nor entirely eliminated.

In the future, however, 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 "Risk Factors Because it is difficult and costly to protect our proprietary rights, and third parties have filed patent applications that are similar to ours, we cannot ensure the proprietary protection of our technologies and products."

Competition

We believe that we are a leader in the field of ZFP TF gene regulation. 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 technology. The field of regulation of gene expression 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 technologies that will compete with our ZFP TF technology platform.

In July 2001, we strengthened our competitive position by completing our acquisition of Gendaq. Gendaq scientists have also focused their research efforts on regulating genes through the engineering of ZFPs. Despite the Gendaq acquisition, any products that we develop using 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 noncompetitive. In addition, many of those competitors 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 TFs or other competitive products before us. If we commence commercial product sales, we will 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 also arise from other drug development technologies and methods of preventing or reducing the incidence of disease, small molecule therapeutics, or other classes of therapeutic agents.

We expect to face intense competition from other companies for collaborative arrangements with pharmaceutical, biotechnology, agricultural and chemical 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;

develop and maintain products that reach the market first, are technologically superior to or are of lower cost than other products in the market;

attract and retain scientific and product development personnel;

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

obtain required regulatory approvals; and

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

Government Regulation

We have not applied for any regulatory approvals with respect to any of our technology or products under development. We anticipate that the production and distribution of any therapeutic or diagnostic products developed, either alone or with our strategic partners or collaborators, will be subject to extensive regulation in the United States and other countries. We intend to pursue

therapeutic, diagnostic, agricultural and industrial biotechnology products, some of which may be subject to different government regulation.

Before marketing in the United States, any pharmaceutical, therapeutic or diagnostic 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. Before commencing clinical investigations in humans, we must submit to, and receive approval from, the FDA of an Investigational New Drug application. We expect to rely on some of our strategic partners to file Investigational New Drug applications and generally direct the regulatory approval process for some products developed using our ZFP TF technology.

Clinical testing must meet requirements for:

institutional review board oversight;

informed consent;

good clinical practices; and

FDA oversight.

Before receiving FDA clearance to market a product, we must demonstrate that the product is safe and effective on the patient population that will be treated. 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 studies. Marketing or promoting a drug for an unapproved indication is generally prohibited. Furthermore, clearance may entail ongoing requirements for post-marketing studies. Even if this regulatory clearance is obtained, a marketed product, its manufacturer and its manufacturing facilities are subject to continual review and periodic inspections by the FDA. Discovery of previously unknown problems with a product, manufacturer or facility may result in restrictions on this product or manufacturer, including costly recalls or withdrawal of the product from the market.

The length of time necessary to complete clinical trials varies significantly and may be difficult to predict. Clinical results are frequently susceptible to varying interpretations that may delay, limit or prevent regulatory approvals. Additional factors that can cause delay or termination of our clinical trials, or the costs of these trials to increase, include:

slow patient enrollment due to the nature of the protocol, the proximity of patients to clinical sites, the eligibility criteria for the study or other factors;

inadequately trained or insufficient personnel at the study site to assist in overseeing and monitoring clinical trials;

delays in approvals from a study site's review board;

longer treatment time required to demonstrate effectiveness or determine the appropriate product dose;

lack of sufficient supplies of the product candidate;

adverse medical events or side effects in treated patients; and

lack of effectiveness of the product candidate being tested.

In addition, the field testing, production and marketing of genetically engineered plants and plant products are subject to federal, state, local and foreign governmental regulation. Regulatory action or private litigation could also 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 applied to foods developed through traditional plant breeding. Genetically engineered food products, however, will be subject to premarket review if these products raise safety questions or are deemed to be food additives. Our products or those of our strategic partners may be subject to lengthy FDA reviews and unfavorable FDA determinations.

International Biosafety Protocols have been announced in which signatory states may require that genetically engineered food products be labeled as such. Additional and more restrictive international or foreign policies may be developed which further limit our ability to pursue our business plan in relation to agricultural biotechnology.

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 Community registration procedures are available to companies wishing to market a product in more than one EC 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 intend to consult with, and when appropriate, to hire personnel with expertise in regulatory affairs to assist us in obtaining appropriate regulatory approvals as required. We also intend to work with our strategic partners and collaborators that have experience in regulatory affairs to assist us in obtaining regulatory approvals for collaborative products. See "Risk Factors Our potential therapeutic products are subject to a lengthy and uncertain regulatory process, and if these potential products are not approved, we will not be able to commercialize those products" and " Regulatory approval, if granted, may be limited to specific uses or geographic areas which could limit our ability to generate revenues."

Employees

As of February 28, 2002, we had 90 full-time employees, 42 of whom hold Ph.D. degrees and 41 of whom hold other graduate or technical degrees. Of our total workforce, 78 are engaged in research and development activities and 12 are engaged in business development, finance and administration. 74 of our employees are located in the United States, and 16 are located in the United Kingdom. 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.

Risk Factors

An investment in our common stock is risky. You should carefully consider the following risks, as well as the other information contained in this report. If any of the following risks actually occurs, it would harm our business. In that case, the trading price of our common stock could decline, and you might lose all or a part of your investment. The risks and uncertainties described below are not the only ones facing us. Additional risks and uncertainties not presently known to us or that we currently see as immaterial, may also harm our business.

Risks Related to Our Business

Our gene regulation technology is 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 new approach to gene regulation. Although we have generated some ZFP TFs for some gene sequences, we have not created ZFP TFs for all gene sequences and we may not be able to create ZFP TFs for all gene sequences 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 done so in humans and many other organisms, and the failure to do so could restrict our ability to develop commercially viable products. If we and our Universal GeneTools collaborators or strategic partners are unable to extend our results to new gene sequences and experimental animal models, we may be unable to use our technology in all its intended applications. Also, delivery of ZFP TFs into cells in these and other environments is limited by a number of technical challenges, which we may be unable to surmount.

The utility of our ZFP TFs is in part based on the belief that the regulation of gene expression may help scientists better understand the role of human, animal, plant and other genes in drug discovery, as well as therapeutic, diagnostic, agricultural and industrial biotechnology applications. There is only a limited understanding of the role of 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 Universal GeneTools collaborators or our strategic partners may not be able to use our technology to identify and validate drug targets or other targets in order to develop commercial products.

If our technology does prove to be effective, it still may not lead to commercially viable products, which would reduce our revenue opportunities.

Even if our Universal GeneTools collaborators or strategic partners are successful in identifying drug targets or other targets based on discoveries made using our ZFP TFs, they may not be able to discover or develop commercially viable products or may determine to pursue products that do not use our technology. To date, no company has developed or commercialized any therapeutic, diagnostic, agricultural or industrial biotechnology 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 plan and future growth.

Our quarterly results will fluctuate.

We believe that period-to-period comparisons of our results of operations are not necessarily meaningful and should not be relied upon as indicators of future performance. The variability of receipt of funds from corporate partners, as well as revenue recognition accounting rules, including the SEC staff accounting bulletin No. 101, will lead to quarterly fluctuations in our revenue. We generally operate with limited backlog in our Universal GeneTools business because our ZFP TFs are typically designed and engineered as orders are received. As a result, product sales in any quarter are generally

dependent on orders received and shipped in that quarter. Universal GeneTools sales are also difficult to forecast because demand varies substantially from customer to customer and from period to period. We have recently begun shifting our commercial development focus from Universal GeneTools collaborations to higher value strategic partnerships with selected pharmaceutical and biotechnology companies. While strategic partnerships may provide us with committed quarterly research funding, the signing of such deals, and the subsequently initiation of revenue recognition, is also uncertain.

Due to all of the foregoing factors, it is likely that in one or more future quarters our results may fall below the expectations of public market analysts and investors. In such event, the trading price of our common stock would likely be adversely impacted.

Our Universal GeneTools collaboration agreements with companies are of limited scope, and if we are not able to expand the scope of our existing collaborations or enter into new ones, our revenues will be negatively impacted and our research initiatives may be slowed or halted.

Our Universal GeneTools collaborations permit us to introduce our technology to many companies by supplying them with a specified ZFP TF for a payment without licensing our technology. The collaboration agreements, however, are of limited scope. Under most of our current Universal GeneTools collaborations we receive a payment for supplying ZFP TFs for gene targets specified by the companies. These companies are not obligated to make continuing payments to us in connection with their research efforts or to pursue any product development program with us. As a result, we may not develop long-term relationships with these companies that could lead to additional revenues. If we are not able to expand the scope of our existing collaborations or enter into new ones, we may have reduced revenues and be forced to slow or halt research initiatives.

Initial evaluations of our engineered ZFP TFs delivered to our Universal GeneTools collaborators have produced mixed results.

Some of our Universal GeneTools collaborators were unable to substantiate the effects of our gene regulation technology. Generally, failures were re-evaluated at Sangamo using our current approach of examining the local chromatin structure for accessible sites and then targeting ZFP TFs to these areas. In most cases, additional ZFP TFs were designed and tested for these targets, and data was generated at Sangamo, or by our partners, confirming the ability to regulate these targets. Sangamo now performs this more extensive validation on all Universal GeneTools targets prior to use by external parties. However, there can be no assurances that we will be able to regulate all gene targets, and repression of a gene is generally more difficult than activation. Although we have been able to achieve repression in numerous genes, the degree of repression may not be sufficient to allow our collaborators to realize their objectives. For example, one of our collaborators has advised us that while some of our ZFP TFs delivered to them repressed certain target gene sequences to a significant extent, the repression was not complete enough to warrant proceeding to develop revised ZFP TFs for this purpose. However this collaborator has advised us that positive results were achieved using our ZFP TFs to regulate other target gene sequences. In addition, some of our collaborators have not yet generated the final results of their testing, and no assurances can be given that our collaborators will be able to achieve satisfactory results. These ZFP TFs, or ones engineered in the future, may not function as intended. 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.

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 using our ZFP TF technology platform will participate in highly competitive markets. Even if we are able to generate ZFP

TFs that achieve useful results, competing technologies may prove to be more effective or less expensive which would limit or eliminate our revenue opportunities. Competing technologies may include other methods of regulating gene expression. ZFP TFs have broad application in the life sciences, and competes 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. Our competitors include biotechnology companies with:

competing proprietary technology;

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

greater manufacturing and marketing capabilities than we do.

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.

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

In order to regulate an endogenous gene, the ZFP TF must be delivered to a cell. We have licensed certain gene transfer technology for use with our Universal GeneTools in pharmaceutical discovery. We are evaluating this and other technologies which may need to be used in the delivery of ZFP TFs into cells for *in vitro* and *in vivo* applications. However, we may not be able to license the gene transfer technologies required to develop and commercialize our ZFP TF technology. We have not developed our own gene transfer technologies and 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.

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 90 employees as of February 28, 2002, 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 academic and other research 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. If we lose the services of personnel with these types of skills, it could impede significantly the achievement of our research and development objectives. If we fail to negotiate additional acceptable collaborations with academic and other research institutions and

scientists, or if our existing collaborations are unsuccessful, our technology development programs may be delayed or may not succeed.

At present the scope of our needs is somewhat limited to the expertise of personnel who are able to engineer ZFP TFs and apply them to gene regulation. In the future, we will need to hire additional personnel and develop additional academic collaborations as we continue to expand our research and development activities and to work on some of our planned projects because these activities and projects will require additional expertise in disciplines applicable to the products we would develop with them. Further, our planned activities will require existing

management to develop additional expertise. We do not know if we will be able to attract, retain or motivate the required personnel to achieve our goals.

We may have difficulty managing our growth, which may slow our growth rate or give rise to inefficiencies which would reduce our profits.

We have recently experienced, and expect to continue to experience, growth in the number of our employees and the scope of our operating and financial systems. This growth has resulted in an increase in responsibilities for both existing and new management personnel. Our ability to manage growth effectively will require us to continue to implement and improve our operational, financial and management information systems and to recruit, train, motivate and manage our employees. We may not be able to manage our growth and expansion, and the failure to do so may slow our growth rate or give rise to inefficiencies which would reduce our profits.

We are at an early stage of development and may not succeed or become profitable.

We began operations in 1995 and are at an early stage of development. We have incurred significant losses to date, and our revenues have been generated from Universal GeneTools collaborators, strategic partners and federal government research grants. Our Universal GeneTools collaborators are evaluating our ZFP TFs. If the ZFP TFs do not provide sufficient value to those collaborators, then they may not continue to work with us. This may also impair our ability to attract additional collaborators. As a result, our business is subject to all of the risks inherent in the development of a new technology, which includes the need to:

attract additional new Universal GeneTools collaborators and strategic partners and expand existing relationships;

attract and retain qualified scientific and technical staff and management, particularly scientific staff with expertise to further apply and develop our early stage technology;

attract and enter into research collaborations with academic and other research institutions and scientists;

obtain sufficient capital to support the expense of developing our technology platform and developing, testing and commercializing products;

develop a market for our products; and

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

In addition to competitive pressures, problems frequently encountered with research, development and commercialization of new technologies and products will likely affect us. Most of our ZFP TF design and testing procedures take place on a relatively small scale. In the future, we intend to apply ZFP TF design and testing procedures at a scale involving hundreds of genes per year. We may not be able to successfully or efficiently achieve this scale. In addition, while we have had success in applying

ZFP TF gene regulation in our laboratories, we may have difficulty in transferring our technology to our collaborators' and strategic partners' laboratories.

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 highly uncertain, and we may not be profitable in 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 partnership agreements and federal government research grants. As of December 31, 2001, we had an accumulated deficit of approximately $43.1 million. Even if we succeed in increasing our current product and research revenue or developing additional commercial products, we expect to incur losses for the foreseeable future. These losses will increase as we expand our research and development activities. 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 should it become necessary, 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 development activities. While we believe our financial resources will be adequate to sustain our current operations for the next 24 months, if we are unable to generate adequate operating cash flows thereafter we may need to seek additional sources of capital through equity or debt financing or by entering into additional Universal GeneTools collaborations, strategic partnerships or licensing arrangements. In addition, if we decide to focus our efforts on proprietary human therapeutics, we may need to seek FDA approval of potential products, a process which would 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 products would be harmed.

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

Volatility in the market for biotechnology stocks could cause you 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 become highly volatile. The market price of our common stock may fluctuate significantly in response to the following factors, some of which are beyond our control:

changes in market valuations of similar companies;

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;

deviations in our results of operations from the estimates of securities analysts; and

future sales of our common stock or other securities.

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 us and our corporate or academic collaborators, strategic partners or scientific advisors or directors, the other party may act in its self-interest which may limit our ability to implement our strategies. Some of our Universal GeneTools or academic collaborators or strategic partners are conducting multiple product development efforts within each area that is the subject of the collaboration with us. Generally, in each of our collaborations, we have agreed not to conduct independently, or with any third party, any research that is competitive with the research conducted under our collaborations. Our collaborations may cause us to limit the areas of research that we pursue, either alone or with others. 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 their withdrawal of support for our product candidates.

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

Commercialization of our technologies depends on strategic partnering with other companies, and if we are not able to find strategic partners in the future, we may not be able to develop our technologies or products, which could slow our growth and decrease our revenues.

We expect to rely, to some extent, on our strategic partners to provide funding in support of our research and to perform some independent research, preclinical and clinical testing. Our technology is broad based and we do not currently possess the resources necessary to develop and commercialize potential products that may result from our technologies, or the resources or capabilities to complete any approval processes that may be required for the products, therefore we must enter into additional strategic partnerships to develop and commercialize products.

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 uses 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.

If we do not enter into additional strategic partnering agreements, we will experience reduced revenues and may not develop or commercialize our products. The loss of our current or any future strategic partnering agreement would not only delay or terminate the potential development or commercialization of any products we may derive from our technologies but 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 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 current Universal GeneTools collaboration 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 fails to meet specific milestones, then the strategic partnership can be terminated which could decrease our revenues.

Our Universal GeneTools collaborators and strategic partners may decide to adopt alternative technologies or may be unable to develop commercially viable products using our technology, which would negatively impact our revenues and our strategy to develop these products.

Our collaborators or strategic partners may adopt alternative technologies of our competitors which could decrease the marketability of our technology. Because many of our Universal GeneTools collaborators or strategic partners are likely to be working on more than one research 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 gene regulation technology. Further, our collaborators and strategic partners may elect not to develop products arising out of our collaborative and strategic partnering arrangements or to devote sufficient resources to the development, manufacturing, marketing or sale of these products. If any of these events occur, we may not be able to develop our technologies or commercialize our products.

We intend to conduct proprietary research programs to discover therapeutic product candidates. These programs increase our risk of product failure, may significantly increase our research expenditures, and may involve conflicts with our collaborators and strategic partners.

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 and the expenditure of significantly greater funds than our current research activities. In addition, these programs will require substantial commitments of time from our management and staff. Moreover, we have no experience in preclinical or clinical testing, obtaining regulatory approval or commercial-scale manufacturing and marketing of therapeutic products, and we currently do not have the resources 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, market and sell products. We do not have these capabilities, and we may not be able to develop or otherwise obtain the requisite preclinical, clinical, regulatory, manufacturing, marketing and sales capabilities.

In addition, disagreements with our Universal GeneTools 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.

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 these patents against third party challenges. The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and 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, and our future licenses 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:

- 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;
- 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 Universal GeneTools collaborators or strategic partners will provide a basis for commercially viable products or will provide us with any competitive advantages or will not be challenged and invalidated by third parties;
- we will develop additional products, processes or technologies that are patentable; or
- the patents of others will not have an adverse effect on our ability to do business.

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 Sangamo has no current plans to use

the associated inventions. If these or other patents issue, it is possible that the holder of any patent or patents granted on these applications may bring an infringement action against our collaborators, strategic partner 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 our Universal GeneTools collaborators, strategic partners or we 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. While we believe that our proprietary intellectual property would give us substantial leverage to secure a cross-license, it is uncertain that any license required under that patent or patents would be made available on commercially acceptable terms, if at all. We believe that there may be significant litigation in the genomics industry regarding patent and other intellectual property rights, which could subject us to litigation. If we become involved in litigation, it could consume a substantial portion of our managerial and financial resources.

We rely on trade secrets to protect technology where we believe patent protection is not appropriate or obtainable. Trade secrets, however, are difficult to protect. While we require employees, academic collaborators and consultants to enter into confidentiality agreements, we may not be able to adequately protect our trade secrets or other proprietary information or enforce these confidentiality agreements.

Our Universal GeneTools 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. See "Business Intellectual Property and Technology Licenses."

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 therapeutic and some diagnostic products based on ZFP TF technology before they can be marketed in the United States. The process for receiving regulatory approval is long and uncertain, and even if we had a potential product, this product may not withstand the rigors of testing under the regulatory approval processes.

Before commencing clinical trials in humans, we must submit and receive approval from the FDA of an Investigational New Drug Application. Clinical trials are subject to oversight by institutional review boards and the FDA and these trials must meet particular conditions, such that they:

- must be conducted in conformance with the FDA's good clinical practice 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 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 Investigational New Drug application or the conduct of these trials.

We must also demonstrate that the product is safe and effective in the patient population that will be treated. Data obtained from preclinical and clinical activities are susceptible to varying interpretations that could delay, limit or prevent regulatory clearances. In addition, we may encounter delays or rejections based upon additional government regulation from future legislation or administrative action or changes in FDA

policy during the period of product development, clinical trials and FDA regulatory review. Failure to comply with applicable FDA or other applicable regulatory requirements may result in criminal prosecution, civil penalties, recall or seizure of products, total or partial suspension of production or injunction, as well as other regulatory action against our potential

products or us. Additionally, we have no experience in conducting and managing the clinical trials necessary to obtain regulatory approval.

In addition, we may also require approval 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 have not submitted an application with the FDA or any other regulatory authority for any product candidate, and neither the FDA nor any other regulatory authority has approved any therapeutic, diagnostic, agricultural or industrial product candidate developed with our technology for commercialization in the United States or elsewhere.

Regulatory approval, if granted, may be limited to specific uses or geographic areas which could limit our ability to generate revenues.

Regulatory approval may limit the indicated use for which we can market a product. Further, once regulatory approval for a product is obtained, it 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 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.

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.

Laws or public sentiment may limit our production of genetically engineered agricultural products in the future, and these laws could reduce our ability to sell these products.

Genetically engineered products are currently subject to publi