SANGAMO BIOSCIENCES INC
Form 424B5
September 17, 2013
Table of Contents

Filed pursuant to Rule 424(b)(5)
Registration File No.: 333-179634

The information in this preliminary prospectus supplement and the accompanying prospectus, relating to an effective registration statement under the Securities Act of 1933, as amended, is not complete and may be changed. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities and we are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED SEPTEMBER 17, 2013

Prospectus Supplement

(To Prospectus dated April 12, 2012)

Shares

Sangamo BioSciences, Inc.

Common Stock

We are offering shares of our common stock. Shares of our common stock trade on The NASDAQ Global Select Market under the symbol SGMO. On September 16, 2013, the last reported sale price of our common stock was $10.73 per share.

Investing in our common stock involves a high degree of risk. See Risk Factor beginning on page S-6 of this prospectus supplement.

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.

	Per Share	Total
Public Offering Price	$	$
Underwriting Discounts and Commission	$	$
Proceeds to Sangamo BioSciences, Inc. (Before Expenses)	$	$

We estimate the total expenses of this offering, excluding the underwriting discounts and commissions, will be approximately $240,000. The underwriters may also purchase up to an additional shares of our common stock from us at the public offering price, less underwriting discounts and commissions, to cover over-allotments, if any, within 30 days of the date of this prospectus supplement.

We anticipate that delivery of the shares of our common stock will be made through the facilities of the Depository Trust Company on or about September , 2013, subject to customary closing conditions.

Joint Book Running Managers

Lazard Capital Markets **JMP Securities** **Piper Jaffray & Co.**

Prospectus Supplement dated September , 2013.

Table of Contents

Table Of Contents

Prospectus Supplement

Prospectus

Table of Contents

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus dated April 12, 2012 is part of a shelf registration statement on Form S-3 we filed on February 22, 2012 with the Securities and Exchange Commission and was declared effective by the Securities and Exchange Commission on April 12, 2012. By using a shelf registration statement, we may sell shares of common stock, preferred stock, debt securities, warrants to purchase common stock and/or warrants to purchase preferred stock, as described in the accompanying prospectus, from time to time in one or more offerings up to a total of $100,000,000.

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this common stock offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference herein. The second part, the accompanying prospectus, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement and the information contained in the accompanying prospectus or any document incorporated by reference therein filed prior to the date of this prospectus supplement, you should rely on the information in this prospectus supplement; provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date for example, a document incorporated by reference in the accompanying prospectus the statement in the document having the later date modifies or supersedes the earlier statement.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

You should rely only on the information contained in this prospectus supplement or the accompanying prospectus, or incorporated by reference herein. We have not authorized, and the underwriters have not authorized, anyone to provide you with information that is different. The information contained in this prospectus supplement or the accompanying prospectus, or incorporated by reference herein, is accurate only as of the respective dates thereof, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or of any sale of our common stock. It is important for you to read and consider all information contained in this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein and therein, in making your investment decision. You should also read and consider the information in the documents to which we have referred you in the sections entitled Where You Can Find More Information and Incorporation of Certain Information by Reference in this prospectus supplement and in the accompanying prospectus.

We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the accompanying prospectus and the offering of the common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus supplement and the accompanying prospectus outside the United States. This prospectus supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

Unless otherwise stated, all references in this prospectus supplement and the accompanying prospectus to we, us, our, Sangamo, the Company and similar designations refer to Sangamo BioSciences, Inc. and its subsidiaries on a consolidated basis.

Table of Contents

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights certain information about us, this offering and selected information contained elsewhere in or incorporated by reference in this prospectus supplement. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our common stock. For a more complete understanding of our company and this offering, we encourage you to read and consider carefully the more detailed information in this prospectus supplement and the accompanying prospectus, including the information referred to under the heading Risk Factors in this prospectus supplement beginning on page S-6 the information incorporated by reference in this prospectus supplement and the accompanying prospectus, and the information included in any free writing prospectus that we have authorized for use in connection with this offering.

Our Business

Overview

We are a clinical stage biopharmaceutical company focused on the research, development and commercialization of engineered DNA-binding proteins for the development of novel therapeutic strategies for unmet medical needs. Our current mission is to develop ZFP Therapeutics, or human therapeutics based on our proprietary ZFP technology, through early stage clinical testing, strategically partner with biopharmaceutical companies at points of value inflection and have the partner execute late-stage clinical trials and commercial development. In the long term, our goal is to integrate marketing and development operations and to capture the value of late-stage and commercial ZFP Therapeutic products for ourselves.

We, and our licensed partners, are the leaders in the research, development and commercialization of zinc finger DNA-binding proteins (ZFPs), a naturally occurring class of proteins. We have used our knowledge and expertise to develop a proprietary technology platform. ZFPs can be engineered to make ZFP nucleases (ZFNs), proteins that can be used to modify DNA sequences in a variety of ways and ZFP transcription factors (ZFP TFs), proteins that can be used to turn genes on or off. As ZFPs act at the DNA level, they have broad potential applications in several areas including human therapeutics, plant agriculture and research reagents, as well as production of transgenic animals and cell-line engineering.

The main focus for our company is the development of novel human therapeutics and we are building a pipeline of ZFP Therapeutics. Our lead ZFP Therapeutic, SB-728-T, a ZFN-modified autologous T-cell product for the treatment of HIV/AIDS, is the first therapeutic application of our ZFN technology and is being evaluated in ongoing clinical trials, the most advanced of which are a Phase 2 study (SB-728-902 Cohort 5) and a Phase 1/2 study (SB-728-1102) in HIV-infected subjects. We expect to present data from these programs at appropriate scientific and medical meetings in 2013.

In January 2012, we established a collaborative partnership with Shire AG (Shire) to research, develop and commercialize some of our preclinical ZFP Therapeutic development programs, including programs in hemophilia, Huntington s disease and other monogenic diseases. We also have several proprietary preclinical programs in monogenic diseases, including hemoglobinopathies such as sickle cell disease and ß-thalassemia and several lysosomal storage disorders. In addition, we have research stage programs in other monogenic diseases, including certain immunodeficiencies.

We believe the potential commercial applications of ZFPs are broad-based and we have also licensed our ZFP platform in fields outside human therapeutics as follows to facilitate the sale or license of ZFNs and ZFP TFs:

We have a license agreement with the research reagent company Sigma-Aldrich Corporation (Sigma). Sigma has the exclusive rights to develop and market high value laboratory research reagents based

Table of Contents

upon our ZFP technology as well as ZFP-modified cell lines for commercial production of protein pharmaceuticals and ZFP-engineered transgenic animals. Sigma is marketing ZFN-derived gene editing tools under the trademark CompoZr®.

We have a license agreement with Dow AgroSciences, LLC (DAS), a wholly owned subsidiary of Dow Chemical Corporation. Under the agreement, we have provided DAS with access to our ZFP technology and the exclusive rights to use it to modify the genomes or alter protein expression of plant cells, plants, or plant cell cultures. DAS markets our ZFN technology under the trademark EXZACT™ Precision Technology. We have retained rights to use plants or plant-derived products to deliver ZFP TFs or ZFNs into human or animals for diagnostic, therapeutic, or prophylactic purposes.

On August 23, 2013, we entered into a definitive agreement to acquire Ceregene, Inc. (Ceregene), a privately held biotechnology company focused on the development of adeno-associated virus (AAV) gene therapies. The acquired assets include all of Ceregene s therapeutic programs, including CERE-110, an AAV vector delivery system for the treatment of Alzheimer s disease that is currently in a Phase 2 clinical trial, certain intellectual property rights relating to the manufacturing of AAV, and certain toxicology and safety data from Ceregene s human clinical trials. We believe that these additional assets provide valuable reference materials for us in the preparation and filing of IND applications for our *in vivo* ZFP Therapeutics, particularly those that target the brain. The acquisition is expected to close in September 2013, subject to customary closing conditions.

We have a substantial intellectual property position in the design, selection, composition, and use of engineered ZFPs to support all of these commercial activities. As of June 30, 2013, we either owned outright or have exclusively licensed the commercial rights to approximately 389 patents issued in the United States and foreign national jurisdictions, and we have 526 patent applications owned and licensed pending worldwide. We continue to license and file new patent applications that strengthen our core and accessory patent portfolio. We believe that our intellectual property position is a critical element in our ability to research, develop, and commercialize products and services based on ZFP technology across our chosen applications.

Recent Development

On September 12, 2013, we presented new data from our ongoing Phase 2 clinical trial (SB-728-902 Cohort 5) to evaluate a single infusion of our novel ZFP Therapeutic, SB-728-T, for treatment of HIV/AIDS at the 53rd Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC). The data demonstrated functional control of the virus at or below the limit of detection in CCR5 delta 32 heterozygote HIV-infected subjects treated with SB-728-T. Also on September 11, 2013, we presented data at ICAAC demonstrating depletion of the HIV viral reservoir in SB-728-T treated subjects in cohorts 1-3 of the SB-728-902 study.

Data from the presentation demonstrated that viral load (VL) became undetectable during a treatment interruption (TI) from standard antiretroviral therapy (ART) in a total of three of seven evaluable CCR5 delta 32 heterozygote HIV-infected subjects, including two of six subjects that had completed TI in the ongoing SB-728-902 Cohort 5 study and an additional subject from an earlier Phase 1 clinical trial of SB-728-T. In one SB-728-T treated subject featured in the presentation, the VL has remained undetectable (at or below the limits of quantification (LOQ) of the current ultra-sensitive assays for HIV) for seven weeks (to last measurement taken) and the TI is ongoing. Reduction in VL from peak during TI showed a statistically significant correlation (p=0.015) with estimated numbers of engrafted ZFN modified cells (SB-728-T) in which both copies of the CCR5 gene had been disrupted (biallelic modification) in line with previously presented data from this program.

In addition, the data we presented on September 11, 2013 demonstrated that treatment of HIV-infected subjects with SB-728-T leads to a long-term increase in CD4 counts. The effect on total CD4 counts in SB-728-T treated subjects was significantly greater than those observed in previously published T-cell infusion studies without CCR5 modification and correlated with increased CD4 central memory and increased CCR5-disrupted

Table of Contents

central memory cells. In addition, a median 0.6 log reduction decrease in the size of the HIV reservoir at twelve months was observed, as demonstrated by measurement of HIV total DNA in peripheral blood mononuclear cells (PBMCs). The decrease in reservoir showed a statistically significant correlation with the improvement in CD4 count. Finally, data were presented describing possible predictors of robust CD4 T-cell reconstitution and immunological response post SB-728-T infusion.

Risk Factors

An investment in our common stock is subject to a number of risks and uncertainties. Before investing in our common stock, you should carefully consider the following, as well as the more detailed discussion of risk factors and other information included in this prospectus supplement:

- ZFP Therapeutics have undergone limited testing in humans and our ZFP Therapeutics may fail safety studies in clinical trials;
- Our progress in early Phase 1 and Phase 2 trials may not be indicative of long-term efficacy in late stage clinical trials;
- Our potential therapeutic products are subject to a lengthy and uncertain regulatory process, and we may encounter unanticipated toxicity or adverse events or fail to demonstrate efficacy of our product candidates;
- While we have stated that we intend to file IND applications for several ZFP Therapeutic programs over the next three years, we may encounter difficulties that may delay, suspend or scale back these efforts;
- We have incurred significant operating losses since inception and anticipate that we will incur continued losses for the foreseeable future;
- If conflicts arise between us and our collaborators or strategic partners, these parties may act in their self-interest, which may limit our ability to implement our strategies; and
- Our collaborators and strategic partners may control aspects of our clinical trials, which could result in delays and other obstacles in the commercialization of our proposed products.

Company and Other Information

Our principal offices are located at 501 Canal Boulevard, Richmond, California, 94804, and our telephone number there is (510) 970-6000. Our website address is www.sangamo.com. We do not incorporate the information on or accessible through our website into this prospectus, and you should not consider any information on, or that can be accessed through, our website as part of this prospectus. 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.

ZFP Therapeutics® is a registered trademark of Sangamo BioSciences, Inc. This prospectus supplement and the accompanying prospectus and information incorporated by reference into this prospectus supplement and the accompanying prospectus also contain trademarks and trade names that are the property of their respective owners.

Table of Contents

THE OFFERING

Common stock offered by us in this offering	shares
Option to purchase additional shares	We have granted the underwriters an option for a period of up to 30 days from the date of this prospectus supplement to purchase up to additional shares of common stock at the public offering price less the underwriting discounts and commissions to cover over-allotments, if any.
Common stock to be outstanding immediately after this offering	shares (or shares if the underwriters exercises in full their over-allotment option to purchase additional shares).
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, clinical trials, 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-24.
Risk Factors	You should carefully read Risk Factors on page S-6 in this prospectus for a discussion of factors that you should consider before deciding to invest in our common stock.
NASDAQ Global Select Market symbol	SGMO

The number of shares of common stock to be outstanding after this offering is based on 53,974,452 shares outstanding on June 30, 2013. It excludes:

- 8,344,138 shares of common stock issuable upon exercise of options outstanding as of June 30, 2013, of which 6,038,091 shares are exercisable under our 2013 Stock Incentive Plan (2013 Plan), at a weighted average exercise price of $6.76 per share;
- 1,006,750 shares of common stock issuable upon settlement of outstanding restricted stock units;
- 4,406,666 shares available for grant as of June 30, 2013 under our 2013 Plan;

1,618,084 shares available for grant as of June 30, 2013 under our employee stock purchase plan; and

100,000 shares to be issued upon closing of the acquisition of Ceregene, Inc.

Except as otherwise indicated, all information in this prospectus supplement assumes no exercise of the underwriter s option to purchase additional shears to cover over-allotment.

Table of Contents

RISK FACTORS

An investment in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should consider carefully the risks described below, together with other information in this prospectus supplement, the accompanying prospectus, the information and documents incorporated by reference, and in any free writing prospectus that we have authorized for use in connection with this offering. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or 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 Relating to Development, Commercialization and Regulatory Approval of our Products and Technology

ZFP Therapeutics have undergone limited testing in humans and our ZFP Therapeutics may fail safety studies in clinical trials.

In December 2008, in collaboration with scientists at the University of Pennsylvania, we filed an Investigational New Drug (IND) application for a Phase 1 trial of our CCR5 ZFN-based therapeutic, SB-728-T, for treatment of HIV/AIDS. In September 2009, we announced the FDA s review and acceptance of our IND application to initiate an open-label, repeat-dosing Phase 1 clinical trial of SB-728-T (SB-728-902). Preliminary data from these studies demonstrated that, to date, treatment of aviremic HIV-infected subjects with SB-728-T has been well-tolerated. We also have an on-going Phase 2 (SB-728-902, Cohort 5) and two Phase 1/2 trials (SB-728-1101 and 1002) for this indication. In addition, we have previously completed enrollment and the treatment phase of a Phase 1 and several Phase 2 clinical trials of our ZFP Therapeutic, SB-509, for diabetic neuropathy and ALS and the drug was well tolerated in these studies. However, if one of our ZFP Therapeutic fails one of its safety studies, it could reduce our ability to attract new investors and corporate partners.

All of these studies are designed primarily to evaluate the safety and tolerability of this ZFP Therapeutic approach. Our clinical studies are a highly visible test of our ZFP Therapeutics. Since we have increased our focus on therapeutic research and development, investors increasingly assess the value of our technology based on the continued progress of ZFP Therapeutic products into and through clinical trials. If clinical trials of our ZFP Therapeutic products were halted due to safety concerns, this would negatively affect our operations and the value of our stock.

Our progress in early Phase 1 and Phase 2 trials may not be indicative of long-term efficacy in late stage clinical trials.

The results in early phases of clinical testing are based upon limited numbers of patients and a limited follow-up period. Typically, our Phase 1 clinical trials for indications of safety enroll less than 25 patients. Our Phase 2 and late-stage clinical trials generally enroll a larger number of patients. Accordingly, any positive data obtained in early Phase 1 and Phase 2 trials may not be indicative of long-term efficacy in late-stage clinical trials. In September 2011, we announced preliminary data from our Phase 1 clinical program to develop SB-728-T for the treatment of HIV/AIDS. The data demonstrated a statistically significant relationship between SB-728-T and the reduction of HIV viral load. In January 2012, we initiated a Phase 2 clinical study (SB-728-902, Cohort 5) and a Phase 1/2 clinical study (SB-728-1101) for the treatment of HIV/AIDS. In May 2013, we presented preliminary data from these two ongoing clinical trials. Two of four evaluable subjects in Cohort 5 showed a decrease of greater than one log in their viral load during a sixteen week treatment interruption (TI) with one subject achieving a transiently undetectable viral load during the TI period. In subjects in which viral load decreased, a measureable anti-HIV immune response was also

observed. Additional data were presented from the Company s Phase 1 study (SB-728-902, Cohorts 1-3) that demonstrated a long-term decrease in the peripheral blood mononuclear cell (PBMC) HIV reservoir. In September 2013, we presented new data from our ongoing

Table of Contents

Phase 2 clinical trial (SB-728-902 Cohort 5) for treatment of HIV/AIDS, demonstrating functional control of the virus at or below the limit of detection in HIV-infected subjects treated with SB-728-T, as well as additional data demonstrating depletion of the HIV viral reservoir in SB-728-T treated subjects in cohorts 1-3 of the SB-728-902 study. We expect to present a full data set from these trials in the second half of 2013. However, there is no guarantee that these and other future studies of SB-728-T in later stage trials involving larger patient groups may produce positive or similar results as those obtained in earlier trials.

In addition, the initial results from the Phase 1 clinical trial of our ZFP Therapeutic product, SB-509, became available in the first half of 2006 and the complete data set was presented in June 2008. The primary end point of the trial was clinical and laboratory safety; however, we collected some preliminary efficacy data that showed trends of clinical improvement in some subjects. Notwithstanding this preliminary efficacy data, the top-line data from our Phase 2b clinical study for SB-509-901 did not meet the key primary or secondary endpoints for the study and as a result we discontinued development of our SB-509 program in October 2011.

A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late stage clinical trials even after achieving promising results in earlier stage clinical trials. If a larger population of patients does not experience positive results, or if these results are not reproducible, our products may not receive approval from the FDA. Failure to confirm favorable results from earlier trials by demonstrating the safety and effectiveness of our ZFP Therapeutic products in late stage clinical trials with larger patient populations could have a material adverse effect on our business that would cause our stock price to decline significantly.

Our potential therapeutic products are subject to a lengthy and uncertain regulatory process, and we may encounter unanticipated toxicity or adverse events or fail to demonstrate efficacy, causing us to delay, suspend or terminate the development of a ZFP Therapeutic. If these potential products are not approved, we will not be able to commercialize those products.

The FDA must approve any human therapeutic product before it can be marketed in the United States. The process for receiving regulatory approval is long and uncertain, and a potential product may not withstand the rigors of testing under the regulatory approval processes.

Before commencing clinical trials in humans, we must submit an IND application to the FDA. The FDA has 30 days to comment on the application and if the agency has no comments, we or our commercial partner may begin clinical trials. While we have stated our intention to file additional IND applications during the next several years, this is only a statement of intent, and we may not be able to do so because the associated product candidates may not meet the necessary preclinical requirements. In addition, there can be no assurance that, once filed, an IND application will result in the actual initiation of clinical trials. Clinical trials are subject to oversight by institutional review boards and the FDA. In addition, our proposed clinical studies require review from the Recombinant DNA Advisory Committee (RAC), which is the advisory board to the National Institutes of Health (NIH), focusing on clinical trials involving gene transfer. We will typically submit a proposed clinical protocol and other product-related information to the RAC three to six months prior to the expected IND application filing date.

Clinical trials:

- must be conducted in conformance with the FDA s good clinical practices, within the guidelines of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) and other applicable regulations;

must meet requirements for Institutional Review Board (IRB) oversight;

must follow Institutional Biosafety Committee (IBC) and NIH RAC guidelines where applicable;

must meet requirements for informed consent;

Table of Contents

are subject to continuing FDA oversight;

may require oversight by a Data Safety Monitoring Board (DSMB);

may require large numbers of test subjects; and

may be suspended by a commercial partner, the FDA, or us at any time if it is believed that the subjects participating in these trials are being exposed to unacceptable health risks or if the FDA finds deficiencies in the IND application or the conduct of these trials.

We have limited experience in conducting clinical trials.

Our ZFP Therapeutics may fail to show the desired safety and efficacy in initial clinical trials. We have an ongoing Phase 2 trial and two Phase 1/2 studies of a ZFP Therapeutic for HIV/AIDS. However, the FDA will require additional clinical testing which involves significantly greater resources, commitments and expertise and so it is likely that we would need to enter into a collaborative relationship with a pharmaceutical company that could assume responsibility for late-stage development and commercialization. We have limited experience in conducting clinical trials and may not possess the necessary resources and expertise to complete such trials, and there is no guarantee that we will be able to enter into collaborative relationships with third parties that can provide us with the funding and expertise for such trials. In our collaborative agreement to develop ZFP Therapeutics with Shire AG (Shire), we are responsible for all activities through submission of IND Applications and European Clinical Trial Applications (CTA) and Shire is responsible for clinical development and commercialization of products arising from the alliance.

While we have stated that we intend to file IND applications for several ZFP Therapeutic programs over the next three years, we may encounter difficulties that may delay, suspend or scale back our efforts.

We have previously announced a strategy for our ZFP Therapeutic programs that enables the potential filing of seven IND applications by the end of 2015. The preparation and submission of IND applications requires us to conduct rigorous and time-consuming pre-clinical testing, studies, and documentation relating to, among other things, the toxicity, safety, manufacturing, chemistry and clinical protocol of new ZFP Therapeutic products. We may experience unforeseen difficulties that could delay or otherwise prevent us from executing this strategy successfully. For example, we may encounter problems in the manufacturing of our ZFP Therapeutic products and fail to demonstrate consistency in the formulation of the drug. Our pre-clinical tests may produce negative or inconclusive results, which may lead us to decide, or regulators may require us, to conduct additional pre-clinical testing. If we cannot obtain positive results in pre-clinical testing, we may decide to abandon the projects altogether. Furthermore, the filing of several IND applications involves significant cost and labor, and we may not have sufficient resources and personnel to complete the filing of all intended IND applications, which may force us to scale back the number of IND applications or forego potential IND applications that we believe are promising. Any delay, suspension or reduction of our efforts to pursue our pre-clinical and IND strategy could have a material adverse effect on our business and cause our stock price to decline.

We may not be able to find acceptable patients or may experience delays in enrolling patients for our clinical trials.

We may experience difficulties or delays in recruiting and enrolling a sufficient number of patients to participate in our clinical trials due to a variety of reasons, including competition from other clinical trial programs for the same indication, failure of patients to meet our enrollment criteria and premature withdraws of patients prior to the

completion of clinical trials. The FDA and institutional review boards may also require large numbers of patients, and the FDA may require that we repeat a clinical trial. Any delay resulting from our failure to enroll a sufficient number of patients on a timely basis may have a material adverse affect on our business.

Table of Contents

As we cannot predict whether or when we will obtain regulatory approval to commercialize our product candidates, we cannot predict the timing of any future revenue from these product candidates.

We cannot commercialize any of our ZFP Therapeutics to generate revenue until the appropriate regulatory authorities have reviewed and approved the applications for the product candidates. We cannot ensure that the regulatory agencies will complete their review processes in a timely manner or that we will obtain regulatory approval for any product candidate that we or our collaborators develop. Satisfaction of regulatory requirements typically takes many years, is dependent upon the type, complexity and novelty of the product and requires the expenditure of substantial resources. Regulatory approval processes outside the United States include all of the risks associated with the FDA approval process. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action or changes in FDA policy during the period of product development, clinical trials and FDA regulatory review.

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

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

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

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

Commercialization of our technologies will depend, in part, on strategic partnering with other companies. If we are not able to find partners in the future or our partners do not diligently pursue product development efforts, we may not be able to develop our technologies or products, which could slow our growth and decrease the value of our stock.

We expect to rely, to some extent, on our strategic partners to provide funding in support of our research and to perform independent research and preclinical and clinical testing. Our technology is broad based, and we do not currently possess the resources necessary to fully develop and commercialize potential products that may result from our technologies or the resources or capabilities to complete the lengthy marketing approval processes that may be required for the products. Therefore, we plan to rely on strategic partnerships to help us develop and commercialize ZFP Therapeutic products. If we are unable to find partners or if the partners we find, such as Shire, are unable or unwilling to advance our programs, or if they do not diligently pursue product approval, this may slow our progress and defer our revenues. Our partners may sublicense or abandon development programs or we may have disagreements with our partners, which would cause associated product development to slow or cease. There can be no assurance that we will be able to establish further strategic collaborations for ZFP Therapeutic product development. We may require significant time to secure collaborations or partners because we need to effectively

market the benefits of our technology to these future collaborators and partners, which may direct the attention and resources of our research and development personnel and management away from our primary business operations. Further, each collaboration or partnering arrangement will involve the negotiation of terms that may be unique to each collaborator or partner. These business development efforts may not result in a collaboration or partnership.

Table of Contents

The loss of partnering agreements would not only delay or terminate the potential development or commercialization of products we may derive from our technologies, but it may also delay or terminate our ability to test ZFP Therapeutic candidates for specific genes. If any 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.

Under typical partnering agreements we would expect to receive revenue for the research and development of a ZFP Therapeutic product based on achievement of specific milestones, as well as royalties based on a percentage of sales of the commercialized products. Achieving these milestones will depend, in part, on the efforts of our partner as well as our own. If we, or any partner, fail to meet specific milestones, then the partnership may be terminated, which could reduce our revenues. For more information on risks relating to our third party collaborative agreements, see Risks Relating to our Collaborative Relationships.

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

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

Our gene regulation and gene modification technology is relatively new, and if we are unable to use this technology in all our intended applications, it would limit our revenue opportunities.

Our technology involves a relatively new approach to gene regulation and gene modification. Although we have generated ZFPs for thousands of gene sequences, we have not created ZFPs for all gene sequences and may not be able do so, which could limit the usefulness of our technology. In addition, while we have demonstrated the function of engineered ZFNs and ZFP TFs in mammalian cells, yeast, insects, plants, and animals, we have not yet demonstrated clinical benefit of this technology in humans, and the failure to do so could restrict our ability to develop commercially viable products. If we, and our collaborators or strategic partners, are unable to extend our results to new commercially important genes, experimental animal models, and human clinical studies, we may be unable to use our technology in all its intended applications.

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

Effective delivery of ZFNs and ZFP TFs into the appropriate target cells and tissues is critical to the success of the therapeutic applications of our ZFP technology. In order to have a meaningful therapeutic effect, the ZFP Therapeutic must be delivered to sufficient numbers of cells in the targeted tissue. The ZFN or ZFP TF must be

Table of Contents

present in that tissue for sufficient time to effect either modification of a therapeutically relevant gene or regulation of its expression. In our current clinical and preclinical programs, we administer our ZFP Therapeutics as a nucleic acid that encodes the ZFN or ZFP TF. We use different formulations to deliver the ZFP Therapeutic depending on the required duration of expression, the targeted tissue and the indication that we intend to treat. However, there can be no assurances that we will be able to effectively deliver our ZFNs and ZFP TFs to produce a beneficial therapeutic effect.

We are conducting proprietary research to discover ZFP Therapeutic product candidates. These programs increase our financial risk of product failure, may significantly increase our research expenditures, and may involve conflicts with future collaborators and strategic partners.

Our proprietary research programs consist of research which is funded solely by us or by grant funding and in which we retain exclusive rights to therapeutic products generated by such research. This is in contrast to certain of our research programs that may be funded by corporate partners and in which we may share rights to any resulting products. Conducting proprietary research programs may not generate corresponding revenue and may create conflicts with our collaborators or strategic partners over rights to our intellectual property with respect to our proprietary research activities. Any conflict with our collaborators or strategic partners could reduce our ability to enter into future collaborations or partnering agreements and negatively impact our relationship with existing collaborators and partners which could reduce our revenue and delay or terminate our product development. As we continue to focus our strategy on proprietary research and therapeutic development, we expect to experience greater business risks, expend significantly greater funds and require substantial commitments of time from our management and staff.

Even if our technology proves to be effective, it still may not lead to commercially viable products.

Even if our collaborators or strategic partners are successful in using our ZFP technology in drug discovery, protein production, therapeutic development, or plant agriculture, they may not be able to commercialize the resulting products or may decide to use other methods competitive with our technology. To date, no company has received marketing approval or has developed or commercialized any therapeutic or agricultural products based on our technology. Should our technology fail to provide safe, effective, useful, or commercially viable approaches to the discovery and development of these products, this would significantly limit our business and future growth and would adversely affect our value.

Even if our product development efforts are successful and even if the requisite regulatory approvals are obtained, our ZFP Therapeutics may not gain market acceptance among physicians, patients, healthcare payers and the medical community.

A number of additional factors may limit the market acceptance of our ZFP Therapeutic products including the following:

rate of adoption by healthcare practitioners;

rate of a product s acceptance by the target population;

timing of market entry relative to competitive products;

availability of alternative therapies;

price of our product relative to alternative therapies;

availability of third-party reimbursement;

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

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

Therefore, even after we have obtained the required regulatory approval for our ZFP Therapeutic products, we may not be able to commercialize these products successfully if we cannot achieve an adequate level of market acceptance.

Table of Contents

We do not currently have the infrastructure or capability to manufacture, market and sell therapeutic products on a commercial scale.

In order for us to commercialize our therapeutic products directly, we would need to develop, or obtain through outsourcing arrangements, the capability to manufacture, market and sell our products on a commercial scale. Currently we do not have the ability nor the financial resources to establish the infrastructure and organizations needed to execute these functions, including such infrastructure needed for the commercialization of any product from our HIV/AIDS programs, which can be complex and costly. If we are unable to establish adequate manufacturing, sales, marketing and distribution capabilities, we will not be able to directly commercialize our therapeutics products, which would limit our future growth.

We may not be able to fully realize the expected benefits from the acquisition of Ceregene, Inc., and the operation of the new business of Ceregene, Inc. may subject us to additional risks.

On August 23, 2013, we entered into a definitive agreement to acquire Ceregene Inc. (Ceregene), including all of its therapeutic programs and related intellectual property and other assets. Although we expect to realize strategic, operational and financial benefits as a result of the acquisition, we cannot be certain whether, and to what extent, such benefits will be achieved in the future. In particular, the success of the acquisition will depend on our ability to efficiently and successfully integrate Ceregene s business, including the prosecution of its CERE-110 Phase 2 clinical trial, and to apply Ceregene s technology for a delivery vector based on adeno-associated virus (AAV) to advance our ZFP Therapeutics. There is no guarantee that any existing and future clinical trials of Ceregene s product candidates, including CERE-110, will produce positive results, and failure to so may adversely affect our ability to validate the AAV delivery technology and apply such technology to our ZFP products as well as negatively impact our stock price. In April 2013, Ceregene reported that its top line data for the CERE-120 Phase 2b clinical trial for Parkinson s disease did not demonstrate statistically significant efficacy in the primary endpoint. In addition, even if we obtain positive data from such clinical trials, there is no guarantee that the AAV delivery technology can be applied to our ZFP Therapeutics safely and effectively.

The acquisition of Ceregene also subjects us to additional operational and financial risks, including the following:

- additional costs that we may need to incur in order to conduct and complete Ceregene s therapeutic programs, including the CERE-110 Phase 2 clinical trial, and to comply with new regulatory requirements;
- difficulties acquiring and developing the necessary expertise to continue the development of AAV technologies and other acquired assets of Ceregene;
- difficulties in coordinating research and development activities;
- uncertainties in the business relationships with our collaborators and suppliers due to the acquisition;
- difficulties integrating Ceregene s accounting systems and procedures, including internal control over financial reporting as required by Sarbanes-Oxley Act; and

lack of previous experiences in conducting Phase 2 trials of a gene therapy based on AAV vector delivery system.

In addition, the market price of our common stock may decline as a result of the merger if the integration of Ceregene is unsuccessful, takes longer than expected or fails to achieve the expected benefits to the extent anticipated by financial analysts or investors, or the effect of the acquisition on our financial results is otherwise not consistent with the expectations of financial analysts or investors.

Table of Contents

Risks Relating to our Industry

If our competitors develop, acquire, or market technologies or products that are more effective than ours, this would reduce or eliminate our commercial opportunity.

Any products that we or our collaborators or strategic partners develop by using our ZFP technology platform will enter into highly competitive markets. Even if we are able to generate ZFP Therapeutics that are safe and effective for their intended use, competing technologies may prove to be more effective or less expensive, which, to the extent these competing technologies achieve market acceptance, will limit our revenue opportunities. In some cases, competing technologies have proven to be effective and less expensive. Competing technologies may include other methods of regulating gene expression or modifying genes. ZFNs and ZFP TFs have broad application in the life sciences industry and compete with a broad array of new technologies and approaches being applied to genetic research by many companies. Competing proprietary technologies with our product development focus include but are not limited to:

For ZFP Therapeutics:

- small molecule drugs;
- monoclonal antibodies;
- recombinant proteins;
- gene therapy/cDNAs;
- antisense;
- siRNA and microRNA approaches, exon skipping;
- TALE proteins; and
- Meganucleases.

For our Non-Therapeutic Applications:

For protein production: gene amplification, meganucleases, TALE technology, insulator technology, mini-chromosomes and CRISPR/Cas9 technology;

For target validation: antisense, siRNA, TALE technology and CRISPR/Cas9 technology;

For plant agriculture: recombination approaches, mutagenesis approaches, meganucleases, TALE technology, CRISPR/Cas9 technology, mini-chromosomes; and

For transgenic animals: somatic nuclear transfer, embryonic stem cell, TALE, CRISPR/Cas9 technology and transposase technologies.

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

substantially greater capital resources than ours;

larger research and development staffs and facilities than ours; and

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

These organizations also compete with us to:

attract qualified personnel;

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

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

Table of Contents

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

Adverse public perception in the field of gene therapy may negatively impact regulatory approval of, or demand for, our potential products.

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

Laws or public sentiment may limit the production of genetically modified agricultural products, and these laws could reduce our partner s ability to sell such products.

Genetically modified products are currently subject to public debate and heightened regulatory scrutiny, either of which could prevent or delay production of agricultural products. We have a research license and commercial option agreement with Dow AgroSciences (DAS) through which we provide DAS with access to our proprietary ZFP technology and the exclusive right to use our ZFP technology to modify the genomes or alter the nucleic acid or protein expression of plant cells, plants, or plant cell cultures. The field-testing, production and marketing of genetically modified plants and plant products are subject to federal, state, local and foreign governmental regulation. Regulatory agencies administering existing or future regulations or legislation may not allow production and marketing of our genetically modified products in a timely manner or under technically or commercially feasible conditions. In addition, regulatory action or private litigation could result in expenses, delays or other impediments to our product development programs or the commercialization of resulting products.

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

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

Table of Contents

Risks Relating to our Finances

We have incurred significant operating losses since inception and anticipate that we will incur continued losses for the foreseeable future.

We have generated operating losses since we began operations in 1995. Our net losses for the years ended December 31, 2012, 2011 and 2010 were $22.3 million, $35.8 million and $24.8 million, respectively. The extent of our future losses and the timing of profitability are uncertain, and we expect to incur losses for the foreseeable future. We have been engaged in developing our ZFP technology since inception, which has and will continue to require significant research and development expenditures. To date, we have generated our funding from issuance of equity securities, revenues derived from strategic partnering agreements, other collaborations in non-therapeutic applications of our technology, federal government research grants and grants awarded by research foundations. As of June 30, 2013, we had an accumulated deficit of $287.8 million. From 2005 to date, we have generated an aggregate of approximately $157.2 million in net proceeds from the sale of our equity securities. We expect to continue to incur additional operating losses for the next several years as we continue to expand and extend our research and development activities into human therapeutic product development. If the time required to generate significant product revenues and achieve profitability is longer than we currently anticipate or if we are unable to generate liquidity through equity financing or other sources of funding, we may be forced to curtail or suspend our operations.

We may be unable to raise additional capital, which would harm our ability to develop our technology and products.

We have incurred significant operating losses and negative operating cash flows since inception and have not achieved profitability. We expect capital outlays and operating expenditures to increase over the next several years as we expand our infrastructure and research and ZFP Therapeutic product development activities. While we believe our financial resources will be adequate to sustain our current operations at least through 2014, we may need to seek additional sources of capital through equity or debt financing. In addition, as we focus our efforts on proprietary human therapeutics, we will need to seek FDA approval of potential products, a process that could cost in excess of hundreds of millions of dollars per product. Furthermore, we may experience difficulties in accessing the capital market due to external factors beyond our control such as volatility in the equity markets for emerging biotechnology companies and general economic and market conditions. We cannot be certain that we will be able to obtain financing on terms acceptable to us, or at all. Our failure to obtain adequate and timely funding will materially adversely affect our business and our ability to develop our technology and ZFP Therapeutic products. Furthermore, any sales of additional equity securities may result in dilutions to our stockholders and any debt financing may include business and financial covenants that restricts our operations.

We are at the development phase of operations and may not succeed or become profitable.

We began operations in 1995 and are in the early phases of ZFP Therapeutic product development, and we have incurred significant losses since inception. To date, our revenues have been generated from strategic partners, other collaborations in non-therapeutic applications of our technology, and federal government and research foundation grants. Our focus on higher-value therapeutic product development and related strategic partnerships requires us to incur substantial expenses associated with product development. In addition, the preclinical or clinical failure of any single product may have a significant effect on the actual or perceived value of our stock. Our business is subject to all of the risks inherent in the development of a new technology, which includes the need to:

attract and retain qualified scientific and technical staff and management, particularly scientific staff with expertise to develop our early-stage technology into therapeutic products;

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

Table of Contents

develop a market for our products; and

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

Risks Relating to our Relationships with Collaborators and Strategic Partners

If conflicts arise between us and our collaborators or strategic partners, these parties may act in their self-interest, which may limit our ability to implement our strategies.

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

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

Our collaborators and strategic partners may control aspects of our clinical trials, which could result in delays and other obstacles in the commercialization of our proposed products.

For some programs, we depend on third party collaborators and strategic partners to design and conduct our clinical trials. As a result, we may not be able to conduct these programs in the manner or on the time schedule we currently contemplate, which may negatively impact our business operations. In addition, if any of these collaborators or strategic partners withdraws support for our programs or proposed products or otherwise impair their development; our business could be negatively affected.

In January 2012, we entered into a research and collaborative agreement with Shire, pursuant to which we are engaging in a joint program with Shire to research, develop and commercialize human therapeutics and diagnostics for hemophilia, Huntington s disease and other monogenic diseases based on our ZFP technology. Under this agreement, we are responsible for all research activities through the submission of an IND or CTA, while Shire is responsible for clinical development and commercialization of products generated from the research program from and after the acceptance of an IND or CTA for the product. Under the agreement, we may be eligible to receive milestone payments upon the achievement of specified clinical development, commercialization and post-commercialization milestones. The total amount of potential milestone payments for each gene target, assuming the achievements of all specified milestones in the agreement, is $213.5 million. We may receive royalty payments based on specified percentages of net sales of