

3,100,000 Shares**SANGAMO BIOSCIENCES, INC.****Common Stock****\$6.75 per share**

- Sangamo BioSciences, Inc. is offering for sale 3,100,000 shares of its common stock.
- The last reported sale price on the Nasdaq National Market of our common stock on June 15, 2006 was \$7.35 per share.
- Trading symbol:
Nasdaq National Market — SGMO

This investment involves a high degree of risk. See “Risk Factors” on page S-3 of this prospectus supplement.

	Per Share	Total
Public offering price	\$ 6.75	\$ 20,925,000.00
Underwriting discount	\$ 0.25	\$ 775,000.00
Proceeds, before expenses, to Sangamo BioSciences, Inc.	\$ 6.50	\$ 20,150,000.00

We have granted the underwriter a 30-day option to purchase up to an additional 465,000 shares of common stock on the same terms and conditions as set forth above solely to cover over-allotments, if any.

The underwriter is offering shares of our common stock as described in “Underwriting” on page S-5 of this prospectus supplement. Delivery of the shares will be made on or about June 21, 2006.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities, or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

Piper Jaffray

The date of this prospectus supplement is June 16, 2006.

TABLE OF CONTENTS

PROSPECTUS SUPPLEMENT

	<u>Page</u>
Statements Regarding Forward-Looking Information	S-1
About this Prospectus Supplement	S-1
The Offering	S-2
Risk Factors	S-3
About Sangamo Biosciences, Inc.	S-3
Use of Proceeds	S-4
Dilution	S-4
Underwriting	S-5
Legal Matters	S-7
Where You Can Find More Information	S-7
Incorporation of Certain Documents by Reference	S-7

PROSPECTUS

	<u>Page</u>
About this Prospectus	1
Statements Regarding Forward-Looking Information	1
About Sangamo Biosciences, Inc.	2
Risk Factors	3
Use of Proceeds	3
Plan of Distribution	3
The Securities We May Offer	5
Description of Common Stock	5
Description of Warrants	6
Legal Matters	7
Experts	7
Where You Can Find More Information	7
Incorporation of Certain Documents by Reference	7

You should rely only on the information contained in or incorporated by reference into this prospectus supplement and the accompanying prospectus. We have not, and the underwriter has not, authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not, and the underwriter is not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. The information in this prospectus supplement and the accompanying prospectus is accurate only as of the date it is presented. Our business, financial condition, results of operations and prospects may have changed since these dates.

STATEMENTS REGARDING FORWARD-LOOKING INFORMATION

Some statements contained in this prospectus supplement and the accompanying prospectus and the information incorporated by reference into this prospectus supplement and the accompanying prospectus are forward-looking with respect to our operations, research, development and commercialization activities and financial condition. Statements that are forward-looking in nature should be read with caution because they involve risks and uncertainties, which are included, for example, in specific and general discussions about:

- our strategy;
- product development and commercialization of our products;
- clinical trials;
- revenues from existing and new collaborations;
- our research and development and other expenses;
- sufficiency of our cash resources;
- our operational and legal risks; and
- our plans, objectives, expectations and intentions and any other statements that are not historical facts.

Various terms and expressions similar to them are intended to identify these cautionary statements. These terms include: “anticipates,” “believes,” “continues,” “could,” “estimates,” “expects,” “intends,” “may,” “plans,” “seeks,” “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.” Sangamo undertakes no obligation to publicly release any revisions to forward-looking statements to reflect events or circumstances arising after the date of this prospectus supplement and the accompanying prospectus.

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus dated June 7, 2006 is part of a “shelf” registration statement on Form S-3 we filed on May 26, 2006 with the Securities and Exchange Commission and was declared effective by the Securities and Exchange Commission on June 7, 2006. By using a “shelf” registration statement, we may sell shares of common stock and/or warrants to purchase common stock as described in the accompanying prospectus from time to time in one or more offerings up to a total of \$50,000,000.

These documents contain important information you should consider when making your investment decision. The accompanying prospectus provides you with a general description of the securities we may offer. This prospectus supplement contains information about the common stock in this offering. This prospectus supplement may add, update or change information in the accompanying prospectus. You should rely only on the information contained in this prospectus supplement, the accompanying prospectus or incorporated by reference into this prospectus supplement and the accompanying prospectus. We have not authorized anyone to provide you with any other information.

This prospectus supplement does not constitute an offer to sell, or a solicitation of an offer to buy, the securities offered hereby in any jurisdiction where, or to any person to whom, it is unlawful to make such offer or solicitation.

The information contained in this prospectus supplement is accurate only as of the date of this prospectus supplement and the accompanying prospectus, regardless of the time of delivery of this prospectus or of any sale of securities.

Table of Contents

THE OFFERING

Common stock offered by us	3,100,000 shares
Common stock to be outstanding after this offering	33,937,508 shares
Over-allotment option	We have granted the underwriter an option to purchase up to an additional 465,000 shares of common stock solely to cover over-allotments, if any, at the public offering price less the underwriting discount shown on the cover page of this prospectus supplement. The underwriter may exercise this option at any time until 30 days after the date of the purchase agreement.
Use of proceeds	We intend to use the net proceeds from this offering for working capital and other general corporate purposes, including support for our continuing research and development of our ZFP Therapeutic product candidates and research programs, commercialization activities, business development activities and, if opportunities arise, acquisitions of businesses, products, technologies or licenses that are complementary to our business. See "Use of Proceeds" on page S-4.
Nasdaq National Market symbol	SGMO
Risk factors	This investment involves a high degree of risk. See "Risk Factors" on page S-3 of this prospectus supplement.
The number of shares of common stock to be outstanding after this offering is based on 30,837,508 shares outstanding on June 15, 2006. It excludes:	
	<ul style="list-style-type: none">• 3,632,141 shares of common stock issuable upon exercise of options outstanding as of June 15, 2006, of which 2,360,042 shares are exercisable under our 2004 stock option plan, at a weighted average exercise price of \$6.12 per share;• 4,192,466 shares available for grant as of June 15, 2006 under our 2004 stock option plan; and• 1,115,146 shares available for grant as of June 15, 2006 under our employee stock purchase plan.

Except as otherwise indicated, all information in this prospectus supplement assumes no exercise of the underwriter's over-allotment option.

RISK FACTORS

An investment in our common stock offered through this prospectus supplement and the accompanying prospectus involves certain risks. You should carefully consider the specific risks relating to this offering set forth below and relating to our business set forth under the caption “Risk Factors” in our filings with the Securities and Exchange Commission pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, incorporated by reference herein, before making an investment decision. The risks and uncertainties we have described are not the only ones facing our company. Additional risks and uncertainties not presently known to us or that we currently consider immaterial may also affect our business operations.

Risks Related to this Offering

Management will have broad discretion as to the use of the proceeds from this offering, and we may not use the proceeds effectively.

We have not designated the amount of net proceeds we will use for any particular purpose. Accordingly, our management will have broad discretion as to the application of the net proceeds and could use them for purposes other than those contemplated at the time of this offering. Our stockholders may not agree with the manner in which our management chooses to allocate and spend the net proceeds. Moreover, our management may use the net proceeds for corporate purposes that may not increase our profitability or our market value. See “Use of Proceeds” on page S-4 for a description of our management’s intended use of the proceeds from this offering.

You will experience immediate dilution in the book value per share of the common stock you purchase.

Because the price per share of our common stock being offered is substantially higher than the book value per share of our common stock, you will suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering. Based on the public offering price of \$6.75 per share, if you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of \$5.13 per share in the net tangible book value of the common stock. See “Dilution” on page S-4 for a more detailed discussion of the dilution you will incur in this offering.

ABOUT SANGAMO BIOSCIENCES, INC.

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

We were incorporated in June 1995. From our inception through December 31, 2006, our activities related primarily to establishing and operating a biotechnology research and development organization and developing relationships with our corporate collaborators. Our scientific and business development endeavors currently focus on the engineering of novel ZFPs for the regulation and modification of genes. Our revenues have consisted primarily of revenues from our corporate partners for ZFP TFs and ZFNs, contractual payments from strategic partners for research programs and research milestones, and Federal government research grant funding.

[Table of Contents](#)

Our principal offices are located at 501 Canal Boulevard, Suite A100, Richmond, California 94804, and our telephone number there is (510) 970-6000.

For further information regarding us and our financial information, you should refer to our recent filings with the Securities and Exchange Commission. See “Where You Can Find More Information” and “Incorporation of Certain Documents by Reference.”

USE OF PROCEEDS

We estimate that the net proceeds we will receive from this offering will be approximately \$20.15 million, after deducting the underwriter’s commission and discounts and before deducting estimated offering expenses payable by us.

We intend to use the net proceeds from this offering for working capital and other general corporate purposes, including support for our continuing research and development of our ZFP Therapeutic product candidates and research programs, commercialization activities, business development activities, and, if opportunities arise, acquisitions of businesses, products, technologies or licenses that are complementary to our business.

The amounts and timing of the expenditures may vary significantly, depending upon numerous factors including our proprietary research and therapeutic programs and our clinical trials as well as the amount of cash used in our operations. Accordingly, our management will have broad discretion in the application of the net proceeds and investors will be relying upon the judgment of our management regarding the application of these proceeds. We reserve the right to change the use of these proceeds.

Pending these uses, we intend to invest the proceeds of this offering in short-term, investment grade interest -bearing securities.

DILUTION

If you purchase our common stock in this offering, your interest will be diluted to the extent of the difference between the public offering price per share and the net tangible book value per share of our common stock after this offering. We calculate net tangible book value per share by dividing the net tangible book value, tangible assets less total liabilities, by the number of outstanding shares of our common stock.

Our net tangible book value at March 31, 2006, was \$35.6 million, or \$1.16 per share, based on 30,700,165 shares of our common stock outstanding. After giving effect to the sale of 3,100,000 shares of common stock by us at a public offering price of \$6.75 per share, less the underwriter’s discount and commission and our estimated offering expenses, our net tangible book value as of March 31, 2006, would have been approximately \$56.34 million, or \$1.67 per share. This represents an immediate increase in the net tangible book value of \$0.51 per share to existing stockholders and an immediate dilution of \$5.08 per share to investors in this offering. The following table illustrates this per share dilution:

Public offering price per share		\$	6.75
Net tangible book value per share as of March 31, 2006		\$	1.16
Increase in net tangible book value per share after this offering		\$	0.51
Net tangible book value per share after this offering		\$	1.67
Dilution per share to new investors		\$	5.08

UNDERWRITING

We have entered into a purchase agreement with Piper Jaffray & Co. with respect to the shares being offered. Subject to the terms and conditions of the purchase agreement, Piper Jaffray has agreed to purchase from us the number of shares of common stock set forth below.

<u>Underwriter</u>	<u>Number of Shares</u>
Piper Jaffray & Co.	3,100,000
Total	3,100,000

Piper Jaffray has advised us that it proposes to offer the shares of common stock to the public at the public offering price per share set forth on the cover page of this prospectus supplement. After an initial offering and distribution to the public, the offering price and other selling terms may be modified by Piper Jaffray.

We have granted to Piper Jaffray an option, exercisable for 30 days from the date of the purchase agreement, to purchase up to 465,000 additional shares of common stock at the public offering price less the underwriting discount described below. Piper Jaffray may exercise the option solely for the purpose of covering over-allotments, if any, in connection with this offering.

The following table shows the per share and total underwriting discount to be paid to Piper Jaffray by us. These amounts are shown assuming both no exercise and full exercise of Piper Jaffray's option to purchase additional shares of common stock.

	<u>No Exercise</u>	<u>Full Exercise</u>
Per Share	\$ 0.25	\$ 0.25
Total	\$ 775,000.00	\$ 891,250.00

In addition to the underwriting discount in the above table, we have agreed to reimburse Piper Jaffray for the fees, disbursements and other charges of its counsel in connection with this offering in an amount not to exceed \$37,500.

The purchase agreement provides that we will indemnify Piper Jaffray against certain liabilities that may be incurred in connection with this offering, including liabilities under the Securities Act, or to contribute payments that Piper Jaffray may be required to make in respect thereof.

We and each of our directors and executive officers have agreed to certain restrictions on the ability to sell shares of our common stock and other securities that they beneficially own, including securities convertible into or exercisable or exchangeable for common stock, for a specified lock-up period following the date of this prospectus supplement — 90 days for the company and 75 days for executive officers and directors. This means that, subject to certain exceptions, for the lock-up period we and such persons may not, directly or indirectly, offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of any shares of common stock, without the prior written consent of Piper Jaffray. Notwithstanding the foregoing, if (x) during the last 17 days of such lock-up periods we announce that we will release earnings results or publicly announce other material news or a material event relating to us occurs or (y) prior to the expiration of the lock-up period, we announce that we will release earnings results during the 16 day period beginning on the last day of the lock-up periods, then in each case the lock-up periods will be extended until the expiration of the 18 day period beginning on the date of release of the earnings results or the public announcement regarding the material news or the occurrence of the material event, as applicable, unless Piper Jaffray waives, in writing, such extension. At any time and without public notice, Piper Jaffray may in its sole discretion release all or some of the securities from these lock-up agreements.

Table of Contents

Piper Jaffray proposes to offer the shares of our common stock, subject to prior sale, when, as and if issued to and accepted by it, subject to approval of legal matters by its counsel, including the validity of the shares, and other conditions contained in the purchase agreement, such as the receipt by Piper Jaffray of officers' certificates and legal opinions. Piper Jaffray reserves the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part. Piper Jaffray is obligated to purchase all the shares (other than those covered by the over-allotment option described above) if it purchases any of the shares.

In connection with the offering, Piper Jaffray may purchase and sell shares of common stock in the open market. These transactions may include short sales and stabilizing transactions. Short sales involve sales of common stock in excess of the number of shares to be purchased by Piper Jaffray in the offering, which creates a short position. "Covered" short sales are sales of shares made in an amount up to the number of shares represented by Piper Jaffray's over-allotment option. In determining the source of shares to close out the covered short position, Piper Jaffray will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which it may purchase shares through the over-allotment option. Transactions to close out the covered short involve either purchases of the common stock in the open market after the distribution has been completed or the exercise of the over-allotment option. Piper Jaffray may also make "naked" short sales of shares in excess of the over-allotment option. Piper Jaffray must close out any naked short position by purchasing shares of common stock in the open market. A naked short position is more likely to be created if Piper Jaffray is concerned that there may be downward pressure on the price of the shares in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of bids for or purchases of shares in the open market while the offering is in progress.

In connection with this offering, Piper Jaffray may also engage in passive market making transactions in the common stock on the Nasdaq National Market. Passive market making consists of displaying bids on the Nasdaq National Market limited by the prices of independent market makers and effecting purchases limited by those prices in response to order flow. Rule 103 of Regulation M promulgated by the Commission limits the amount of the net purchases that each passive market maker may make and the displayed size of each bid. Passive market making may stabilize the market price of the common stock at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

In the ordinary course of its business, Piper Jaffray has provided in the past, and may provide in the future, investment banking services (including capital markets and merger and acquisition advisory services) to us for which it has received, and may receive in the future, customary fees for such services.

LEGAL MATTERS

The validity of the common stock offered by this prospectus supplement has been passed upon for us by Morgan, Lewis & Bockius LLP, San Francisco, California. As of June 12, 2006, partners of Morgan, Lewis & Bockius LLP beneficially owned a total of approximately 402,360 shares of our common stock. The underwriter is being represented in connection with this offering by Lowenstein Sandler PC, New York, New York.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus supplement and the accompanying prospectus is part of a “shelf” registration statement that we filed with the Securities and Exchange Commission. The “shelf” registration statement that contains this prospectus supplement and the accompanying prospectus, including the exhibits to the “shelf” registration statement, contains additional information about us and the securities offered by this prospectus supplement and the accompanying prospectus.

We file annual, quarterly and special reports, proxy statements and other information with the Commission. You may read and copy any document we file at the Commission’s Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the Commission at 1-800-SEC-0330 for further information on the Public Reference Room. Our public filings, including reports, proxy and information statements, are also available on the Commission’s web site at <http://www.sec.gov>.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The Securities and Exchange Commission allows us to “incorporate by reference” information from other documents that we file with them, which means that we can disclose important information by referring to those documents. The information incorporated by reference is considered to be part of this prospectus supplement and the accompanying prospectus, and information that we file later with the Commission will automatically update and supersede this information. We incorporate by reference into this prospectus supplement and the accompanying prospectus the documents listed below, and any future filings (other than the portions thereof deemed to be “furnished” to the Commission pursuant to Item 2.02 or Item 7.01 of Current Report on Form 8-K) we make with the Commission under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934 prior to the termination of this offering:

- our annual report on Form 10-K for the year ended December 31, 2005, filed with the Commission on March 16, 2006;
- our quarterly report on Form 10-Q for the quarter ended March 31, 2006, filed with the Commission on May 10, 2006;
- our current report on Form 8-K filed with the Commission on April 27, 2006;
- our current report on Form 8-K filed with the Commission on June 16, 2006; and
- the description of our common stock contained in our registration statement on Form 8-A filed under Section 12(g) of the Securities Exchange Act of 1934 with the Commission on March 31, 2000, including any amendment or reports filed for the purpose of updating such description

To the extent that any statement in this prospectus supplement or the accompanying prospectus is inconsistent with any statement that is incorporated by reference and that was made on or before the date of this prospectus supplement or the accompanying prospectus, the statement in this prospectus supplement or the accompanying prospectus shall supersede such incorporated statement. The incorporated statement shall not be deemed, except as modified or superseded, to constitute a part of this prospectus supplement, the accompanying prospectus or the registration statement. Statements

Table of Contents

contained in this prospectus supplement and the accompanying prospectus as to the contents of any contract or other document are not necessarily complete and, in each instance, we refer you to the copy of each contract or document filed as an exhibit to the registration statement.

We will furnish without charge to each person, including any beneficial owner of our securities, to whom a copy of this prospectus supplement and the accompanying prospectus is delivered, upon written or oral request, a copy of the information that has been incorporated into this prospectus supplement and the accompanying prospectus by reference (except exhibits, unless they are specifically incorporated into this prospectus supplement and the accompanying prospectus by reference). You should direct any requests for copies to:

Sangamo BioSciences, Inc.
501 Canal Boulevard, Suite A100
Richmond, CA 94804
Attention: Investor Relations
(510) 970-6000

PROSPECTUS

SANGAMO BIOSCIENCES, INC.

\$50,000,000

of

Common Stock and Warrants

We may offer the shares of common stock and warrants to purchase shares of common stock covered by this prospectus from time to time in one or more issuances. We refer to the common stock and warrants to purchase common stock collectively as the “securities”.

This prospectus provides you with a general description of the securities that we may offer. Each time we sell securities, we will provide a prospectus supplement that will contain specific information about the terms of that offering. The prospectus supplement may also add information or update information contained in this prospectus. You should read both this prospectus and any prospectus supplement together with the documents incorporated by reference and described under the heading “Where You Can Find More Information” before you make your investment decision.

We will sell the securities to underwriters or dealers, through agents, or directly to investors.

An investment in the securities offered under this prospectus involves a high degree of risk. You should carefully consider the risk factors described in the applicable prospectus supplement and certain of our filings with the Securities and Exchange Commission, as described under “Risk Factors” on page 2.

Our common stock trades on the Nasdaq National Market under the symbol SGMO. On May 25, 2006, the last reported sale price of our common stock on the Nasdaq National Market was \$6.03.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is June 7, 2006.

Table of Contents

	<u>Page</u>
About this Prospectus	1
Statements Regarding Forward-looking Information	1
About Sangamo Biosciences, Inc.	2
Risk Factors	3
Use of Proceeds	3
Plan of Distribution	3
The Securities We May Offer	5
Description of Common Stock	5
Description of Warrants	6
Legal Matters	7
Experts	7
Where You Can Find More Information	7
Incorporation of Certain Documents by Reference	7

ABOUT THIS PROSPECTUS

This prospectus is part of a “shelf” registration statement we filed with the Securities and Exchange Commission. By using a shelf registration statement, we may sell any combination of securities described in this prospectus from time to time for an aggregate offering price of up to \$50,000,000.

You should rely only on the information contained in or specifically incorporated by reference into this prospectus or a supplement. No dealer, sales person or other individual has been authorized to give any information or to make any representations not contained in this prospectus. If given or made, such information or representations must not be relied upon as having been authorized by us.

This prospectus does not constitute an offer to sell or a solicitation of an offer to buy, the securities offered hereby in any jurisdiction where, or to any person to whom, it is unlawful to make such offer or solicitation.

The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of securities. Neither the delivery of this prospectus nor any sale made hereunder shall, under any circumstances, create an implication that there has not been any change in the facts set forth in this prospectus or in our affairs since the date of this prospectus.

STATEMENTS REGARDING FORWARD-LOOKING INFORMATION

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

- our strategy;
- product development and commercialization of our products;
- clinical trials;
- revenues from existing and new collaborations;
- our research and development and other expenses;
- sufficiency of our cash resources;
- our operational and legal risks; and
- our plans, objectives, expectations and intentions and any other statements that are not historical facts.

Various terms and expressions similar to them are intended to identify these cautionary statements. These terms include: “anticipates,” “believes,” “continues,” “could,” “estimates,” “expects,” “intends,” “may,” “plans,” “seeks,” “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.” Sangamo undertakes no obligation to publicly release any revisions to forward-looking statements to reflect events or circumstances arising after the date of this prospectus.

ABOUT SANGAMO BIOSCIENCES, INC.

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

We were incorporated in June 1995. From our inception through December 31, 2005, our activities related primarily to establishing and operating a biotechnology research and development organization and developing relationships with our corporate collaborators. Our scientific and business development endeavors currently focus on the engineering of novel ZFPs for the regulation and modification of genes. Our revenues have consisted primarily of revenues from our corporate partners for ZFP TFs and ZFNs, contractual payments from strategic partners for research programs and research milestones, and Federal government research grant funding.

Our principal offices are located at 501 Canal Boulevard, Suite A100, Richmond, California 94804, and our telephone number there is (510) 970-6000.

RISK FACTORS

An investment in the securities offered through this prospectus involves certain risks. You should carefully consider the specific risks set forth under the caption “Risk Factors” in the applicable prospectus supplement and under the caption “Risk Factors” in our filings with the Securities and Exchange Commission pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, incorporated by reference herein, before making an investment decision. The risks and uncertainties we have described are not the only ones facing our company. Additional risks and uncertainties not presently known to us or that we currently consider immaterial may also affect our business operations. To the extent that a particular offering implicates additional significant risks, we will include a discussion of those risks in the applicable prospectus supplement.

USE OF PROCEEDS

Except as may be otherwise set forth in the prospectus supplement accompanying this prospectus, we will use the net proceeds we receive from sales of the securities offered hereby for general corporate purposes, including support for our continuing research and development, commercialization activities, business development activities, and, if opportunities arise, acquisitions of businesses, products, technologies or licenses that are complementary to our business.

PLAN OF DISTRIBUTION

We may sell the securities being offered by us in this prospectus:

- directly to purchasers;
- through agents;
- through dealers;
- through underwriters; or
- through a combination of any of these methods of sale.

We and our agents and underwriters may sell the securities being offered by us in this prospectus from time to time in one or more transactions:

- at a fixed price or prices which may be changed;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

Offers to purchase securities may be solicited directly by us, or by agents designated by us, from time to time. Any such agent, which may be deemed to be an underwriter as that term is defined in the Securities Act of 1933, as amended (the “Securities Act”), involved in the offer or sale of the securities in respect of which this prospectus is delivered will be named, and any commissions payable by us to such agent will be set forth, in the applicable prospectus supplement.

If an underwriter is, or underwriters are, utilized in the offer and sale of securities in respect of which this prospectus and the accompanying prospectus supplement are delivered, we will execute an underwriting agreement with such underwriter(s) for the sale to it or them and the name(s) of the underwriter(s) and the terms of the transaction, including any underwriting discounts and other items constituting compensation of the underwriters and dealers, if any, will be set forth in such prospectus supplement, which will be used by the underwriter(s) to make resales of the securities in respect of which this prospectus and such prospectus supplement are delivered to the public. The securities will

Table of Contents

be acquired by the underwriters for their own accounts and may be sold by the underwriters from time to time in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. Any public offering price and any discounts or concessions allowed or reallocated or paid to dealers may be changed from time to time.

If a dealer is utilized in the sale of the securities in respect of which this prospectus is delivered, we will sell such securities to the dealer, as principal. The dealer may then resell such securities to the public at varying prices to be determined by such dealer at the time of resale. The name of the dealer and the terms of the transaction will be identified in the applicable prospectus supplement.

If an agent is used in an offering of securities being offered by this prospectus, the agent will be named, and the terms of the agency will be described, in the applicable prospectus supplement relating to the offering. Unless otherwise indicated in the prospectus supplement, an agent will act on a best efforts basis for the period of its appointment.

If indicated in the applicable prospectus supplement, we will authorize underwriters or their agents to solicit offers by certain institutional investors to purchase our securities pursuant to contracts providing for payment and delivery at a future date. Institutional investors with which these contracts may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and others. In all cases, these purchasers must be approved by us. The obligations of any purchaser under any of these contracts will not be subject to any conditions except that (a) the purchase of the securities must not at the time of delivery be prohibited under the laws of any jurisdiction to which that purchaser is subject and (b) if the securities are also being sold to underwriters, we must have sold to these underwriters the securities not subject to delayed delivery. Underwriters and other agents will not have any responsibility in respect of the validity or performance of these contracts.

Certain of the underwriters, dealers or agents utilized by us in any offering hereby may be customers of, including borrowers from, engage in transactions with, and perform services for us or one or more of our affiliates in the ordinary course of business. Underwriters, dealers, agents and other persons may be entitled, under agreements which may be entered into with us, to indemnification against and contribution toward certain civil liabilities, including liabilities under the Securities Act.

Until the distribution of the securities is completed, rules of the Commission may limit the ability of the underwriters and certain selling group members, if any, to bid for and purchase the securities. As an exception to these rules, the representatives of the underwriters, if any, are permitted to engage in certain transactions that stabilize the price of the securities in accordance with Regulation M, but only in the case of a fixed-price offering. Such transactions may consist of bids or purchases for the purpose of pegging, fixing or maintaining the price of the securities.

If underwriters create a short position in the securities in connection with the offering thereof (i.e., if they sell more securities than are set forth on the cover page of the applicable prospectus supplement), the representatives of such underwriters may reduce that short position by purchasing securities in the open market. Any such representatives also may elect to reduce any short position by exercising all or part of any over-allotment option described in the applicable prospectus supplement.

Any such representatives also may impose a penalty bid on certain underwriters and selling group members. This means that if the representatives purchase securities in the open market to reduce the underwriters' short position or to stabilize the price of the securities, they may reclaim the amount of the selling concession from the underwriters and selling group members who sold those shares as part of the offering thereof.

In general, purchases of a security for the purpose of stabilization or to reduce a syndicate short position could cause the price of the security to be higher than it might otherwise be in the absence of such purchases. The imposition of a penalty bid might have an effect on the price of a security to the extent that it were to discourage resales of the security by purchasers in the offering.

Table of Contents

Neither we nor any of the underwriters, if any, makes any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of the securities. In addition, neither we nor any of the underwriters, if any, makes any representation that the representatives of the underwriters, if any, will engage in such transactions or that such transactions, once commenced, will not be discontinued without notice.

The anticipated date of delivery of the securities offered by this prospectus will be described in the applicable prospectus supplement relating to the offering. The securities offered by this prospectus may or may not be listed on a national securities exchange or a foreign securities exchange. We cannot give any assurances that there will be a market for any of the securities offered by this prospectus and any prospectus supplement.

THE SECURITIES WE MAY OFFER

The descriptions of the securities contained in this prospectus, together with the applicable prospectus supplement, summarize the material terms and provisions of the various types of securities that we may offer. We will describe in the applicable prospectus supplement relating to any securities the particular terms of the securities offered by that prospectus supplement; however, the prospectus supplement may not change the information related to our plan of distribution or the securities we are offering. We will also include in the prospectus supplement information, where applicable, about material United States federal income tax considerations relating to the securities, and the securities exchange or market, if any, on which the securities will be listed.

We may sell from time to time, in one or more offerings, one or more of the following securities:

- common stock; and
- warrants to purchase common stock.

These securities may be offered and sold from time to time for an aggregate offering price not to exceed \$50,000,000.

This prospectus may not be used to consummate a sale of securities unless it is accompanied by a prospectus supplement.

DESCRIPTION OF COMMON STOCK

For a description of the material terms and provisions of our common stock and each other class of our securities which qualifies or limits our common stock, please see the applicable prospectus supplement, as well as the description of our capital stock in our Registration Statement on Form 8-A dated March 31, 2000 which is incorporated by reference in this prospectus.

DESCRIPTION OF WARRANTS

We may issue warrants to purchase common stock. The warrants may be issued independently or together with any other securities and may be attached to or separate from the other securities. Each series of warrants may be issued under a separate warrant agreement to be entered into between us and a bank or trust company, as warrant agent. The warrants will be evidenced by warrant certificates. Unless otherwise specified in the prospectus supplement, the warrant certificates may be traded separately from the common stock with which the warrant certificates were issued. Warrant certificates may be exchanged for new warrant certificates of different denominations at the office of an agent that we will appoint. Until a warrant is exercised, the holder of a warrant does not have any of the rights of a holder of our common stock and is not entitled to any payments on any common stock issuable upon exercise of the warrants.

The prospectus supplement relating to a series of warrants will describe the specific terms of the warrants including the following:

- the title of the warrants;
- the aggregate number of the warrants;
- the price or prices at which the warrants will be issued and the currency in which the price for the warrants may be paid;
- the price at which and the currency in which the common stock purchasable upon exercise of the warrants may be purchased and the various factors considered in determining that price;
- the dates on which the right to exercise the warrants will commence and expire and whether the exercise of warrants will be at the option of holders, at our option, or automatic;
- whether the warrants are exercisable by payment of cash, surrender of other securities, or both;
- provisions for changes to or adjustments in the exercise price of the warrants;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
- if applicable, the designation and terms of the other securities with which the warrants are issued and the number of the warrants issued with each such other security;
- if applicable, the date on and after which the warrants and the related other securities will be separately transferable;
- whether the warrants will be issued in registered form or bearer form;
- information with respect to book-entry procedures, if any;
- if applicable, a discussion of material U.S. federal income tax considerations; and
- any other terms of the warrants, including terms, procedures, and
- limitations relating to the exchange or exercise of the warrants.

LEGAL MATTERS

The legality of the securities offered by this prospectus has been passed upon for us by Morgan, Lewis & Bockius LLP, San Francisco, California. As of May 26, 2006, members of Morgan, Lewis & Bockius LLP beneficially owned a total of 401,360 shares of our common stock.

EXPERTS

The consolidated financial statements of Sangamo Biosciences, Inc. appearing in Sangamo Biosciences, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2005, and Sangamo Biosciences, Inc. management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2005 included therein, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their reports thereon, included therein, and incorporated herein by reference. Such consolidated financial statements and management's assessment are incorporated herein by reference in reliance upon such reports given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission. The registration statement that contains this prospectus, including the exhibits to the registration statement, contains additional information about us and the securities offered by this prospectus.

We file annual, quarterly and special reports, proxy statements and other information with the Commission. You may read and copy any document we file at the Commission's Public Reference Room at 100 F. Street, N.E., Washington, D.C. 20549. Please call the Commission at 1-800-SEC-0330 for further information on the Public Reference Room. Our public filings, including reports, proxy and information statements, are also available on the Commission's web site at <http://www.sec.gov>.

INCORPORATION OF CERTAIN DOCUMENTS BY REFERENCE

The Securities and Exchange Commission allows us to "incorporate by reference" information from other documents that we file with them, which means that we can disclose important information by referring to those documents. The information incorporated by reference is considered to be part of this prospectus, and information that we file later with the Commission will automatically update and supersede this information. We incorporate by reference into this prospectus the documents listed below, and any future filings (other than the portions thereof deemed to be "furnished" to the Commission pursuant to Item 2.02 or Item 7.01 of Current Report on Form 8-K) we make with the Commission under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934 prior to the termination of this offering:

our annual report on Form 10-K for the year ended December 31, 2005, filed with the Commission on March 16, 2006;

our quarterly report on Form 10-Q for the quarter ended March 31, 2006, filed with the SEC on May 10, 2006;

our current report on Form 8-K filed with the SEC on April 27, 2006; and

the description of our common stock contained in our registration statement on Form 8-A filed under Section 12(g) of the Securities Exchange Act of 1934 with the Commission on March 31, 2000, including any amendment or reports filed for the purpose of updating such description

Table of Contents

To the extent that any statement in this prospectus is inconsistent with any statement that is incorporated by reference and that was made on or before the date of this prospectus, the statement in this prospectus shall supersede such incorporated statement. The incorporated statement shall not be deemed, except as modified or superseded, to constitute a part of this prospectus or the registration statement. Statements contained in this prospectus as to the contents of any contract or other document are not necessarily complete and, in each instance, we refer you to the copy of each contract or document filed as an exhibit to the registration statement.

We will furnish without charge to each person, including any beneficial owner, to whom a copy of this prospectus is delivered, upon written or oral request, a copy of the information that has been incorporated into this prospectus by reference (except exhibits, unless they are specifically incorporated into this prospectus by reference). You should direct any requests for copies to:

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

3,100,000 Shares

SANGAMO BIOSCIENCES, INC.

Common Stock



PROSPECTUS SUPPLEMENT

Piper Jaffray

June 16, 2006
