

SANGAMO THERAPEUTICS, INC

Form 424B5

April 24, 2018

Table of Contents

Filed pursuant to Rule 424(b)(5)
Registration No. 333-224418

The information in this preliminary prospectus supplement is not complete and may be changed. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities and are not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

Subject to completion, dated April 24, 2018

Preliminary Prospectus Supplement

(To Prospectus dated April 24, 2018)

\$200,000,000

Common Stock

We are offering \$200,000,000 of shares of our common stock.

Our common stock is listed on The Nasdaq Global Select Market under the symbol SGMO. On April 23, 2018, the last reported sale price of our common stock as reported on The Nasdaq Global Select Market was \$18.15 per share. Based on an assumed public offering price of \$18.15 per share, the last reported sale price of our common stock on The Nasdaq Global Select Market on April 23, 2018, we would expect to offer approximately 11,019,284 shares hereby.

	Per Share	Total
Public offering price	\$	\$
Underwriting discounts and commissions ⁽¹⁾	\$	\$
Proceeds to Sangamo Therapeutics, before expenses	\$	\$

(1) See the section entitled "Underwriting" for additional disclosure regarding underwriter compensation and estimated offering expenses.

We have granted the underwriters an option for a period of 30 days to purchase up to \$30,000,000 of additional shares of our common stock, solely to cover overallotments.

Investing in our common stock involves a high degree of risk. See Risk Factors beginning on page S-13 of this prospectus supplement and in the Current Report on Form 8-K filed with the Securities and Exchange Commission on April 17, 2018, as well as our other filings that are incorporated by reference into this prospectus supplement and the accompanying prospectus.

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.

Gilead Sciences, Inc. has indicated an interest in purchasing up to approximately \$50,000,000 of the shares of common stock offered hereby at the price offered to the public. Because this indication of interest is not a binding agreement or commitment to purchase, this entity may elect not to purchase any shares in this offering, or the underwriters may elect not to sell any shares in this offering to it.

The underwriters expect to deliver the shares to purchasers on or about April , 2018.

Joint Book-Running Managers

BofA Merrill Lynch

J.P. Morgan

Cowen

April , 2018

Table of Contents

TABLE OF CONTENTS

Prospectus Supplement

	Page
<u>About this Prospectus Supplement</u>	S-ii
<u>Prospectus Supplement Summary</u>	S-1
<u>Risk Factors</u>	S-13
<u>Special Note Regarding Forward-Looking Statements</u>	S-17
<u>Use of Proceeds</u>	S-19
<u>Dividend Policy</u>	S-19
<u>Dilution</u>	S-20
<u>Price Range of Common Stock</u>	S-22
<u>Material U.S. Federal Income Tax Consequences for Non-U.S. Holders of Common Stock</u>	S-23
<u>Underwriting</u>	S-27
<u>Legal Matters</u>	S-34
<u>Experts</u>	S-34
<u>Where You Can Find More Information</u>	S-34
<u>Incorporation of Certain Information by Reference</u>	S-34

Prospectus

	Page
<u>About this Prospectus</u>	ii
<u>Prospectus Summary</u>	1
<u>Risk Factors</u>	5
<u>Forward-Looking Statements</u>	5
<u>Financial Ratios</u>	7
<u>Use of Proceeds</u>	8
<u>Description of Capital Stock</u>	9
<u>Description of Debt Securities</u>	13
<u>Description of Warrants</u>	20
<u>Legal Ownership of Securities</u>	22
<u>Selling Securityholders</u>	26
<u>Plan of Distribution</u>	27
<u>Legal Matters</u>	29
<u>Experts</u>	29
<u>Where You Can Find More Information</u>	29
<u>Incorporation of Certain Information by Reference</u>	29

Table of Contents

We have not, and the underwriters have not, authorized anyone to provide you with information different than or inconsistent with the information contained in or incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectus that we have authorized for use in connection with this offering. We and the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We are not, and the underwriters are not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and in any free writing prospectus that we have authorized for use in connection with this offering, is accurate only as of the date of those respective documents, regardless of the time of delivery of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering, in their entirety before making an investment decision. You should also read and consider the information in the documents to which we have referred you in the sections of this prospectus supplement entitled **Where You Can Find More Information and **Incorporation of Certain Information by Reference**.**

ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the terms of this offering of common stock and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus dated April 24, 2018, including the documents incorporated by reference therein, 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, on the one hand, and the information contained in the accompanying prospectus or in any document incorporated by reference that was filed with the Securities and Exchange Commission, or SEC, before the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. 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.

All references in this prospectus supplement and the accompanying prospectus to Sangamo, the Company, we, us, or similar references refer to Sangamo Therapeutics, Inc., a Delaware corporation, and its subsidiaries on a consolidated basis, except where the context otherwise requires or as otherwise indicated.

This prospectus supplement, the accompanying prospectus, and the information incorporated herein and therein by reference include trademarks, trade names and service marks owned by us or other companies. SANGAMO®, SANGAMO THERAPEUTICS®, Better Therapeutics By Design®, ZFP Therapeutic®, Engineering Genetic Cures®, and Pioneering Genetic Cures® are our registered trademarks in the United States. All other trademarks or trade names referred to in this prospectus supplement, the accompanying prospectus and the information incorporated herein and therein by reference are the property of their respective owners.

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 into 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, you should read and consider carefully the more detailed information included or incorporated by reference in this prospectus supplement and the accompanying prospectus, including the factors described under the heading *Risk Factors* of this prospectus supplement, in our Current Report on Form 8-K filed with the SEC on April 17, 2018 and in our other filings that are incorporated by reference into this prospectus supplement and the accompanying prospectus, as well as the information included in any free writing prospectus that we have authorized for use in connection with this offering.*

Our Business

We are a clinical stage biotechnology company focused on translating ground-breaking science into genomic therapies that transform patients' lives using our industry-leading platform technologies in genome editing, gene therapy, gene regulation and cell therapy.

We are a leader in the research and development of zinc finger proteins, or ZFPs, a naturally occurring class of proteins found in humans. We have used our knowledge and expertise to develop a proprietary technology platform in both genome editing and gene regulation. ZFPs can be engineered to make zinc finger nucleases, or ZFNs, proteins that can be used to specifically modify DNA sequences by adding or knocking out specific genes, or genome editing, and ZFP transcription factors or ZFP TFs, proteins that can be used to increase or decrease gene expression, or gene regulation. In the process of developing this platform, we have accrued significant scientific, manufacturing and regulatory capabilities and know-how that are generally applicable in the broader field of gene therapy and have capitalized this knowledge into a conventional gene therapy platform based on adeno-associated viral vector, or AAV, cDNA gene transfer.

Our strategy is to maximize the value and therapeutic use of our technology platforms. In certain therapeutic areas we intend to capture the value of our proprietary genome editing and gene therapy products by forward integrating into manufacturing, development and commercial operations. In other therapeutic areas we intend to partner with biopharmaceutical companies to develop products.

We are focused on the development of human therapeutics for diverse diseases with well-characterized genetic causes. We have several proprietary clinical and preclinical product candidates in development and have strategically partnered certain programs with biopharmaceutical companies to obtain funding for our own programs and to expedite clinical and commercial development.

We have an ongoing Phase 1/2 clinical trial evaluating SB-525, a gene therapy for the treatment of hemophilia A, a bleeding disorder. We also have ongoing Phase 1/2 clinical trials evaluating three product candidates using our proprietary *in vivo* genome editing approach: SB-FIX for the treatment of hemophilia B, a bleeding disorder; SB-318, for the treatment of Mucopolysaccharidosis Type I, or MPS I; and SB-913 for the treatment of Mucopolysaccharidosis Type II, or MPS II. MPS I and MPS II are rare lysosomal storage disorders, or LSDs. We are also initiating a Phase 1/2 clinical trial evaluating ST-400, developed using our proprietary ZFN-mediated *ex vivo* cell therapy platform, for the treatment of beta-thalassemia, a blood disorder. In addition, we have proprietary preclinical and discovery stage programs in other LSDs, hematological disorders and monogenic diseases, including certain central nervous system, or CNS, disorders, cancer immunotherapy, immunology and infectious disease.

S-1

Table of Contents

In February 2018, we entered into a global collaboration and license agreement with Kite Pharma, Inc., or Kite, a wholly owned subsidiary of Gilead Sciences, Inc., or Gilead, for the research, development and commercialization of potential engineered cell therapies for cancer. In this collaboration, we will work together with Kite on a research program under which we will design ZFNs and AAVs to disrupt and insert certain genes in T cells and natural killer, or NK, cells, including the insertion of genes that encode chimeric antigen receptors, or CARs, T-cell receptors, or TCRs and NK-cell receptors, or NKRs, directed to mutually agreed targets. Kite will be responsible for all clinical development and commercialization of any resulting products.

In December 2017, we entered into a new research collaboration and license agreement with Pfizer Inc., or Pfizer, for the development and commercialization of potential gene therapy products that use ZFP TFs to treat amyotrophic lateral sclerosis, or ALS, and frontotemporal lobar degeneration, or FTL, linked to mutations of the *C9ORF72* gene. Under this agreement, we are working with Pfizer on a research program to identify, characterize and preclinically develop ZFP TFs that satisfy pre-agreed criteria. Pfizer is responsible for subsequent development, manufacturing and commercialization of licensed products.

In May 2017, we entered into a global collaboration and license agreement with Pfizer for the research, development and commercialization of SB-525, our gene therapy product candidate for hemophilia A, and closely related products. Under this agreement, we are responsible for conducting the Phase 1/2 clinical trial and certain manufacturing activities for SB-525, while Pfizer is responsible for subsequent worldwide development, manufacturing, marketing and commercialization of SB-525. We and Pfizer may also collaborate in the research and development of additional AAV-based gene therapy products for hemophilia A.

We have also established a collaborative partnership with Bioverativ, Inc., or Bioverativ, a wholly owned subsidiary of Sanofi, to research, develop and commercialize therapeutic gene-edited cell therapy products in hemoglobinopathies, including beta-thalassemia and sickle cell disease, or SCD. We expect to begin enrolling patients in a Phase 1/2 clinical study for beta-thalassemia in the first half of 2018. Bioverativ is responsible for subsequent development, manufacturing and commercialization of licensed products.

We have a substantial intellectual property position in the genome editing field including the design, selection, composition and use of engineered ZFPs to support our research and development activities. As of February 15, 2018, we either owned outright or have exclusively licensed the commercial rights to over 860 patents issued in the United States and foreign jurisdictions, and over 610 patent applications pending worldwide. We continue to license and file new patent applications that strengthen our core and accessory patent portfolio. We believe that our intellectual property position is a critical element in our ability to research, develop and commercialize products and services based on genome editing, gene therapy, gene regulation and cell therapy.

Table of Contents

Our Product Development

Hemophilia A and B

Hemophilia is a rare bleeding disorder in which the blood does not clot normally. It is also a monogenic disease, or a disease that is caused by a genetic defect in a single gene. There are several types of hemophilia caused by mutations in genes that encode factors which help the blood clot and stop bleeding when blood vessels are injured. Individuals with hemophilia experience bleeding episodes after injuries and spontaneous bleeding episodes that often lead to joint disease such as arthritis. The most severe forms of hemophilia affect males. The standard treatment for individuals with hemophilia is replacement of the defective clotting factor with regular infusion of recombinant clotting factors or plasma concentrates. These therapies are expensive and sometimes stimulate the body to produce antibodies against the factors that inhibit the benefits of treatment. In these situations, other clotting factors such as Factor VII and X may be used to treat patients.

The most prevalent form of the disease, hemophilia A, is caused by a defect in the clotting Factor 8 gene. According to the National Hemophilia Foundation and the World Federation of Hemophilia, hemophilia A occurs in about one in every 5,000 male births in the United States, with approximately 16,000 males currently affected. Defects in clotting Factor 9 gene lead to hemophilia B. Hemophilia B occurs in about one in every 25,000 male births in the United States, with approximately 4,000 males currently affected.

SB-525 Hemophilia A

We are developing SB-525, a gene therapy product candidate utilizing an AAV carrying a clotting Factor 8 gene construct that is driven by our proprietary synthetic liver specific promoter. In 2016, we presented preclinical data demonstrating production of supraphysiological levels of human Factor VIII clotting protein, or hFVIII, in mice and non-human primates, or NHPs. In these dose-ranging preclinical studies, mean hFVIII levels of 5 – 230% of normal were observed using AAV doses in the range of 6.00E+11 – 6.00E+12 vg/kg, the most potent dose response reported in NHPs for a human Factor 8 gene construct at the time.

In 2017, we initiated a Phase 1/2 clinical trial, the Alta Study, to evaluate the safety and efficacy of SB-525 in adults with severe hemophilia A. The Alta Study is an open-label, ascending-dose study designed to enroll up

Table of Contents

to 20 adult subjects across six potential dose cohorts. In August 2017, we announced that the first subject was treated in our Alta Study. Currently, there are four patients dosed with SB-525. We expect to release preliminary data from the Alta Study in the third quarter of 2018.

SB-525 has been granted Orphan Drug and Fast Track designations by the U.S. Food and Drug Administration, or FDA, as well as Orphan Medicinal Product designation by the European Medicines Agency, or EMA.

SB-FIX Hemophilia B

We are developing SB-FIX, an *in vivo* genome editing product candidate, to treat hemophilia B. Utilizing our ZFN genome editing technology, we are adding a new therapeutic copy of the Factor 9 gene precisely into the Albumin gene locus in liver cells, and using the strong endogenous Albumin promoter to drive expression of the newly inserted gene. We believe the potential of this approach to provide a permanent correction for a patient may be optimal for a pediatric population by reducing or eliminating the need for chronic infusions of replacement proteins or clotting factor products. We have published data demonstrating the potential utility of this approach for several different monogenic disease applications in addition to hemophilia B.

Preclinical studies of the Albumin genome editing approach have demonstrated that therapeutic levels of Factor IX clotting protein could be generated in a dose-dependent manner in NHPs. There were no significant alterations in circulating Albumin levels. Studies in mice also demonstrated stable Factor IX production for over one year. Preclinical studies in wildtype mice have demonstrated expression of therapeutic levels of human clotting Factor IX protein, or hFIX, from the liver and into the blood for the duration of the 60-week study. Additional preclinical studies in mouse models of hemophilia B demonstrated expression of therapeutic levels of hFIX from the liver and into the blood, which resulted in the correction of the clotting defect in hemophilia B mice treated with a single dose of SB-FIX. SB-FIX was also evaluated in preclinical NHP studies and demonstrated dose-dependent, therapeutic levels of hFIX expression, between 20-50% of normal, in wildtype cynomolgus monkeys, after a single administration of SB-FIX. Levels of hFIX were stable for up to three months in treated NHPs. Furthermore, there was a strong dose-response correlation between the level of gene modification at the Albumin locus and the levels of hFIX measured in the blood.

In 2016, we initiated a Phase 1/2, open-label, ascending dose clinical trial, the FIXtendz Study, to evaluate safety and efficacy of SB-FIX in adult males with severe hemophilia B. The FIXtendz Study is designed to enroll up to 12 subjects across three dose cohorts. In February 2018, the Medicines and Healthcare Products Regulatory Agency, or MHRA, of the United Kingdom granted Clinical Trial Authorisation, or CTA, for enrollment of subjects into the ongoing Phase 1/2 clinical trial evaluating SB-FIX for hemophilia B. The CTA permits evaluation of SB-FIX in both adults and adolescents. We expect to open clinical trial sites in the United Kingdom in the second half of 2018. Once preliminary safety has been demonstrated in the ongoing SB-FIX Phase 1/2 clinical trial in adults (18 years of older), we may begin enrolling adolescents (12 – 17 years of age) into the study.

SB-FIX has been granted Orphan Drug and Fast Track designations by the FDA.

Lysosomal Storage Disorders

LSDs are a heterogeneous group of rare inherited metabolic disorders including: MPS I, MPS II, Fabry disease, Gaucher disease and many others. These disorders are caused by defects in genes that encode proteins known as enzymes, which break down and eliminate unwanted substances in cells. These enzymes are found in structures called lysosomes which act as recycling sites in cells, breaking down unwanted material into simple products. A defect in a lysosomal enzyme leads to the accumulation of toxic levels of the substance that the enzyme would normally

eliminate. These toxic levels may cause cell damage which can lead to serious health problems.

S-4

Table of Contents

MPS I is caused by mutations in the gene encoding the alpha-L-iduronidase, or IDUA, enzyme, resulting in a deficiency of IDUA enzyme, which is required for the degradation of the glycosaminoglycans, or GAGs, dermatan sulfate and heparin sulfate. The inability to degrade GAGs leads to their accumulation within the lysosomes throughout the body. Individuals with this mutation experience multi-organ dysfunction and damage. Depending on the severity of the mutations and degree of residual enzyme activity, affected individuals may develop enlarged internal organs, joint stiffness, skeletal deformities, corneal clouding, hearing loss and cognition impairments. Three forms of MPS I, in order of increasing severity, include Scheie, Hurler-Scheie and Hurler syndromes. According to the National MPS Society, one in 500,000 births in the United States will result in Scheie syndrome, one in 115,000 births in Hurler/Scheie, and one in 100,000 births results in Hurler syndrome. There are approximately 1,000 MPS I patients in the United States.

MPS II is an X-linked disorder primarily affecting males and caused by mutations in the gene encoding the iduronate-2-sulfatase, or IDS, enzyme. This results in a deficiency of IDS enzyme, which is required for the degradation of GAGs. Similar to MPS I, the inability to degrade GAGs leads to their accumulation within the lysosomes throughout the body. Individuals with this mutation experience multi-organ dysfunction and damage. Children with MPS II appear normal at birth but begin showing symptoms of developmental delay by age 2-3 years. Depending on the severity of the mutations and degree of residual enzyme activity, affected individuals may develop delayed development, enlarged internal organs, cardiovascular disorders, stunted growth and skeletal abnormalities and hearing loss. The disorder is progressive and symptoms range from mild (normal cognitive function) to severe (cognitively impaired). According to the National MPS Society, one in 100,000 male births in the United States will result in MPS II. There are approximately 500 MPS II patients in the United States.

Fabry disease is an X-linked disorder primarily affecting males and caused by a mutation in the gene encoding the alpha-galactosidase A, or alpha-Gal A, enzyme, resulting in a deficiency of alpha-Gal A enzyme, which is required for the degradation of the ganglioside globotriaosylceramide, a particular type of fatty substance. The inability to degrade this fatty substance leads to its accumulation within the lysosomes throughout the body. Individuals with this mutation experience multi-organ dysfunction and damage. Depending on the severity of the mutations and degree of residual enzyme activity, affected individuals may develop progressive kidney damage, heart attack, stroke, gastrointestinal complications, corneal opacity, tinnitus and hearing loss. Milder forms of the disorder present later in life and affect only the heart or kidneys. According to the National Institutes of Health U.S. National Library of Medicine, one in 40,000 to one in 60,000 male births in the United States will result in Fabry disease. There are approximately 2,200 males with Fabry disease in the United States. This mutation can also occur in females, however is less common and the frequency is unknown.

There are limited treatments currently available for MPS I, MPS II and Fabry disease. For individuals with MPS I, there are only two options: hematopoietic stem cell transplantation, or HSCT, for those with the most severe form of the disease (Hurler) and enzyme replacement therapy, or ERT, for patients with the attenuated forms of the disease (Hurler-Scheie, Scheie). However, the reported mortality rate after HSCT is approximately 15% and the survival rate with successful engraftment is 56%. Most patients with milder forms of the disease receive weekly ERT, usually in a doctor's office. These IDUA enzyme infusions take on average four to six hours to administer. Weekly and bi-weekly ERT infusions are the only available options for MPS II and Fabry disease, respectively. Because of the availability of few treatment options that effectively and safely treat these diseases, there remains significant unmet medical need.

SB-913 MPS II

We are developing SB-913, an *in vivo* genome editing product candidate, to treat MPS II. Similar to SB-318, we are using our ZFN genome editing technology to add a new therapeutic copy of the IDS gene precisely into the *Albumin* gene locus in the genome of liver cells, using the strong endogenous Albumin promoter to drive expression of the

newly inserted gene.

S-5

Table of Contents

Preclinical mouse model data demonstrated robust levels of IDS enzyme expression in the liver, blood plasma and spleen of SB-913 treated mice, resulting in a 100-fold increase in IDS activity, with sustained elevated levels in the blood plasma over the course of the entire study. Additional preclinical mouse model data demonstrated stable production of therapeutic levels of IDS enzyme from the liver into the circulation and additional secondary tissues, including the spleen, lung, muscle, heart and brain, after a single intravenous administration of SB-913. This resulted in the significant reduction of GAG biomarkers across all the tissues. Behavioral data from Barnes maze tests, collected at the end of the four-month study demonstrated statistically significant preservation of cognitive learning and memory in mice treated with SB-913, compared to untreated mice.

In 2017, we initiated an open-label, dose-ascending Phase 1/2 clinical trial, the CHAMPIONS Study, to evaluate the safety and efficacy of SB-913 in adult male subjects with attenuated MPS II, designed to enroll up to nine subjects across three ascending dose cohorts. In November 2017, we announced that the first subject had been treated in the CHAMPIONS Study. In February 2018, we presented preliminary six-week safety data from the first subject enrolled in the CHAMPIONS Study. The data demonstrated that the subject tolerated the infusion well. Mild (Grade 1) adverse events related to the study drug were reported on the fourth day after dosing. These were dizziness, weakness and frequent urination, all of which resolved within one day without treatment. No other adverse events related to the study drug have been observed. Liver function tests have remained within normal limits for the patient since the infusion. Currently, there are four patients dosed with SB-913. We expect to present additional safety and preliminary efficacy data from the CHAMPIONS Study in the third quarter of 2018. We submitted a CTA in the first half of 2018 to initiate enrollment of adolescent and pediatric subjects in the United Kingdom into the Phase 1/2 clinical trial. We expect to open clinical trial sites in the United Kingdom in the second half of 2018.

SB-913 has been granted Orphan Drug, Rare Pediatric Disease and Fast Track designations by the FDA, as well as Orphan Medicinal Product designation by the EMA.

SB-318 MPS I

We are developing SB-318, an *in vivo* genome editing product candidate, to treat MPS I. Using the same approach as our hemophilia B product candidate, SB-FIX, we are adding a new therapeutic copy of the IDUA gene precisely into the *Albumin* gene locus in the genome of liver cells, using the strong endogenous Albumin promoter to drive expression of the newly inserted gene. We believe the potential of this approach to provide a permanent correction for a patient may be optimal for a pediatric population by reducing or eliminating the need for chronic ERT infusions.

Preclinical mouse model data demonstrated robust levels of IDUA enzyme expression in the liver, blood plasma and spleen of SB-318 treated mice, resulting in a 10-fold increase in IDUA activity, with sustained elevated levels in the blood plasma over the course of the two-month study. Additional preclinical mouse model data demonstrated stable production of therapeutic levels of IDUA enzyme from the liver into the circulation and secondary tissues, including the spleen, lung, muscle, heart and brain, after a single intravenous administration of SB-318. This resulted in the significant reduction of GAG biomarkers in all of the tissues. Behavioral data from Barnes maze tests, collected at the end of the four-month study, demonstrated statistically significant preservation of cognitive learning and memory in mice treated with SB-318, compared to untreated mice.

In 2017, we initiated an open-label, dose-ascending Phase 1/2 clinical trial, the EMPOWERS Study, to evaluate SB-318 in adult subjects with attenuated MPS I. The EMPOWERS Study is designed to enroll up to nine subjects across three ascending dose cohorts. Based on the preliminary safety data from the CHAMPIONS Study discussed above, in April 2018, we amended the protocol for the EMPOWERS Study so that the patients would initiate treatment in the study at the mid-dose level. We expect to present preliminary safety and efficacy

S-6

Table of Contents

data from the EMPOWERS Study in 2018. We submitted a CTA to initiate enrollment of adolescent and pediatric subjects in the United Kingdom into the Phase 1/2 clinical trial. We expect to open clinical trial sites in the United Kingdom in the second half of 2018.

SB-318 MPS I has been granted Orphan Drug, Rare Pediatric Disease and Fast Track designations by the FDA, as well as Orphan Medicinal Product designation by the EMA.

ST-920 Fabry Disease

We are developing ST-920 for Fabry disease. ST-920 is a gene therapy product candidate utilizing an AAV, carrying a galactosidase alpha, or GLA, gene construct, coding for the alpha-Gal A enzyme, driven by our proprietary synthetic liver specific promoter. We are currently conducting IND-enabling studies for ST-920 and expect to file an IND application with the FDA in 2018.

Hemoglobinopathies: Beta-thalassemia and Sickle Cell Disease

Mutations in the gene encoding beta-globin, the oxygen carrying protein of red blood cells, lead to hemoglobinopathies such as beta-thalassemia and sickle cell disease, or SCD. Both diseases manifest in the months after birth, when patients switch from producing functional fetal gamma-globin to a mutant form of adult beta-globin, which results in their condition. Naturally occurring increased levels of fetal hemoglobin have been shown to reduce the severity of both beta-thalassemia and SCD.

Beta-thalassemia is a rare disorder that results in greatly impaired production of healthy red blood cells despite bone marrow over activity, leading to life-threatening anemia, enlarged spleen, liver and heart, and bone abnormalities. We are focused on Beta-thalassemia major which is a severe form of thalassemia that requires regular, often monthly, blood transfusions and subsequent iron-chelation therapy to treat iron overload. The Centers for Disease Control and Prevention, or CDC, estimates that 1,000 people have beta-thalassemia major in the United States, and an unknown number carry the genetic trait and can pass it on to their children.

In SCD, the mutation causes the red blood cells to form an abnormal sickle or crescent shape. The cells are fragile and deliver less oxygen to the body's tissues. They can also get stuck more easily in small blood vessels and break into pieces that can interrupt healthy blood flow which further decrease the amount of oxygen flowing to body tissues. Almost all patients with SCD experience these painful vaso-occlusive crises, which can last from hours to days and may cause irreversible organ damage. Current standard of care is to manage and control symptoms, and to limit the number of crises. Treatments include administration of hydroxyurea, blood transfusions, iron-chelation therapy, pain medications and antibiotics. The CDC estimates that there are 90,000 to 100,000 Americans living with SCD, which occurs in approximately one out of every 365 African-American births and one out of every 16,300 Hispanic-American births.

ST-400 Beta-thalassemia; BIVV-003 SCD

We are developing ST-400 for the treatment of beta-thalassemia and our collaboration partner, Bioverativ, is developing BIVV-003 for the treatment of SCD. Both ST-400 and BIVV-003 are genome-edited cell therapies that use our ZFN genome editing technology to modify a patient's own, or autologous, hematopoietic stem/progenitor cells, or HSPCs, to produce functional red blood cells using fetal hemoglobin. Our genome editing technology can be used in HSPCs to precisely disrupt regulatory sequences that control the expression of key transcriptional regulators, such as the BCL11A erythroid enhancer sequence, to reverse the switch from expression of the mutant adult beta-globin back to the production of functional fetal gamma-globin.

The current standard of care for beta-thalassemia includes chronic blood transfusions, while the standard of care for SCD is a bone marrow transplant, or BMT, of HSPCs from a matched related donor, or an allogeneic

S-7

Table of Contents

BMT. However, these therapies are limited due to the risk of iron overload with blood transfusions, requiring subsequent iron chelation therapy, and the scarcity of matched donors and the significant risk of Graft versus Host Disease, or GvHD, with BMTs after transplantation of the foreign cells. By performing genome editing in HSPCs that are isolated from and subsequently returned to the same patient (i.e., an autologous HSPC transplant), our approach has the potential to address these limitations. The goal of this approach is to develop a one-time long-lasting treatment for beta-thalassemia and SCD.

Preclinical data from clinical-scale *in vitro* studies have demonstrated that ST-400 and BIVV-003 can be manufactured by reproducible, high-level, ZFN-mediated modification in HSPCs mobilized in peripheral blood at clinical production scale (>10⁸ cells), with an on-target modification efficiency of greater than 80%. Furthermore, erythroid differentiation of enhancer targeted cells showed modification of both BCL11A erythroid enhancer alleles in more than 50% of the erythroid colonies and resulted in a greater than four-fold increase in gamma globin mRNA and protein production, compared to controls. Specificity studies of ST-400 and BIVV-003 revealed no detectable off-target activity using state-of-the art, unbiased, highly sensitive oligo-capture assays. Preclinical data from *in vivo* studies in immune-deficient mice demonstrated robust long-term (19 weeks) engraftment and that targeted gene modification was maintained through multi-lineage differentiation in the bone marrow and peripheral blood.

Our IND for ST-400 was cleared by the FDA in September 2017, and we have designed an open-label, single arm Phase 1/2 clinical trial to evaluate the safety and efficacy of ST-400 in up to six adult subjects with beta-thalassemia. In March 2018, we initiated the first clinical site for this beta-thalassemia study and we expect to begin enrolling patients in the first half of 2018.

Bioverativ is our partner for ST-400 and is responsible for the clinical development of BIVV-003 for SCD.

CNS-Tauopathies

We are using our ZFP-TF gene regulation platform to develop potential gene therapies for tauopathy disorders, including Alzheimer's disease and other neurodegenerative diseases. We believe a reduction in tau protein levels can help reduce intracellular tau protein aggregation and the formation of neurofibrillary tangles in neurons, potentially ameliorating or reversing disease progression. We believe this approach may have a significant advantage compared to monoclonal antibody-based approaches to Alzheimer's disease and other tauopathy disorders because it is designed to selectively down-regulate the *tau* gene in neurons with the goal of reducing all forms of the tau protein globally across the CNS. In contrast, monoclonal antibody-based approaches are limited in that they can only bind to certain forms of tau proteins.

Preclinical studies in wildtype mice demonstrated that a single administration of *tau*-targeting ZFP-TFs resulted in up to 70% reduction of tau mRNA and protein expression across the entire CNS, as well as sustained and well-tolerated ZFP-TF expression with minimal impact on inflammatory markers. Additional preclinical studies in amyloid mouse models of Alzheimer's disease demonstrated up to 80% reduction of tau protein levels in the brain and cerebrospinal fluid, as well as significantly reduced neuritic dystrophy after a single administration of ZFP-TFs in mice with established disease pathology.

We are currently conducting preclinical studies in NHPs to evaluate our ZFP-TFs in larger mammalian species. We intend to seek a partner with disease area expertise for the clinical development and commercialization of this program.

C9ORF72 linked ALS/FTLD

In December 2017, we entered into a research collaboration and license agreement with Pfizer to develop and commercialize gene therapy products that use our ZFP TFs to treat ALS and FTLN linked to mutations of the

S-8

Table of Contents

C9ORF72 gene. ALS and FTLN are part of a spectrum of neurodegenerative disorders caused by mutations in the C9ORF72 gene that involve hundreds of additional repetitions of a six base pair sequence of DNA. This ultimately leads to the deterioration of motor neurons, in the case of ALS, or neurons in the frontal and temporal lobes, in the case of FTLN. Currently, there are no cures to halt or reverse the progression of ALS or FTLN. The C9ORF72 mutation is linked to approximately one-third of cases of familial ALS. We and Pfizer plan to investigate allele-specific ZFP-TFs with the potential to differentiate the mutant C9ORF72 allele from the wildtype allele and to specifically down-regulate expression of the mutant form of the gene.

Huntington's Disease

Huntington's disease is an inherited, progressive neurologic disease for which there is no treatment or cure. The disease is caused by a particular type of mutation in a single gene, the HTT gene. Most patients inherit one normal and one defective or mutant copy of the HTT gene, which causes Huntington's disease. The mutation is characterized by expansion of a repeated stretch of DNA sequence within the gene called a CAG repeat. A normal copy of the HTT gene usually has 10 to 29 of these CAG repeats but a defective copy has many more—generally greater than 39 repeats. While the protein produced by the normal copy of the gene appears to be essential for development (mice lacking the gene do not survive to birth), the product of the mutated gene is damaging to cells. Symptoms, which include deterioration of muscle control, cognition and memory, usually develop between 35 and 44 years of age. It is known that the greater the number of CAG repeats, the earlier the onset. Huntington's disease is usually fatal within 15 to 20 years after the onset of symptoms. The disease has a high prevalence for an inherited disorder. According to the Huntington's Disease Society of America, approximately 30,000 people in the United States have Huntington's disease. In addition, it is estimated that approximately 200,000 people in the United States are at risk of developing the disease.

Research in animal models of the disease has shown that lowering the levels of the mutant HTT protein can prevent, or even reverse, disease progression. However, to date most HTT-lowering methods decrease levels of both the normal and mutant forms of HTT, raising potential safety concerns given the importance of normal HTT protein. In collaboration with Shire, we are developing ZFP TFs that can selectively repress the expression of the mutant disease-causing form of HTT while leaving expression levels of the normal gene unchanged. Preclinical studies in animal models of the disease are ongoing and Shire is responsible for all clinical development activities including filing the IND application.

We previously announced a data security incident involving the compromise of a senior executive's company email account. While we are continuing to analyze the effects of the incident, along with the appropriate remediation of our information technology systems, at this time we do not believe that our ongoing clinical trials or any data from these trials have been compromised, particularly because we restrict the receipt of data from our clinical trials to a very limited number of employees.

New ZFN Architectures

In 2017, our scientists reported on platform advancements that substantially enhanced the precision, efficiency and specificity of ZFNs for therapeutic genome editing. We believe these advances enable rapid development of ZFNs to target chosen genomic sites with high levels of targeted modification and with no detectable off-target activity. These advances include the development of new linkers that enable base skipping between adjacent zinc finger modules as well as a reconfiguring of the ZFN architecture to allow optional placement of the FokI nuclease domain at either the carboxy terminal or the amino terminal end. The enhancements also include the identification of key amino acid substitutions that can be used to tune biochemical properties and remove non-specific binding contacts between the ZFN and the DNA backbone.

S-9

Table of Contents

Advancements in T Cell Editing Capabilities

In 2018, we presented preclinical data demonstrating our ability to accomplish highly efficient multiplex genome editing of T cells. Efficient multiplex editing, the ability to make multiple genetic changes in a single step, enables simultaneous disruption of certain genes to prevent the body from rejecting the treatment and integration of new genes to equip the modified T cells with targeted antitumor functions. In the presented data, we described a T cell with four edits achieved in a single step. The four simultaneous edits included triple knockout of TCR (93% efficiency), b2 microglobulin, or B2M, (96% efficiency), CISH, a checkpoint gene (93% efficiency), and targeted insertion of green fluorescent protein, or GFP, (91% efficiency), resulting in 76% of the modified T cells with all four edits.

Our T cell engineering capabilities have advanced rapidly in the last two years with improvements in our ZFN design capabilities. These novel architectural enhancements have resulted in a 300-fold increase in potential design options for a given genetic sequence, yielding higher on-target modification activity in preclinical testing, with *ex vivo* editing efficiencies now reaching as high as 99.5%, and off-target cleavage consistently below the level of detection. We believe these improvements potentially allow for the use of substantially reduced doses of mRNA and AAV, enabling a highly efficient gene editing process that maintains T cell phenotypes, functions and proliferative capacity during *ex vivo* cell expansion.

Certain Preliminary Financial Results

As of March 31, 2018, we had approximately \$234.9 million of cash, cash equivalents and investments. This amount is unaudited and preliminary, is subject to completion of financial closing procedures that could result in changes to the amount, and does not present all information necessary for an understanding of our financial condition as of March 31, 2018. This amount also does not reflect \$150.0 million that we received in April 2018 under the terms of our collaboration agreement with Kite.

Corporate Information

We were incorporated in June 1995 in the state of Delaware and in January 2017, we changed our name from Sangamo BioSciences, Inc. to Sangamo Therapeutics, Inc. Our principal executive offices are located at 501 Canal Boulevard, Richmond, California 94804. Our telephone number is (510) 970-6000. Our website is www.sangamo.com. Information found on, or accessible through, our website is not a part of, and is not incorporated into, this prospectus supplement or the accompanying prospectus, and you should not consider it part of this prospectus supplement or the accompanying prospectus. Our website address is included in this document as an inactive textual reference only.

Table of Contents

The Offering

Common stock offered by us	shares
Common stock to be outstanding immediately after this offering	shares
Option to purchase additional shares	The underwriters have an option to purchase up to additional shares of our common stock, solely to cover overallocments. The underwriters may exercise this option at any time within 30 days from the date of this prospectus supplement.
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 own and our partnered gene therapy, genome editing, cell therapy and gene regulation product candidates and research programs, our manufacturing facilities and other business development activities. See Use of Proceeds.
Nasdaq Global Select Market Symbol	SGMO
Risk factors	Investing in our common stock involves a high degree of risk. See Risk Factors.
The number of shares of our common stock to be outstanding immediately after this offering as shown above is based on 85,598,534 shares of common stock outstanding as of December 31, 2017 and excludes:	

8,287,456 shares of our common stock issuable upon the exercise of options outstanding as of December 31, 2017, having a weighted-average exercise price of \$7.77 per share;

80,172 shares of our common stock issuable upon the vesting of restricted stock units outstanding as of December 31, 2017;

3,601,633 shares of our common stock reserved for future issuance under our Amended and Restated 2013 Stock Incentive Plan, or the 2013 Plan, as of December 31, 2017; and

835,674 additional shares of our common stock reserved for future issuance under our 2010 Employee Stock Purchase Plan, or the ESPP, as of December 31, 2017.

In addition, the number of shares of our common stock to be outstanding immediately after this offering as shown above excludes the up to \$75.0 million of our common stock that remained available for sale at December 31, 2017 pursuant to an Amended and Restated At-the-Market Offering Program Sales Agreement, or the ATM Agreement, that we entered into with Cowen and Company, LLC, or Cowen, on May 26, 2017. Moreover, our compensation committee has reserved an additional 2,500,000 shares of our common stock for issuance under the ESPP, subject to the receipt of stockholder approval at our 2018 annual meeting of stockholders anticipated to be held on June 11, 2018, or the 2018 annual meeting. At the 2018 annual meeting, we will also be asking our stockholders to approve our 2018 Equity Incentive Plan, or the 2018 Plan, which is intended to be the successor of the 2013 Plan, and which will include a new reserve of 8,800,000 shares of our common stock (in addition to the shares of our common stock that are, or would become, available under our 2013 Plan). The number of shares of our common stock to be outstanding immediately after this offering as shown above does not reflect these additional shares.

S-11

Table of Contents

Except as otherwise indicated, all information in this prospectus supplement assumes no exercise by the underwriters of their option to purchase additional shares.

Gilead Sciences, Inc. has indicated an interest in purchasing up to approximately \$50 million of the shares of common stock offered hereby at the price offered to the public. Because this indication of interest is not a binding agreement or commitment to purchase, this entity may elect not to purchase any shares in this offering, or the underwriters may elect not to sell any shares in this offering to it.

S-12

Table of Contents

RISK FACTORS

Investing 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 and discussed under the section captioned Risk Factors contained in our Current Report on Form 8-K filed with the SEC on April 17, 2018 and in our other filings that are incorporated by reference in this prospectus supplement and the accompanying prospectus in its entirety, together with the other information in this prospectus supplement, the accompanying prospectus, and the 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 occur, our business, financial condition, results of operations or prospects 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.

Risks Relating to this Offering and our Common Stock

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

Our stock price has been volatile and may continue to be volatile, which could cause investors in this offering to incur substantial losses. An active public market for our common stock may not be sustained, and the market price of our common stock may continue to be highly volatile. The market price of our common stock has fluctuated significantly and may continue to be subject to substantial volatility in response to various factors, some of which are beyond our control, including but not limited to the following:

announcements by us or collaborators providing updates on the progress or development status of product candidates;

data from clinical trials;

initiation or termination of clinical trials;

changes in market valuations of similar companies;

overall market and economic conditions, including the equity markets for emerging biotechnology companies;

deviations in our results of operations from the guidance given by us;

announcements by us or our competitors of new or enhanced products, technologies or services or significant contracts, acquisitions, strategic relationships, joint ventures or capital commitments;

announcement of changes in business and operations by our collaborators and partners, or changes in our existing collaboration agreements;

regulatory developments;

changes, by one or more of our security analysts, in recommendations, ratings or coverage of our stock;

additions or departures of key personnel;

future sales of our common stock or other securities by us, management or directors, liquidation of institutional funds that comprised large holdings of our stock; and

decreases in our cash balances.

Actual or potential sales of our common stock by our employees, including our executive officers, pursuant to pre-arranged stock trading plans could cause our stock price to fall or prevent it from increasing for numerous reasons, and actual or potential sales by such persons could be viewed negatively by other investors.

In accordance with the guidelines specified under Rule 10b5-1 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and our policies regarding stock transactions, a number of our employees,

Table of Contents

including executive officers and members of our board of directors, have adopted and may continue to adopt stock trading plans pursuant to which they have arranged to sell shares of our common stock from time to time in the future. Generally, sales under such plans by our executive officers and directors require public filings. Actual or potential sales of our common stock by such persons could cause the price of our common stock to fall or prevent it from increasing for numerous reasons.

If you purchase shares of common stock in this offering, you will experience immediate and substantial dilution in your investment.

Because the price per share of our common stock being offered is substantially higher than the net tangible book value per share of our common stock, you will suffer immediate and substantial dilution with respect to the net tangible book value of the common stock you purchase in this offering. Based on the public offering price of \$ _____ per share and our net tangible book value as of December 31, 2017, if you purchase shares of common stock in this offering, you would suffer immediate and substantial dilution of \$ _____ per share with respect to the net tangible book value of the common stock. See the section entitled "Dilution" for a more detailed discussion of the dilution you will incur if you purchase common stock in this offering.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders, including investors in this offering, and could cause our stock price to fall.

Additional capital will be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, including pursuant to the ATM Agreement, our stockholders, including investors in this offering, may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, our stockholders, including investors who purchase shares of common stock in this offering, will experience additional dilution, and any such issuances may result in downward pressure on the price of our common stock. We also cannot assure you that we will be able to sell shares or other securities in any other offering at a price per share that is equal to or greater than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders.

We will have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

We will have broad discretion in the use of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. Our failure to apply these funds effectively could have a material adverse effect on our business, impair or delay our ability to develop our product candidates, and cause the price of our common stock to decline.

Our stock price is also influenced by public perception of gene therapy and government regulation of potential products.

Reports of serious adverse events in a retroviral gene transfer trial for infants with X-linked severe combined immunodeficiency (X-linked SCID) in France and subsequent FDA actions putting related trials on hold in the United States had a significant negative impact on the public perception and stock price of certain companies involved in gene therapy. Stock prices of these companies declined whether or not the specific company was involved with retroviral gene transfer for the treatment of infants with X-linked SCID, or whether the specific company's clinical trials were placed on hold in connection with these events. Other potential adverse events in the field of gene therapy

may occur in the future that could result in greater governmental regulation of our potential products and potential regulatory delays relating to the testing or approval of our potential products. These external events may have a negative impact on public perception of our business, which could cause our stock price to decline.

S-14

Table of Contents

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our stock price and trading volume could decline.

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. In the event securities or industry analysts who cover us downgrade our stock or publish inaccurate or unfavorable research about our business, our stock price would likely decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.

We have never declared or paid any cash dividends on our common stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders, including investors in this offering, will therefore be limited to the appreciation of their stock.

Anti-takeover provisions in our certificate of incorporation and Delaware law could make an acquisition of our company more difficult and could prevent attempts by our stockholders, including investors in this offering, to remove or replace current management.

Anti-takeover provisions of Delaware law and in our certificate of incorporation and our bylaws may discourage, delay or prevent a change in control of our company, even if a change in control would be beneficial to our stockholders. In addition, these provisions may frustrate or prevent any attempts by our stockholders, including investors in this offering, to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. In particular, under our certificate of incorporation our board of directors may issue up to 5,000,000 shares of preferred stock with rights and privileges that might be senior to our common stock, without the consent of the holders of the common stock. Moreover, without any further vote or action on the part of the stockholders, the board of directors would have the authority to determine the price, rights, preferences, privileges, and restrictions of the preferred stock. This preferred stock, if it is ever issued, may have preference over, and harm the rights of, the holders of common stock. Although the issuance of this preferred stock would provide us with flexibility in connection with possible acquisitions and other corporate purposes, this issuance may make it more difficult for a third party to acquire a majority of our outstanding voting stock.

Similarly, our authorized but unissued common stock is available for future issuance without stockholder approval. Our certificate of incorporation further provides that stockholders may not take action by written consent.

In addition, our amended and restated bylaws, as amended:

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

prohibit stockholders from calling a special meeting of stockholders.

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

our voting stock. The application of Section 203 may, in some circumstances, deter or prevent a change in control of our company even when such change may be beneficial to our stockholders.

S-15

Table of Contents

Our amended and restated bylaws, as amended, provide that the Court of Chancery of the State of Delaware will be the exclusive forum for the adjudication of certain disputes, which could limit the ability of investors in this offering to obtain a favorable judicial forum for disputes with us or our directors, officers, or employees.

Our amended and restated bylaws, as amended, provide that the Court of Chancery of the State of Delaware is the sole and exclusive forum for:

any derivative action or proceeding brought on our behalf;

any action asserting a claim of breach of a fiduciary duty owed by any director, officer or other employee of Sangamo to us or our stockholders;

any action asserting a claim arising pursuant to any provision of the General Corporation Law of the State of Delaware; and

any action asserting a claim governed by the internal affairs doctrine.

This provision further provides that any person or entity that acquires any interest in shares of our capital stock, including investors in this offering, will be deemed to have notice of and consented to the provisions of such provision.

This provision may limit the ability of investors in this offering to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, or other employees, which may discourage lawsuits against us and our directors, officers, and other employees. If a court were to find this provision to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving the dispute in other jurisdictions, which could seriously harm our business.

Table of Contents

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus, the documents incorporated by reference and any free writing prospectus that we have authorized for use in connection with this offering contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Exchange Act. These statements relate to future events or to our future operating or financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. Forward-looking statements may include, but are not limited to, statements about:

our strategy;

anticipated product candidate development and potential commercialization of any resulting products;

the initiation, scope, rate of progress, enrollment, anticipated results and timing of our preclinical studies and clinical trials and those of our collaborators or strategic partners;

the therapeutic and commercial potential of, and the ability of Sangamo and our collaborators or strategic partners to advance the development of, product candidates using our ZFP technology platform, including our ability to effectively deliver our ZFNs and ZFP TFs to produce a beneficial therapeutic effect;

our ability to establish and maintain collaborative, licensing and other similar arrangements;

anticipated revenues from existing and new collaborations and the timing thereof;

our research and development and other expenses;

our ability to obtain adequate preclinical and clinical supplies of our product candidates from current and potential new suppliers and manufacturers;

the ability of Sangamo and our collaborators or strategic partners to obtain and maintain regulatory approvals for product candidates using our ZFP technology platform;

our ability to comply with, and the impact of, regulatory requirements, obligations and restrictions on our business;

our ability to protect our intellectual property and operate our business without infringing upon the intellectual property rights of others, including our ability to obtain rights to the gene transfer technologies required to develop and commercialize our product candidates;

our estimates regarding the sufficiency of our cash resources and our expenses, capital requirements and need for additional financing, and our ability to obtain additional financing;

our ability to manage the growth of our business;

our projected operating and financial performance;

our operational and legal risks;

our intended use of the net proceeds from this offering; and

our plans, objectives, expectations and intentions and any other statements that are not historical facts. In some cases, you can identify forward-looking statements by terms such as anticipates, believes, could, estimates, expects, may, plans, potential, predicts, projects, should, would, will and similar expressions intended to identify forward-looking statements. These statements reflect our current views with respect to future events, are based on assumptions and are subject to risks and uncertainties. Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. We

Table of Contents

discuss many of these risks, uncertainties and other factors in greater detail under the heading **Risk Factors** of this prospectus supplement and under the section captioned **Risk Factors** contained in our Current Report on 8-K filed with the SEC on April 17, 2018 and in our other filings that are incorporated by reference in this prospectus supplement and the accompanying prospectus. Also, these forward-looking statements represent our estimates and assumptions only as of the date of the document containing the applicable statement. Unless required by law, we undertake no obligation to update or revise any forward-looking statements to reflect new information or future events or developments. Thus, you should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-looking statements. You should read carefully this prospectus supplement and the accompanying prospectus, the documents incorporated herein by reference as described under the heading

Incorporation of Certain Information by Reference in this prospectus supplement, and any free writing prospectus that we have authorized for use in connection with this offering completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in the foregoing documents by these cautionary statements.

S-18

Table of Contents

USE OF PROCEEDS

We estimate that the net proceeds we will receive from the sale of the \$200,000,000 of shares of our common stock that we are offering will be approximately \$187.7 million (or approximately \$215.9 million if the underwriters exercise in full their over-allotment option to purchase up to an additional \$30,000,000 of shares of our common stock), after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

Assuming we issue 11,019,284 shares in this offering, a \$1.00 increase (decrease) in the assumed public offering price of \$18.15 per share would increase (decrease) the net proceeds to us from this offering by approximately \$10.4 million, assuming that the number of shares offered by us, as set forth above, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. Similarly, a one million share increase (decrease) in the number of shares offered by us, as set forth above, would increase (decrease) the net proceeds to us by \$17.1 million, assuming the assumed public offering price of \$18.15 per share remains the same, and after deducting the estimated underwriting discounts and commissions and 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 own and our partnered gene therapy, genome editing, cell therapy and gene regulation product candidates and research programs, our manufacturing facilities and other business development activities. In addition, we may use a portion of the net proceeds to acquire drugs or drug candidates, technologies, businesses or other assets, although we have no current plans, commitments or agreements to do so as of the date of this prospectus supplement.

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.

DIVIDEND POLICY

We have not paid dividends on our common stock, and currently do not plan to pay any cash dividends in the foreseeable future.

Table of Contents**DILUTION**

Our net tangible book value as of December 31, 2017 was \$186.3 million, or approximately \$2.18 per share. Net tangible book value is total assets minus the sum of liabilities and intangible assets. Net tangible book value per share is net tangible book value divided by the total number of shares of common stock outstanding as of December 31, 2017.

Dilution in net tangible book value per share represents the difference between the amount per share paid by purchasers of shares of common stock in this public offering and the net tangible book value per share of our common stock immediately after completion of this public offering. After giving effect to the sale of _____ shares of our common stock in this offering at the public offering price of \$ _____ per share, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of December 31, 2017 would have been approximately \$ _____ million, or \$ _____ per share. This represents an immediate increase in net tangible book value of \$ _____ per share to existing stockholders and immediate dilution in net tangible book value of \$ _____ per share to investors purchasing our common stock in this offering at the public offering price. The following table illustrates this dilution on a per share basis:

Public offering price per share	\$
Net tangible book value per share as of December 31, 2017	\$ 2.18
Increase in net tangible book value per share attributable to this offering	

As adjusted net tangible book value per share as of December 31, 2017 after giving effect to this offering

Dilution per share to investors purchasing our common stock in this offering	\$
--	----

If the underwriters exercise in full their option to purchase _____ additional shares of common stock at the public offering price of \$ _____ per share, the as adjusted net tangible book value after this offering would be \$ _____ per share, representing an increase in net tangible book value of \$ _____ per share to existing stockholders and immediate dilution in net tangible book value of \$ _____ per share to investors purchasing our common stock in this offering at the public offering price.

The above discussion and table are based on 85,598,534 shares of common stock issued and outstanding as of December 31, 2017 and exclude:

8,287,456 shares of our common stock issuable upon the exercise of options outstanding as of December 31, 2017, having a weighted-average exercise price of \$7.77 per share;

80,172 shares of our common stock issuable upon the vesting of restricted stock units outstanding as of December 31, 2017;

3,601,633 shares of our common stock reserved for future issuance under the 2013 Plan as of December 31, 2017; and

835,674 additional shares of our common stock reserved for future issuance under the ESPP as of December 31, 2017.

In addition, the above discussion and table exclude the up to \$75.0 million of our common stock that remained available for sale at December 31, 2017 pursuant to the ATM Agreement with Cowen. Moreover, our compensation committee has reserved an additional 2,500,000 shares of our common stock for issuance under the ESPP, subject to the receipt of stockholder approval at the 2018 annual meeting. At the 2018 annual meeting, we will also be asking our stockholders to approve our 2018 Plan, which is intended to be the successor of the 2013 Plan, and which will include a new reserve of 8,800,000 shares of our common stock (in addition to the shares of

Table of Contents

our common stock that are, or would become, available under our 2013 Plan). The above discussion and table do not reflect these additional shares.

To the extent that outstanding options are exercised or restricted stock unit awards vest, you will experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations, including pursuant to the ATM Agreement, even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of our common stock, or securities convertible into or exchangeable or exercisable for common stock, the issuance of these securities could result in further dilution to investors in this offering.

S-21

Table of Contents**PRICE RANGE OF COMMON STOCK**

Our common stock is traded on The Nasdaq Global Select Market under the symbol SGMO. The following table sets forth, for the periods indicated, the reported high and low intraday sales prices per share of our common stock as reported on The Nasdaq Global Select Market:

	High	Low
2016		
First Quarter	\$ 9.22	\$ 4.63
Second Quarter	7.60	5.06
Third Quarter	6.91	4.08
Fourth Quarter	4.87	2.65
2017		
First Quarter	\$ 4.87	\$ 2.65
Second Quarter	9.65	4.05
Third Quarter	15.30	8.00
Fourth Quarter	18.40	11.30
2018		
First Quarter	\$ 27.50	\$ 16.30
Second Quarter (through April 23, 2018)	20.55	16.35

The last reported sale price of our common stock on The Nasdaq Global Select Market on April 23, 2018 was \$18.15 per share.

Table of Contents

MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES FOR NON-U.S. HOLDERS OF COMMON STOCK

The following summary describes the material U.S. federal income tax consequences of the acquisition, ownership and disposition of our common stock acquired in this offering by Non-U.S. Holders (as defined below). This discussion is not a complete analysis of all potential U.S. federal income tax consequences relating thereto, and does not deal with foreign, state and local consequences that may be relevant to Non-U.S. Holders in light of their particular circumstances, nor does it address U.S. federal tax consequences (such as gift and estate taxes) other than income taxes. Special rules different from those described below may apply to certain Non-U.S. Holders that are subject to special treatment under the Internal Revenue Code of 1986, as amended (or the Code), such as financial institutions, insurance companies, tax-exempt organizations, broker-dealers and traders in securities, U.S. expatriates, controlled foreign corporations, passive foreign investment companies, corporations that accumulate earnings to avoid U.S. federal income tax, corporations organized outside of the United States, any state thereof or the District of Columbia that are nonetheless treated as United States income taxpayers for United States federal tax purposes, persons that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or integrated investment or other risk reduction strategy, persons who acquire our common stock through the exercise of an option or otherwise as compensation, accrual-method taxpayers subject to special tax accounting rules under Section 451(b) of the Code, persons subject to the alternative minimum tax or federal Medicare contribution tax on net investment income, partnerships and other pass-through entities or arrangements, and investors in such pass-through entities or arrangements. Such Non-U.S. Holders are urged to consult their own tax advisors to determine the U.S. federal, state, local and other tax consequences that may be relevant to them. Furthermore, the discussion below is based upon the provisions of the Code, and U.S. Treasury regulations, rulings and judicial decisions thereunder as of the date hereof, and such authorities may be repealed, revoked or modified, perhaps retroactively, so as to result in U.S. federal income tax consequences different from those discussed below. We have not requested a ruling from the U.S. Internal Revenue Service, or IRS, with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS will agree with such statements and conclusions. This discussion assumes that the Non-U.S. Holder holds our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, property held for investment).

Persons considering the purchase of our common stock pursuant to this offering should consult their own tax advisors concerning the U.S. federal income, estate and other tax consequences of acquiring, owning and disposing of our common stock in light of their particular situations as well as any consequences arising under the laws of any other taxing jurisdiction, including any state, local or foreign tax consequences.

For the purposes of this discussion, a Non-U.S. Holder is, for U.S. federal income tax purposes, a beneficial owner of common stock that is neither a U.S. Holder, nor a partnership (or other entity treated as a partnership for U.S. federal income tax purposes regardless of its place of organization or formation). A U.S. Holder means a beneficial owner of our common stock that is for U.S. federal income tax purposes any of the following:

an individual who is a citizen or resident of the United States;

a corporation or other entity treated as a corporation for U.S. federal income tax purposes created or organized in or under the laws of the U.S., any state thereof or the District of Columbia;

an estate the income of which is subject to U.S. federal income taxation regardless of its source; or

a trust if it (1) is subject to the primary supervision of a court within the U.S. and one or more U.S. persons have the authority to control all substantial decisions of the trust or (2) has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person.

S-23

Table of Contents**Distributions**

Distributions, if any, made on our common stock to a Non-U.S. Holder to the extent made out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles) generally will constitute dividends for U.S. tax purposes and will be subject to withholding tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty, subject to the discussion below regarding foreign accounts. To obtain a reduced rate of withholding under a treaty, a Non-U.S. Holder generally will be required to provide us with a properly executed IRS Form W-8BEN (in the case of individuals) or IRS Form W-8BEN-E (in the case of entities), or other appropriate form, including a U.S. taxpayer identification number, or in certain circumstances, a foreign tax identifying number, and certifying the Non-U.S. Holder's entitlement to benefits under that treaty. This certification must be provided to us or our paying agent prior to the payment of dividends and must be updated periodically. In the case of a Non-U.S. Holder that is an entity, U.S. Treasury regulations and the relevant tax treaty provide rules to determine whether, for purposes of determining the applicability of a tax treaty, dividends will be treated as paid to the entity or to those holding an interest in that entity. If a Non-U.S. Holder holds stock through a financial institution or other agent acting on the holder's behalf, the holder will be required to provide appropriate documentation to such agent. The holder's agent will then be required to provide certification to us or our paying agent, either directly or through other intermediaries. If you are eligible for a reduced rate of U.S. federal withholding tax under an income tax treaty and you do not timely file the required certification, you may be able to obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim for a refund with the IRS.

We generally are not required to withhold tax on dividends paid to a Non-U.S. Holder that are effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, are attributable to a permanent establishment that such holder maintains in the United States) if a properly executed IRS Form W-8ECI, stating that the dividends are so connected, is furnished to us (or, if stock is held through a financial institution or other agent, to such agent). In general, such effectively connected dividends will be subject to U.S. federal income tax, on a net income basis at the regular graduated rates applicable to U.S. residents. A corporate Non-U.S. Holder receiving effectively connected dividends may also be subject to an additional branch profits tax, which is imposed, under certain circumstances, at a rate of 30% (or such lower rate as may be specified by an applicable treaty) on the corporate Non-U.S. Holder's effectively connected earnings and profits, subject to certain adjustments. Non-U.S. Holders should consult their tax advisors regarding any applicable income tax treaties that may provide for different rules.

To the extent distributions on our common stock, if any, exceed our current and accumulated earnings and profits, they will first reduce the Non-U.S. Holder's adjusted basis in our common stock, but not below zero, and then will be treated as gain to the extent of any excess, and taxed in the same manner as gain realized from a sale or other disposition of common stock as described in the next section.

Gain on Disposition of Our Common Stock

Subject to the discussion below regarding backup withholding and foreign accounts, a Non-U.S. Holder generally will not be subject to U.S. federal income tax with respect to gain realized on a sale or other disposition of our common stock unless (a) the gain is effectively connected with a trade or business of such holder in the United States (and, if required by an applicable income tax treaty, is attributable to a permanent establishment that such holder maintains in the United States), (b) the Non-U.S. Holder is a nonresident alien individual and is present in the United States for 183 or more days in the taxable year of the disposition and certain other conditions are met or (c) we are or have been a United States real property holding corporation within the meaning of Code Section 897(c)(2) at any time within the shorter of the five-year period preceding such disposition or such holder's holding period. In general, we would be a U.S. real property holding corporation if interests in U.S. real estate comprise (by fair market value) at least half of

our business assets. We believe that we have not been and we are not, and do not anticipate becoming, a U.S. real property holding corporation. Even if we are treated as a U.S. real property holding corporation, gain realized by a Non-U.S. Holder on a disposition

S-24

Table of Contents

of our common stock will not be subject to U.S. federal income tax so long as (1) the Non-U.S. Holder owned, directly, indirectly and constructively, no more than five percent of our common stock at all times within the shorter of (i) the five-year period preceding the disposition or (ii) the holder's holding period and (2) our common stock is regularly traded on an established securities market. There can be no assurance that our common stock will continue to qualify as regularly traded on an established securities market. If any gain on your disposition is taxable because we are a United States real property holding corporation and your ownership of our common stock exceeds 5%, you will be taxed on such disposition generally in the manner applicable to U.S. persons.

If you are a Non-U.S. Holder described in (a) above, you will be required to pay tax on the net gain derived from the sale at regular graduated U.S. federal income tax rates, and corporate Non-U.S. Holders described in (a) above may be subject to the additional branch profits tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. Gain described in (b) above will be subject to U.S. federal income tax at a flat 30% rate or such lower rate as may be specified by an applicable income tax treaty, which gain may be offset by certain U.S.-source capital losses (even though you are not considered a resident of the U.S.), provided that the Non-U.S. Holder has timely filed U.S. federal income tax returns with respect to such losses.

Information Reporting Requirements and Backup Withholding

Generally, we must report information to the IRS with respect to any dividends we pay on our common stock (even if the payments are exempt from withholding), including the amount of any such dividends, the name and address of the recipient, and the amount, if any, of tax withheld. A similar report is sent to the holder to whom any such dividends are paid. Pursuant to tax treaties or certain other agreements, the IRS may make its reports available to tax authorities in the recipient's country of residence.

Dividends paid by us (or our paying agents) to a Non-U.S. Holder may also be subject to U.S. backup withholding. U.S. backup withholding generally will not apply to a Non-U.S. Holder who provides a properly executed IRS Form W-8BEN, IRS Form W-8BEN-E, or IRS Form W-ECI, or otherwise establishes an exemption. Notwithstanding the foregoing, backup withholding may apply if the payor has actual knowledge, or reason to know, that the holder is a U.S. person who is not an exempt recipient.

U.S. information reporting and backup withholding requirements generally will apply to the proceeds of a disposition of our common stock effected by or through a U.S. office of any broker, U.S. or foreign, except that information reporting and such requirements may be avoided if the holder provides a properly executed IRS Form W-8BEN or IRS Form W-8BEN-E or otherwise meets documentary evidence requirements for establishing non-U.S. person status or otherwise establishes an exemption. Generally, U.S. information reporting and backup withholding requirements will not apply to a payment of disposition proceeds to a Non-U.S. Holder where the transaction is effected outside the U.S. through a non-U.S. office of a non-U.S. broker. Information reporting and backup withholding requirements may, however, apply to a payment of disposition proceeds if the broker has actual knowledge, or reason to know, that the holder is, in fact, a U.S. person. For information reporting purposes, certain brokers with substantial U.S. ownership or operations will generally be treated in a manner similar to U.S. brokers.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be credited against the tax liability of persons subject to backup withholding, provided that the required information is timely furnished to the IRS.

Foreign Accounts

Sections 1471 through 1474 of the Code (commonly referred to as FATCA) impose a U.S. federal withholding tax of 30% on certain payments, including dividends paid on and the gross proceeds of a disposition of our common stock paid to a foreign financial institution (as specifically defined by applicable rules) unless

S-25

Table of Contents

such institution enters into an agreement with the U.S. government to withhold on certain payments and to collect and provide to the U.S. tax authorities substantial information regarding U.S. account holders of such institution (which includes certain equity holders of such institution, as well as certain account holders that are foreign entities with U.S. owners). FATCA also generally imposes a federal withholding tax of 30% on certain payments, including dividends paid on and the gross proceeds of a disposition of our common stock to a non-financial foreign entity unless such entity provides the withholding agent with either a certification that it does not have any substantial direct or indirect U.S. owners or provides information regarding substantial direct and indirect U.S. owners of the entity. An intergovernmental agreement between the United States and an applicable foreign country may modify those requirements. The withholding tax described above will not apply if the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from the rules. Holders are encouraged to consult with their own tax advisors regarding the possible implications of FATCA on their investment in our common stock.

The withholding provisions described above currently apply to payments of dividends, and will apply to payments of gross proceeds from a sale or other disposition of common stock on or after January 1, 2019.

EACH PROSPECTIVE INVESTOR SHOULD CONSULT ITS OWN TAX ADVISOR REGARDING THE TAX CONSEQUENCES OF PURCHASING, HOLDING AND DISPOSING OF OUR COMMON STOCK, INCLUDING THE CONSEQUENCES OF ANY PROPOSED OR RECENT CHANGE IN APPLICABLE LAW.

Table of Contents**UNDERWRITING**

Merrill Lynch, Pierce, Fenner & Smith Incorporated, J.P. Morgan Securities LLC and Cowen and Company, LLC are acting as representatives of each of the underwriters named below. Subject to the terms and conditions set forth in an underwriting agreement among us and the underwriters, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the number of shares of common stock set forth opposite its name below.

<u>Underwriter</u>	Number of Shares
Merrill Lynch, Pierce, Fenner & Smith Incorporated	
J.P. Morgan Securities LLC	
Cowen and Company, LLC	
Total	

Subject to the terms and conditions set forth in the underwriting agreement, the underwriters have agreed, severally and not jointly, to purchase all of the shares sold under the underwriting agreement if any of these shares are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the nondefaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make in respect of those liabilities.

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the shares, and other conditions contained in the underwriting agreement, such as the receipt by the underwriters of officer's certificates and legal opinions. Sales of shares made outside of the United States may be made by affiliates of the underwriters. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commissions and Discounts

The representatives have advised us that the underwriters propose initially to offer the shares to the public at the public offering price set forth on the cover page of this prospectus and to dealers at that price less a concession not in excess of \$ _____ per share. After the initial offering, the public offering price, concession or any other term of the offering may be changed.

The following table shows the public offering price, underwriting discount and proceeds before expenses to us. The information assumes either no exercise or full exercise by the underwriters of their option to purchase additional shares.

Per Share	Without Option	With Option
------------------	-----------------------	--------------------

Public offering price	\$	\$	\$
Underwriting discount	\$	\$	\$
Proceeds, before expenses, to Sangamo	\$	\$	\$

The expenses of the offering, not including the underwriting discount, are estimated at \$295,000 and are payable by us.

Option to Purchase Additional Shares

We have granted an option to the underwriters, exercisable for 30 days after the date of this prospectus, to purchase up to additional shares at the public offering price, less the underwriting discount,

S-27

Table of Contents

solely to cover overallotments. If the underwriters exercise this option, each will be obligated, subject to conditions contained in the underwriting agreement, to purchase a number of additional shares proportionate to that underwriter's initial amount reflected in the above table.

No Sales of Similar Securities

We have agreed not to sell or transfer any common stock or securities convertible into, exchangeable for, exercisable for, or repayable with common stock, for 90 days after the date of this prospectus without first obtaining the written consent of the Representatives. Our executive officers and directors have agreed not to sell or transfer any common stock or securities convertible into, exchangeable for, exercisable for, or repayable with common stock, for 45 days after the date of this prospectus without first obtaining the written consent of the Representatives. Specifically, we and these other persons have agreed, with certain limited exceptions, not to directly or indirectly:

offer, pledge, sell or contract to sell any common stock,

sell any option or contract to purchase any common stock,

purchase any option or contract to sell any common stock,

grant any option, right or warrant for the sale of any common stock,

lend or otherwise dispose of or transfer any common stock,

request or demand that we file a registration statement related to the common stock, or

enter into any swap or other agreement that transfers, in whole or in part, the economic consequence of ownership of any common stock whether any such swap or transaction is to be settled by delivery of shares or other securities, in cash or otherwise.

This lock-up provision applies to common stock and to securities convertible into or exchangeable or exercisable for or repayable with common stock. It also applies to common stock owned now or acquired later by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition.

Nasdaq Global Select Market Listing

The shares are listed on the Nasdaq Global Select Market under the symbol SGMO.

Price Stabilization, Short Positions

Until the distribution of the shares is completed, SEC rules may limit underwriters and selling group members from bidding for and purchasing our common stock. However, the representatives may engage in transactions that stabilize

the price of the common stock, such as bids or purchases to peg, fix or maintain that price.

In connection with the offering, the underwriters may purchase and sell our common stock in the open market. These transactions may include short sales, purchases on the open market to cover positions created by short sales and stabilizing transactions. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering. Covered short sales are sales made in an amount not greater than the underwriters option to purchase additional shares described above. The underwriters may close out any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option granted to them. Naked short sales are sales in

Table of Contents

excess of such option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of our common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of shares of common stock made by the underwriters in the open market prior to the completion of the offering.

Similar to other purchase transactions, the underwriters' purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. The underwriters may conduct these transactions on the Nasdaq Global Select Market, in the over-the-counter market or otherwise.

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

Passive Market Making

In connection with this offering, underwriters and selling group members may engage in passive market making transactions in the common stock on the Nasdaq Global Market in accordance with Rule 103 of Regulation M under the Exchange Act during a period before the commencement of offers or sales of common stock and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, that bid must then be lowered when specified purchase limits are exceeded. Passive market making may cause the price of our common stock to be higher than the price that otherwise would exist in the open market in the absence of those transactions. The underwriters and dealers are not required to engage in passive market making and may end passive market making activities at any time.

Electronic Distribution

In connection with the offering, certain of the underwriters or securities dealers may distribute prospectuses by electronic means, such as e-mail.

Other Relationships

Some of the underwriters and their affiliates have engaged in, and may in the future engage in, investment banking and other commercial dealings in the ordinary course of business with us or our affiliates. They have received, or may in the future receive, customary fees and commissions for these transactions. Cowen is the sales agent under our ATM Agreement.

In addition, in the ordinary course of their business activities, the underwriters and their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

S-29

Table of Contents

European Economic Area

In relation to each member state of the European Economic Area, no offer of shares which are the subject of the offering has been, or will be made to the public in that Member State, other than under the following exemptions under the Prospectus Directive:

- (a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;
- (b) to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), subject to obtaining the prior consent of the Representatives for any such offer; or
- (c) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of shares referred to in (a) to (c) above shall result in a requirement for the Company or any Representative to publish a prospectus pursuant to Article 3 of the Prospectus Directive, or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

Each person located in a Member State to whom any offer of shares is made or who receives any communication in respect of an offer of shares, or who initially acquires any shares will be deemed to have represented, warranted, acknowledged and agreed to and with each Representative and the Company that (1) it is a qualified investor within the meaning of the law in that Member State implementing Article 2(1)(e) of the Prospectus Directive; and (2) in the case of any shares acquired by it as a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, the shares acquired by it in the offer have not been acquired on behalf of, nor have they been acquired with a view to their offer or resale to, persons in any Member State other than qualified investors, as that term is defined in the Prospectus Directive, or in circumstances in which the prior consent of the Representatives has been given to the offer or resale; or where shares have been acquired by it on behalf of persons in any Member State other than qualified investors, the offer of those shares to it is not treated under the Prospectus Directive as having been made to such persons.

The Company, the Representatives and their respective affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgments and agreements.

This prospectus has been prepared on the basis that any offer of shares in any Member State will be made pursuant to an exemption under the Prospectus Directive from the requirement to publish a prospectus for offers of shares. Accordingly any person making or intending to make an offer in that Member State of shares which are the subject of the offering contemplated in this prospectus may only do so in circumstances in which no obligation arises for the Company or any of the Representatives to publish a prospectus pursuant to Article 3 of the Prospectus Directive in relation to such offer. Neither the Company nor the Representatives have authorized, nor do they authorize, the making of any offer of shares in circumstances in which an obligation arises for the Company or the Representatives to publish a prospectus for such offer.

For the purposes of this provision, the expression an offer of shares to the public in relation to any ordinary shares in any Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the ordinary shares to be offered so as to enable an investor to decide to purchase or subscribe the ordinary shares, as the same may be varied in that Member State by any measure implementing the Prospectus

Directive in that Member State, the expression Prospectus Directive means Directive 2003/71/EC (as amended) and includes any relevant implementing measure in each Member State.

The above selling restriction is in addition to any other selling restrictions set out below.

Notice to Prospective Investors in the United Kingdom

In addition, in the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are qualified investors (as defined in the

S-30

Table of Contents

Prospectus Directive) (i) who have professional experience in matters relating to investments falling within Article 19 (5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the Order) and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as relevant persons). This document must not be acted on or relied on in the United Kingdom by persons who are not relevant persons. In the United Kingdom, any investment or investment activity to which this document relates is only available to, and will be engaged in with, relevant persons.

Notice to Prospective Investors in Switzerland

The shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange (SIX) or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the shares or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, the Company, the shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA (FINMA), and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes (CISA). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares.

Notice to Prospective Investors in the Dubai International Financial Centre

This prospectus supplement relates to an Exempt Offer in accordance with the Offered Securities Rules of the Dubai Financial Services Authority (DFSA). This prospectus supplement is intended for distribution only to persons of a type specified in the Offered Securities Rules of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus supplement nor taken steps to verify the information set forth herein and has no responsibility for the prospectus supplement. The shares to which this prospectus supplement relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the shares offered should conduct their own due diligence on the shares. If you do not understand the contents of this prospectus supplement you should consult an authorized financial advisor.

Notice to Prospective Investors in Australia

No placement document, prospectus, product disclosure statement or other disclosure document has been lodged with the Australian Securities and Investments Commission (ASIC), in relation to the offering. This prospectus does not constitute a prospectus, product disclosure statement or other disclosure document under the Corporations Act 2001 (the Corporations Act), and does not purport to include the information required for a prospectus, product disclosure statement or other disclosure document under the Corporations Act.

Any offer in Australia of the shares may only be made to persons (the Exempt Investors) who are sophisticated investors (within the meaning of section 708(8) of the Corporations Act), professional investors (within the meaning of section 708(11) of the Corporations Act) or otherwise pursuant to one or more exemptions contained in section 708

of the Corporations Act so that it is lawful to offer the shares without disclosure to investors under Chapter 6D of the Corporations Act.

The shares applied for by Exempt Investors in Australia must not be offered for sale in Australia in the period of 12 months after the date of allotment under the offering, except in circumstances where disclosure to investors under Chapter 6D of the Corporations Act would not be required pursuant to an exemption under

S-31

Table of Contents

section 708 of the Corporations Act or otherwise or where the offer is pursuant to a disclosure document which complies with Chapter 6D of the Corporations Act. Any person acquiring shares must observe such Australian on-sale restrictions.

This prospectus contains general information only and does not take account of the investment objectives, financial situation or particular needs of any particular person. It does not contain any securities recommendations or financial product advice. Before making an investment decision, investors need to consider whether the information in this prospectus is appropriate to their needs, objectives and circumstances, and, if necessary, seek expert advice on those matters.

Notice to Prospective Investors in Hong Kong

The securities have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to professional investors as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or (b) in other circumstances which do not result in the document being a prospectus as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance. No advertisement, invitation or document relating to the securities has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to professional investors as defined in the Securities and Futures Ordinance and any rules made under that Ordinance.

Notice to Prospective Investors in Japan

The securities have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948, as amended) and, accordingly, will not be offered or sold, directly or indirectly, in Japan, or for the benefit of any Japanese Person or to others for re-offering or resale, directly or indirectly, in Japan or to any Japanese Person, except in compliance with all applicable laws, regulations and ministerial guidelines promulgated by relevant Japanese governmental or regulatory authorities in effect at the relevant time. For the purposes of this paragraph, Japanese Person shall mean any person resident in Japan, including any corporation or other entity organized under the laws of Japan.

Notice to Prospective Investors in Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of Non-CIS Securities may not be circulated or distributed, nor may the Non-CIS Securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the SFA), (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275, of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the Non-CIS Securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- (a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

S-32

Table of Contents

securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the Non-CIS Securities pursuant to an offer made under Section 275 of the SFA except:

- (a) to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;
- (b) where no consideration is or will be given for the transfer;
- (c) where the transfer is by operation of law;
- (d) as specified in Section 276(7) of the SFA; or
- (e) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

Notice to Prospective Investors in Canada

The securities may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 *Prospectus Exemptions* or subsection 73.3(1) of the *Securities Act* (Ontario), and are permitted clients, as defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*. Any resale of the securities must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus supplement (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 (or, in the case of securities issued or guaranteed by the government of a non-Canadian jurisdiction, section 3A.4) of National Instrument 33-105 *Underwriting Conflicts* (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Table of Contents

LEGAL MATTERS

The validity of the shares of common stock offered by this prospectus supplement and the accompanying prospectus will be passed upon for us by Cooley LLP, San Francisco, California. Proskauer Rose LLP, New York, New York, is counsel for the underwriters in connection with this offering.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2017, and the effectiveness of our internal control over financial reporting as of December 31, 2017, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus supplement and the accompanying prospectus are part of the registration statement on Form S-3 we filed with the SEC under the Securities Act and do not contain all the information set forth or incorporated by reference in the registration statement. Whenever a reference is made in this prospectus supplement or the accompanying prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference into this prospectus supplement and the accompanying prospectus for a copy of such contract, agreement or other document. Because we are subject to the information and reporting requirements of the Exchange Act, we file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at <http://www.sec.gov>. You may also read and copy any document we file at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference information from other documents that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus supplement and the accompanying prospectus. Information in this prospectus supplement supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus supplement, while information that we file later with the SEC will automatically update and supersede the information in this prospectus supplement and the accompanying prospectus. We incorporate by reference the documents listed below and any future filings (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items) we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus supplement and prior to the termination of the offering of the common stock covered by this prospectus supplement (Commission File No. 000-30171):

our annual report on Form 10-K for the year ended December 31, 2017, which was filed with the SEC on March 1, 2018, as amended by Form 10-K/A, which was filed with the SEC on April 24, 2018;

the information specifically incorporated by reference into our annual report on Form 10-K for the year ended December 31, 2017 from our revised definitive proxy statement relating to our 2018 annual meeting of stockholders, which was filed with the SEC on April 24, 2018;

S-34

Table of Contents

our current reports on Form 8-K which were filed with the SEC on January 3, 2018, February 22, 2018 (except for the information furnished under Item 2.02 thereof and the accompanying exhibit 99.1), March 23, 2018 and April 17, 2018; and

the description of our common stock in our registration statement on Form 8-A, which was filed with the SEC on March 31, 2000, including all amendments and reports filed for the purpose of updating such description.

We will furnish without charge to each person, including any beneficial owner, to whom a prospectus is delivered, upon written or oral request, a copy of any or all of the documents incorporated by reference, including exhibits to these documents. Any such request may be made by writing or telephoning us at the following address or phone number:

Sangamo Therapeutics, Inc.

501 Canal Boulevard

Richmond, California 94804

(510) 970-6000

Attention: Investor Relations

S-35

Table of Contents

Prospectus

Common Stock

Preferred Stock

Debt Securities

Warrants

From time to time, we or selling securityholders may offer and sell any combination of the securities described in this prospectus, either individually or in combination with other securities. We or selling securityholders may also offer common stock or preferred stock upon conversion of debt securities, common stock upon conversion of preferred stock, or common stock, preferred stock or debt securities upon the exercise of warrants.

Each time we sell securities pursuant to this prospectus, we will provide the specific terms of these offerings and securities in one or more supplements to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus may also add, update or change information contained in this prospectus. You should carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as the documents incorporated by reference, before buying any of the securities being offered.

Our common stock is listed on The Nasdaq Global Select Market under the trading symbol SGMO. On April 23, 2018, the last reported sale price of our common stock was \$18.15 per share. The applicable prospectus supplement will contain information, where applicable, as to other listings, if any, on The Nasdaq Global Select Market or other securities exchange of the securities covered by the applicable prospectus supplement.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading Risk Factors contained in the applicable prospectus supplement and in any free writing prospectuses we have authorized for use in connection with a specific offering, and under similar headings in the documents that are incorporated by reference into this prospectus.

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

The securities may be sold directly to investors, through agents designated from time to time or to or through underwriters or dealers, on a continuous or delayed basis. For additional information on the methods of sale, you should refer to the section entitled Plan of Distribution in this prospectus. If any agents, underwriters or dealers are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such agents, underwriters or dealers and any applicable fees, commissions, discounts and over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive

from such sale will also be set forth in a prospectus supplement. Unless the applicable prospectus supplement provides otherwise, we will not receive any proceeds from the sale of securities by selling securityholders.

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 April 24, 2018.

Table of Contents

TABLE OF CONTENTS

<u>ABOUT THIS PROSPECTUS</u>	ii
<u>PROSPECTUS SUMMARY</u>	1
<u>RISK FACTORS</u>	5
<u>FORWARD-LOOKING STATEMENTS</u>	5
<u>FINANCIAL RATIOS</u>	7
<u>USE OF PROCEEDS</u>	8
<u>DESCRIPTION OF CAPITAL STOCK</u>	9
<u>DESCRIPTION OF DEBT SECURITIES</u>	13
<u>DESCRIPTION OF WARRANTS</u>	20
<u>LEGAL OWNERSHIP OF SECURITIES</u>	22
<u>SELLING SECURITYHOLDERS</u>	26
<u>PLAN OF DISTRIBUTION</u>	27
<u>LEGAL MATTERS</u>	29
<u>EXPERTS</u>	29
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	29
<u>INCORPORATION OF CERTAIN INFORMATION BY REFERENCE</u>	29

Table of Contents

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or SEC, utilizing a shelf registration process. Under this shelf registration process, we or selling securityholders may offer and sell shares of our common stock and preferred stock, various series of debt securities and/or warrants to purchase any of such securities, either individually or in combination with other securities, in one or more offerings. There is no limit on the aggregate amount of the securities that we or selling securityholders may offer pursuant to the registration statement of which this prospectus is a part. This prospectus provides you with a general description of the securities we or selling securityholders may offer.

Each time we or selling securityholders offer securities under this prospectus, we will provide a prospectus supplement that will contain more specific information about the terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change any of the information contained in this prospectus or in the documents that we have incorporated by reference into this prospectus. We urge you to read carefully this prospectus, any applicable prospectus supplement and any free writing prospectuses we have authorized for use in connection with a specific offering, together with the information incorporated herein by reference as described under the heading Incorporation of Certain Information by Reference, before buying any of the securities being offered.

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

You should rely only on the information contained in, or incorporated by reference into, this prospectus and the applicable prospectus supplement, along with the information contained in any free writing prospectuses we have authorized for use in connection with a specific offering. We have not authorized anyone to provide you with different or additional information. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so.

The information appearing in this prospectus, any applicable prospectus supplement and any related free writing prospectus is accurate only as of the date on the front of the document and any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus, the applicable prospectus supplement or any related free writing prospectus, or any sale of a security. Our business, financial condition, results of operations and prospects may have changed since those dates.

This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under the section entitled Where You Can Find More Information.

Unless the context indicates otherwise, as used in this prospectus, the terms Sangamo, we, us and our refer to Sangamo Therapeutics, Inc., a Delaware corporation, and its subsidiaries on a consolidated basis. SANGAMO®, SANGAMO THERAPEUTICS®, Better Therapeutics By Design®, ZFP Therapeutic®, Engineering Genetic Cures®, and Pioneering Genetic Cures® are our registered trademarks in the United States. All other trademarks or trade names referred to in this prospectus and any prospectus supplement are the property of their respective owners.

Table of Contents

PROSPECTUS SUMMARY

This summary highlights selected information contained elsewhere in this prospectus or incorporated by reference in this prospectus, and does not contain all of the information that you need to consider in making your investment decision. You should carefully read the entire prospectus, the applicable prospectus supplement and any related free writing prospectus, including the risks of investing in our securities discussed under the heading Risk Factors contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus. You should also carefully read the information incorporated by reference into this prospectus, including our financial statements, and the exhibits to the registration statement of which this prospectus is a part.

Sangamo Therapeutics, Inc.

We are a clinical stage biotechnology company focused on translating ground-breaking science into genomic therapies that transform patients' lives using our industry-leading platform technologies in genome editing, gene therapy, gene regulation and cell therapy.

We are a leader in the research and development of zinc finger proteins, or ZFPs, a naturally occurring class of proteins found in humans. We have used our knowledge and expertise to develop a proprietary technology platform in both genome editing and gene regulation. ZFPs can be engineered to make zinc finger nucleases, or ZFNs, proteins that can be used to specifically modify DNA sequences by adding or knocking out specific genes, or genome editing, and ZFP transcription factors or ZFP TFs, proteins that can be used to increase or decrease gene expression, or gene regulation. In the process of developing this platform, we have accrued significant scientific, manufacturing and regulatory capabilities and know-how that are generally applicable in the broader field of gene therapy and have capitalized this knowledge into a conventional gene therapy platform based on adeno-associated viral vector cDNA gene transfer.

We were incorporated in June 1995 in the state of Delaware and in January 2017, we changed our name from Sangamo BioSciences, Inc. to Sangamo Therapeutics, Inc. Our website is www.sangamo.com. Information found on, or accessible through, our website is not a part of, and is not incorporated into, this prospectus, and you should not consider it part of this prospectus or part of any prospectus supplement. Our website address is included in this prospectus as an inactive textual reference only.

Description of Securities

We or selling securityholders may offer shares of our common stock and preferred stock, various series of debt securities and/or warrants to purchase any of such securities, either individually or in combination with other securities, from time to time under this prospectus, together with the applicable prospectus supplement and any related free writing prospectus, at prices and on terms to be determined by market conditions at the time of any offering. This prospectus provides you with a general description of the securities we or selling securityholders may offer. Each time we or selling securityholders offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

designation or classification;

aggregate principal amount or aggregate offering price;

maturity date, if applicable;

original issue discount, if any;

rates and times of payment of interest or dividends, if any;

Table of Contents

redemption, conversion, exercise, exchange or sinking fund terms, if any;

ranking;

restrictive covenants, if any;

voting or other rights, if any;

conversion or exchange prices or rates, if any, and, if applicable, any provisions for changes to or adjustments in the conversion or exchange prices or rates and in the securities or other property receivable upon conversion or exchange; and

material or special U.S. federal income tax considerations, if any.

The applicable prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change any of the information contained in this prospectus or in the documents we have incorporated by reference.

We or selling securityholders may sell the securities directly to investors or to or through agents, underwriters or dealers. If we or selling securityholders do offer securities to or through agents or underwriters, we will include in the applicable prospectus supplement:

the names of those agents or underwriters;

applicable fees, discounts and commissions to be paid to them;

details regarding over-allotment or other options, if any; and

the net proceeds to us, if any.

Common Stock. We may issue shares of our common stock from time to time. The holders of common stock are entitled to one vote per share on all matters to be voted on by the stockholders. Subject to the preferences of any outstanding shares of preferred stock, the holders of common stock are entitled to receive ratably any dividends our board of directors declares out of funds legally available for the payment of dividends. If we are liquidated, dissolved or wound up, the holders of common stock are entitled to share pro rata all assets remaining after payment of liabilities and liquidation preferences of any outstanding shares of preferred stock. Holders of common stock have no preemptive rights or rights to convert their common stock into any other securities. There are no redemption or sinking fund provisions applicable to the common stock. In this prospectus, we have summarized certain general features of the common stock under the heading *Description of Capital Stock Common Stock*. We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be

provided to you) related to any common stock being offered.

Preferred Stock. We may issue shares of our preferred stock from time to time, in one or more series. Under our seventh amended and restated certificate of incorporation, as amended, our board of directors has the authority to designate up to 5,000,000 shares of preferred stock in one or more series and determine or alter the designation, rights, preferences, privileges and restrictions granted to or imposed upon any series of preferred stock, any or all of which may be greater than the rights of the common stock. If we sell any new series of preferred stock under this prospectus and any applicable prospectus supplement, our board of directors will determine the rights, preferences and privileges of the preferred stock being offered, as well as the qualifications, limitations or restrictions thereof, including dividend rights, conversion rights, voting rights, preemptive rights, terms of redemption or repurchase, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of any series. Preferred stock may be convertible into our common stock or other securities of ours, or may be exchangeable for debt securities. Conversion may be mandatory or at the holder's option and would be at prescribed conversion rates. We will file as an exhibit to the registration

Table of Contents

statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of the certificate of designation that describes the terms of the series of preferred stock being offered before the issuance of the related series of preferred stock. In this prospectus, we have summarized certain general features of the preferred stock under the heading **Description of Capital Stock Preferred Stock**. We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to the series of preferred stock being offered, as well as the complete certificate of designation that contains the terms of the applicable series of preferred stock.

Debt Securities. We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. Convertible or exchangeable debt securities will be convertible into or exchangeable for our common stock or our other securities. Conversion or exchange may be mandatory or optional (at our option or the holders' option) and would be at prescribed conversion or exchange prices.

The debt securities will be issued under an indenture that we will enter into with a national banking association or other eligible party, as trustee. In this prospectus, we have summarized certain general features of the debt securities under the heading **Description of Debt Securities**. We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to the series of debt securities being offered, as well as the complete indenture and any supplemental indentures that contain the terms of the debt securities. We have filed the form of indenture as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

Warrants. We may issue warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series. We may issue warrants independently or in combination with common stock, preferred stock and/or debt securities offered by any prospectus supplement. In this prospectus, we have summarized certain general features of the warrants under the heading **Description of Warrants**. We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to the particular series of warrants being offered, as well as the form of warrant and/or the warrant agreement and warrant certificate, as applicable, that contain the terms of the warrants. We have filed the forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants that we may offer as exhibits to the registration statement of which this prospectus is a part. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of warrant and/or the warrant agreement and warrant certificate, as applicable, that contain the terms of the particular series of warrants we are offering, and any supplemental agreements, before the issuance of such warrants.

Warrants may be issued under a warrant agreement that we enter into with a warrant agent. We will indicate the name and address of the warrant agent, if any, in the applicable prospectus supplement relating to a particular series of warrants.

Selling Securityholders

Selling securityholders are persons or entities that, directly or indirectly, have acquired or will from time to time acquire from us, our securities. Information about selling securityholders, if any, will be set forth in a prospectus supplement. See **Selling Securityholders** on page 26 of this prospectus.

Table of Contents

Use of Proceeds

Except as described in any applicable prospectus supplement or in any free writing prospectuses we have authorized for use in connection with a specific offering, we intend to use the net proceeds from the sale of the securities under this prospectus for working capital and other general corporate purposes, including support for our continuing research and development of our genomic therapy product candidates and research programs, clinical trials and business development activities. See **Use of Proceeds** on page 8 of this prospectus. Unless the applicable prospectus supplement provides otherwise, we will not receive any of the proceeds from the sale of our securities by selling securityholders.

Nasdaq Global Select Market Listing

Our common stock is listed on The Nasdaq Global Select Market under the symbol **SGMO**.

Table of Contents

RISK FACTORS

Investing in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should consider carefully the risks and uncertainties described under the heading **Risk Factors** contained in the applicable prospectus supplement and any related free writing prospectus, and described under the section entitled **Risk Factors** contained in our current report on Form 8-K filed with the SEC on April 17, 2018, as well as any amendments thereto reflected in subsequent filings with the SEC, and in our other filings that are incorporated by reference into this prospectus in their entirety, together with other information in this prospectus, the documents incorporated by reference and any free writing prospectus that we may authorize for use in connection with a specific offering. The risks described in these documents are not the only ones we face, but those that we consider to be material. There may be other unknown or unpredictable economic, business, competitive, regulatory or other factors that could have material adverse effects on our future results. Past financial performance may not be a reliable indicator of future performance, and historical trends should not be used to anticipate results or trends in future periods. 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 securities to decline, resulting in a loss of all or part of your investment. Please also carefully read the section below entitled **Forward-Looking Statements**.

FORWARD-LOOKING STATEMENTS

This prospectus and any accompanying prospectus supplement, as well as the documents incorporated by reference in this prospectus or any accompanying prospectus supplement, contain **forward-looking statements** within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. These statements relate to future events or to our future operating or financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. Forward-looking statements may include, but are not limited to, statements about:

our strategy;

anticipated product candidate development and potential commercialization of any resulting products;

the initiation, scope, rate of progress, enrollment, anticipated results and timing of our preclinical studies and clinical trials and those of our collaborators or strategic partners;

the therapeutic and commercial potential of, and the ability of Sangamo and our collaborators or strategic partners to advance the development of, product candidates using our ZFP technology platform, including our ability to effectively deliver our ZFNs and ZFP TFs to produce a beneficial therapeutic effect;

our ability to establish and maintain collaborative, licensing and other similar arrangements;

anticipated revenues from existing and new collaborations and the timing thereof;

our research and development and other expenses;

our ability to obtain adequate preclinical and clinical supplies of our product candidates from current and potential new suppliers and manufacturers;

the ability of Sangamo and our collaborators or strategic partners to obtain and maintain regulatory approvals for product candidates using our ZFP technology platform;

our ability to comply with, and the impact of, regulatory requirements, obligations and restrictions on our business;

Table of Contents

our ability to protect our intellectual property and operate our business without infringing upon the intellectual property rights of others, including our ability to obtain rights to the gene transfer technologies required to develop and commercialize our product candidates;

our estimates regarding the sufficiency of our cash resources and our expenses, capital requirements and need for additional financing, and our ability to obtain additional financing;

our ability to manage the growth of our business;

our projected operating and financial performance;

our operational and legal risks;

our intended use of the net proceeds from offerings of our securities under this prospectus; and

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

In some cases, you can identify forward-looking statements by terms such as anticipates, believes, could, estimates, expects, may, plans, potential, predicts, projects, should, would, will and similar expressions intended to identify forward-looking statements. These statements reflect our current views with respect to future events, are based on assumptions and are subject to risks and uncertainties. Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. We discuss in greater detail, and incorporate by reference into this prospectus in their entirety, many of these risks and uncertainties under the heading Risk Factors contained in the applicable prospectus supplement, in any free writing prospectus we may authorize for use in connection with a specific offering, and in our most recent annual report on Form 10-K, in our most recent quarterly report on Form 10-Q, as well as any amendments thereto reflected in subsequent filings with the SEC, and in our other filings that are incorporated by reference into this prospectus. Also, these forward-looking statements represent our estimates and assumptions only as of the date of the document containing the applicable statement. Unless required by law, we undertake no obligation to update or revise any forward-looking statements to reflect new information or future events or developments. Thus, you should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-looking statements. You should read this prospectus, the applicable prospectus supplement, together with the documents we have filed with the SEC that are incorporated by reference and any free writing prospectus we have authorized for use in connection with a specific offering completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in the foregoing documents by these cautionary statements.

Table of Contents**FINANCIAL RATIOS**

The following table sets forth our ratio of earnings to fixed charges and the ratio of our earnings to combined fixed charges and preferred stock dividends to earnings for each of the periods presented. Our net losses were insufficient to cover fixed charges and combined fixed charges and preferred stock dividends for each of the periods presented. Because of these deficiencies, the ratio information is not applicable for those periods. The extent to which earnings were insufficient to cover fixed charges and combined fixed charges and preferred stock dividends for those periods is shown below. Amounts shown are in thousands, except for ratios.

	Year Ended December 31,				
	2013	2014	2015	2016	2017
Ratio of earnings to fixed charges(1)	N/A	N/A	N/A	N/A	N/A
Ratio of earnings to combined fixed charges and preferred stock dividends	N/A	N/A	N/A	N/A	N/A
Deficiency of earnings available to cover fixed charges	\$ (26,624)	\$ (26,417)	\$ (46,425)	\$ (71,672)	\$ (54,568)
Deficiency of earnings available to cover combined fixed charges and preferred stock dividends	\$ (26,624)	\$ (26,417)	\$ (46,425)	\$ (71,672)	\$ (54,568)

(1) Earnings are the sum of loss from continuing operations before income taxes plus fixed charges. Fixed charges consist of interest expense and interest capitalized related to build-to-suit leases.

Table of Contents

USE OF PROCEEDS

Except as described in any applicable prospectus supplement or in any free writing prospectuses we have authorized for use in connection with a specific offering, we intend to use the net proceeds from the sale of the securities under this prospectus for working capital and other general corporate purposes, including support for our continuing research and development of our genomic therapy product candidates and research programs, clinical trials and business development activities. We will set forth in the applicable prospectus supplement our intended use for the net proceeds received from the sale of any securities. Pending the use of the net proceeds, we intend to invest the net proceeds in short-term, investment-grade, interest-bearing securities.

Unless the applicable prospectus supplement provides otherwise, we will not receive any of the proceeds from the sale of our securities by selling securityholders.

Table of Contents

DESCRIPTION OF CAPITAL STOCK

As of the date of this prospectus, our seventh amended and restated certificate of incorporation, as amended, or the Restated Certificate, authorizes us to issue 160,000,000 shares of common stock, par value \$0.01 per share, and 5,000,000 shares of preferred stock, par value \$0.01 per share. As of March 31, 2018, 87,041,208 shares of common stock were outstanding and no shares of our preferred stock were outstanding.

The following summary description of our capital stock is based on the provisions of the Restated Certificate, our second amended and restated bylaws, as amended, or our Bylaws, and the applicable provisions of the General Corporation Law of the State of Delaware, or DGCL. This information may not be complete in all respects and is qualified entirely by reference to the provisions of the Restated Certificate, our Bylaws and the DGCL. For information on how to obtain copies of the Restated Certificate and our Bylaws, which are exhibits to the registration statement of which this prospectus forms a part, see [Where You Can Find More Information](#).

Common Stock

The holders of common stock are entitled to one vote per share on all matters to be voted on by the stockholders. Stockholders have no cumulative voting rights. Subject to the preferences of any outstanding shares of preferred stock, the holders of common stock are entitled to receive ratably any dividends our board of directors declares out of funds legally available for the payment of dividends. If we are liquidated, dissolved or wound up, the holders of common stock are entitled to share pro rata all assets remaining after payment of liabilities and liquidation preferences of any outstanding shares of preferred stock. Holders of common stock have no preemptive rights or rights to convert their common stock into any other securities. There are no redemption or sinking fund provisions applicable to the common stock. When we issue shares of common stock under this prospectus, the shares will be fully paid and nonassessable.

Additional shares of authorized common stock may be issued, as authorized by our board of directors from time to time, without stockholder approval, except as may be required by applicable stock exchange requirements.

Preferred Stock

Pursuant to the Restated Certificate, our board of directors has the authority, without further action by the stockholders, to issue shares of preferred stock in one or more series. Our board of directors also has the authority to determine or alter the designation, rights, preferences, privileges and restrictions granted to or imposed upon any unissued series of preferred stock, any or all of which may be greater than the rights of the common stock. Our board of directors, without stockholder approval, may issue preferred stock with voting, conversion or other rights that are superior to the voting and other rights of the holders of common stock. The issuance of preferred stock may have the effect of delaying, deferring or preventing a change of control of Sangamo without further action by the stockholders, and may have the effect of delaying or preventing changes in management of Sangamo. In addition, the issuance of preferred stock may have the effect of decreasing the market price of the common stock and may adversely affect the voting power of holders of common stock and reduce the likelihood that common stockholders will receive dividend payments and payments upon liquidation.

Our board of directors will determine the rights, preferences, privileges and restrictions of the preferred stock of each series that we sell under this prospectus and applicable prospectus supplements in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of the certificate of designation that describes the terms of the series of preferred stock that we are offering before the issuance of the related series of

preferred stock. This description will include:

the title and stated value;

Table of Contents

the number of shares we are offering;

the liquidation preference per share;

the purchase price per share;

the dividend rate per share, dividend period and payment dates and method of calculation for dividends;

whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;

our right, if any, to defer payment of dividends and the maximum length of any such deferral period;

the procedures for any auction and remarketing, if any;

the provisions for a sinking fund, if any;

the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;

any listing of the preferred stock on any securities exchange or market;

whether the preferred stock will be convertible into our common stock or other securities of ours, including warrants, and, if applicable, the conversion period, the conversion price, or how it will be calculated, and under what circumstances it may be adjusted;

whether the preferred stock will be exchangeable for debt securities, and, if applicable, the exchange period, the exchange price, or how it will be calculated, and under what circumstances it may be adjusted;

voting rights, if any, of the preferred stock;

preemption rights, if any;

restrictions on transfer, sale or other assignment, if any;

a discussion of any material or special United States federal income tax considerations applicable to the preferred stock;

the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;

any limitations on issuances of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock being issued as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and

any other specific terms, rights, preferences, privileges, qualifications or restrictions of the preferred stock. When we issue shares of preferred stock under this prospectus, the shares will be fully paid and nonassessable.

Unless we specify otherwise in the applicable prospectus supplement, the preferred stock will rank, with respect to dividends and upon our liquidation, dissolution or winding up:

senior to all classes or series of our common stock and to all of our equity securities ranking junior to the preferred stock;

on a parity with all of our equity securities the terms of which specifically provide that the equity securities rank on a parity with the preferred stock; and

Table of Contents

junior to all of our equity securities the terms of which specifically provide that the equity securities rank senior to the preferred stock.

The term "equity securities" does not include convertible debt securities.

The General Corporation Law of the State of Delaware, the state of our incorporation, provides that the holders of preferred stock will have the right to vote separately as a class on any proposal involving fundamental changes in the rights of holders of that preferred stock. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

Antitakeover Effects of Provisions of Charter Documents and Delaware Law

Charter Documents

As noted above, our board of directors, without stockholder approval, has the authority under our Restated Certificate to issue preferred stock with rights superior to the rights of the holders of common stock. As a result, the issuance of preferred stock may have the effect of delaying, deferring or preventing a change of control of Sangamo without further action by the stockholders and may adversely affect the voting and other rights of the holders of common stock.

Our Restated Certificate also requires that any action required or permitted to be taken by our stockholders must be effected at a duly called annual or special meeting of the stockholders and may not be effected by a consent in writing. Our Bylaws provide that a special meeting of the stockholders may be called only by the chairman of our board or our president and shall be called by the chairman of our board, our president or our secretary at the request in writing of a majority of the board of directors. These provisions may have the effect of delaying, deferring or preventing a change in control and may also delay or prevent changes in management of Sangamo, which could have an adverse effect on the market price of our stock.

These and other provisions are intended to enhance the likelihood of continued stability in the composition of our board of directors and to discourage certain types of transactions that may involve an actual or threatened change of control. However, such provisions could have the effect of discouraging others from making tender offers for our shares and, as a consequence, such provisions also may inhibit fluctuations in the market price of our shares that could result from actual or rumored takeover attempts.

Section 203 of the General Corporation Law of the State of Delaware

We are subject to Section 203 of the DGCL which regulates acquisitions of some Delaware corporations. In general, Section 203 prohibits, with some exceptions, a publicly held Delaware corporation such as us from engaging in a business combination with an interested stockholder for a period of three years following the time that the stockholder became an interested stockholder, unless:

prior to the time the stockholder became an interested stockholder, the board of directors of the corporation approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;

upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the number of shares outstanding (but not the outstanding voting stock owned by the interested stockholder) those shares owned by (a) persons who are directors and also officers and (b) employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or

at or subsequent to the time the stockholder became an interested stockholder, the business combination is approved by the board and authorized at an annual or special meeting of stockholders,

Table of Contents

and not by written consent, by the affirmative vote of at least 66 $\frac{2}{3}$ % of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 of the DGCL generally defines a "business combination" to include any of the following:

any merger or consolidation involving the corporation and the interested stockholder;

any sale, transfer, pledge or other disposition involving the interested stockholder (in one transaction or a series of transactions) of assets of the corporation having an aggregate market value equal to 10% or more of the aggregate market value of either all of the assets of the corporation or its outstanding stock;

subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;

subject to exceptions, any transaction involving the corporation that has the effect, directly or indirectly, of increasing the proportionate share of the stock or any class or series of the corporation beneficially owned by the interested stockholder; and

the receipt by the interested stockholder of the benefit, directly or indirectly (except proportionately as a stockholder of such corporation), of any loans, advances, guarantees, pledges or other financial benefits, other than certain benefits set forth in Section 203, provided by or through the corporation.

In general, Section 203 defines an "interested stockholder" as an entity or person who, together with the person's affiliates and associates, beneficially owns, or within three years prior to the time of determination of interested stockholder status did own, 15% or more of the outstanding voting stock of the corporation.

Section 203 of the DGCL could depress our stock price and delay, discourage or prohibit transactions not approved in advance by our board of directors, such as takeover attempts that might otherwise involve the payment to our stockholders of a premium over the market price of our common stock.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare, Inc. Its address is 250 Royall Street, Canton, MA 02021 and its telephone number is (781) 575-3951. The transfer agent for any series of preferred stock that we or selling securityholders may offer under this prospectus will be named and described in the applicable prospectus supplement for that series.

Listing on The Nasdaq Global Select Market

Our common stock is listed on The Nasdaq Global Select Market under the symbol **SGMO**.

Table of Contents

DESCRIPTION OF DEBT SECURITIES

We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. While the terms we have summarized below will apply generally to any debt securities that we may offer under this prospectus, we will describe the particular terms of any debt securities that we or selling securityholders may offer in more detail in the applicable prospectus supplement. The terms of any debt securities offered under a prospectus supplement may differ from the terms described below. Unless the context requires otherwise, whenever we refer to the indenture, we also are referring to any supplemental indentures that specify the terms of a particular series of debt securities.

We will issue the debt securities under the indenture that we will enter into with the trustee named in the indenture. The indenture will be qualified under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act. We have filed the form of indenture as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

The following summary of material provisions of the debt securities and the indenture is subject to, and qualified in its entirety by reference to, all of the provisions of the indenture applicable to a particular series of debt securities. We urge you to read the applicable prospectus supplements and any related free writing prospectuses related to the debt securities that we or selling securityholders may offer under this prospectus, as well as the complete indenture that contains the terms of the debt securities.

General

The indenture does not limit the amount of debt securities that we may issue. It provides that we may issue debt securities up to the principal amount that we may authorize and may be in any currency or currency unit that we may designate. Except for the limitations on consolidation, merger and sale of all or substantially all of our assets contained in the indenture, the terms of the indenture do not contain any covenants or other provisions designed to give holders of any debt securities protection against changes in our operations, financial condition or transactions involving us.

We may issue the debt securities issued under the indenture as discount securities, which means they may be sold at a discount below their stated principal amount. These debt securities, as well as other debt securities that are not issued at a discount, may be issued with original issue discount, or OID, for U.S. federal income tax purposes because of interest payment and other characteristics or terms of the debt securities. Material U.S. federal income tax considerations applicable to debt securities issued with OID will be described in more detail in the applicable prospectus supplement.

We will describe in the applicable prospectus supplement the terms of the series of debt securities being offered, including:

the title of the series of debt securities;

any limit upon the aggregate principal amount that may be issued;

the maturity date or dates;

the form of the debt securities of the series;

the applicability of any guarantees;

whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;

whether the debt securities rank as senior debt, senior subordinated debt, subordinated debt or any combination thereof, and the terms of any subordination;

Table of Contents

if the price (expressed as a percentage of the aggregate principal amount thereof) at which such debt securities will be issued is a price other than the principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof, or if applicable, the portion of the principal amount of such debt securities that is convertible into another security or the method by which any such portion shall be determined;

the interest rate or rates, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;

our right, if any, to defer payment of interest and the maximum length of any such deferral period;

if applicable, the date or dates after which, or the period or periods during which, and the price or prices at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;

the date or dates, if any, on which, and the price or prices at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder's option to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;

the denominations in which we will issue the series of debt securities, if other than denominations of \$1,000 and any integral multiple thereof;

any and all terms, if applicable, relating to any auction or remarketing of the debt securities of that series and any security for our obligations with respect to such debt securities and any other terms which may be advisable in connection with the marketing of debt securities of that series;

whether the debt securities of the series shall be issued in whole or in part in the form of a global security or securities; the terms and conditions, if any, upon which such global security or securities may be exchanged in whole or in part for other individual securities; and the depositary for such global security or securities;

if applicable, the provisions relating to conversion or exchange of any debt securities of the series and the terms and conditions upon which such debt securities will be so convertible or exchangeable, including the conversion or exchange price, as applicable, or how it will be calculated and may be adjusted, any mandatory or optional (at our option or the holders' option) conversion or exchange features, the applicable conversion or exchange period and the manner of settlement for any conversion or exchange;

if other than the full principal amount thereof, the portion of the principal amount of debt securities of the series which shall be payable upon declaration of acceleration of the maturity thereof;

additions to or changes in the covenants applicable to the particular debt securities being issued, including, among others, the consolidation, merger or sale covenant;

additions to or changes in the events of default with respect to the securities and any change in the right of the trustee or the holders to declare the principal, premium, if any, and interest, if any, with respect to such securities to be due and payable;

additions to or changes in or deletions of the provisions relating to covenant defeasance and legal defeasance;

additions to or changes in the provisions relating to satisfaction and discharge of the indenture;

additions to or changes in the provisions relating to the modification of the indenture both with and without the consent of holders of debt securities issued under the indenture;

the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars;

Table of Contents

whether interest will be payable in cash or additional debt securities at our or the holders' option and the terms and conditions upon which the election may be made;

the terms and conditions, if any, upon which we will pay amounts in addition to the stated interest, premium, if any and principal amounts of the debt securities of the series to any holder that is not a United States person for federal tax purposes;

any restrictions on transfer, sale or assignment of the debt securities of the series; and

any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, any other additions or changes in the provisions of the indenture, and any terms that may be required by us or advisable under applicable laws or regulations.

Conversion or Exchange Rights

We will set forth in the applicable prospectus supplement the terms on which a series of debt securities may be convertible into or exchangeable for our common stock or our other securities. We will include provisions as to settlement upon conversion or exchange and whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock or our other securities that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the indenture will not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of our assets as an entirety or substantially as an entirety. However, any successor to or acquirer of such assets (other than a subsidiary of ours) must assume all of our obligations under the indenture or the debt securities, as appropriate.

Events of Default under the Indenture

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the following are events of default under the indenture with respect to any series of debt securities that we may issue:

if we fail to pay any installment of interest on any series of debt securities, as and when the same shall become due and payable, and such default continues for a period of 90 days; provided, however, that a valid extension of an interest payment period by us in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of interest for this purpose;

if we fail to pay the principal of, or premium, if any, on any series of debt securities as and when the same shall become due and payable whether at maturity, upon redemption, by declaration or otherwise, or in any payment required by any sinking or analogous fund established with respect to such series; provided, however, that a valid extension of the maturity of such debt securities in accordance with the terms of any

indenture supplemental thereto shall not constitute a default in the payment of principal or premium, if any;

if we fail to observe or perform any other covenant or agreement contained in the debt securities or the indenture, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive written notice of such failure, requiring the same to be remedied and stating that such is a notice of default thereunder, from the trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and

if specified events of bankruptcy, insolvency or reorganization occur.

Table of Contents

If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series, by notice to us in writing, and to the trustee if notice is given by such holders, may declare the unpaid principal of, premium, if any, and accrued interest, if any, due and payable immediately. If an event of default specified in the last bullet point above occurs with respect to us, the principal amount of and accrued interest, if any, of each issue of debt securities then outstanding shall be due and payable without any notice or other action on the part of the trustee or any holder.

The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indenture, if an event of default under an indenture shall occur and be continuing, the trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the trustee reasonable indemnity. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, or exercising any trust or power conferred on the trustee, with respect to the debt securities of that series, provided that:

the direction so given by the holder is not in conflict with any law or the applicable indenture; and

subject to its duties under the Trust Indenture Act, the trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

A holder of the debt securities of any series will have the right to institute a proceeding under the indenture or to appoint a receiver or trustee, or to seek other remedies only if:

the holder has given written notice to the trustee of a continuing event of default with respect to that series;

the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request, such holders have offered to the trustee indemnity satisfactory to it against the costs, expenses and liabilities to be incurred by the trustee in compliance with the request; and

the trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities.

We will periodically file statements with the trustee regarding our compliance with specified covenants in the indenture.

Modification of Indenture; Waiver

We and the trustee may change an indenture without the consent of any holders with respect to specific matters:

to cure any ambiguity, defect or inconsistency in the indenture or in the debt securities of any series;

Table of Contents

to comply with the provisions described above under the heading Description of Debt Securities Consolidation, Merger or Sale;

to provide for uncertificated debt securities in addition to or in place of certificated debt securities;

to add to our covenants, restrictions, conditions or provisions such new covenants, restrictions, conditions or provisions for the benefit of the holders of all or any series of debt securities, to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default or to surrender any right or power conferred upon us in the indenture;

to add to, delete from or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication and delivery of debt securities, as set forth in the indenture;

to make any change that does not adversely affect the interests of any holder of debt securities of any series in any material respect;

to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided above under the heading Description of Debt Securities General to establish the form of any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;

to evidence and provide for the acceptance of appointment under any indenture by a successor trustee; or

to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act.

In addition, under the indenture, the rights of holders of a series of debt securities may be changed by us and the trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected. However, unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, we and the trustee may make the following changes only with the consent of each holder of any outstanding debt securities affected:

extending the fixed maturity of any debt securities of any series;

reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption of any series of any debt securities; or

reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

Discharge

Each indenture provides that we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

provide for payment;

register the transfer or exchange of debt securities of the series;

replace stolen, lost or mutilated debt securities of the series;

pay principal of and premium and interest on any debt securities of the series;

maintain paying agencies;

hold monies for payment in trust;

recover excess money held by the trustee;

Table of Contents

compensate and indemnify the trustee; and

appoint any successor trustee.

In order to exercise our rights to be discharged, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, any premium, if any, and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we provide otherwise in the applicable prospectus supplement, in denominations of \$1,000 and any integral multiple thereof. The indenture provides that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company, or DTC, or another depository named by us and identified in the applicable prospectus supplement with respect to that series. To the extent the debt securities of a series are issued in global form and as book-entry, a description of terms relating to any book-entry securities will be set forth in the applicable prospectus supplement.

At the option of the holder, subject to the terms of the indenture and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indenture and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will impose no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

If we elect to redeem the debt securities of any series, we will not be required to:

issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or

register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Trustee

The trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the trustee is under no obligation to exercise any of the powers given it by the indenture at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Table of Contents

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in the applicable prospectus supplement, we will designate the corporate trust office of the trustee as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

Governing Law

The indenture and the debt securities will be governed by and construed in accordance with the internal laws of the State of New York, except to the extent that the Trust Indenture Act is applicable.

Table of Contents

DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplement and free writing prospectus, summarizes the material terms and provisions of the warrants that we may offer under this prospectus, which may consist of warrants to purchase common stock, preferred stock or debt securities and may be issued in one or more series. Warrants may be offered independently or in combination with common stock, preferred stock or debt securities offered by any prospectus supplement. While the terms we have summarized below will apply generally to any warrants that we may offer under this prospectus, we will describe the particular terms of any series of warrants in more detail in the applicable prospectus supplement. The following description of warrants will apply to the warrants offered by this prospectus unless we provide otherwise in the applicable prospectus supplement. The applicable prospectus supplement for a particular series of warrants may specify different or additional terms.

We have filed forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants that may be offered as exhibits to the registration statement of which this prospectus is a part. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of warrant and/or the warrant agreement and warrant certificate, as applicable, that contain the terms of the particular series of warrants we are offering, and any supplemental agreements, before the issuance of such warrants. The following summaries of material terms and provisions of the warrants are subject to, and qualified in their entirety by reference to, all the provisions of the form of warrant and/or the warrant agreement and warrant certificate, as applicable, and any supplemental agreements applicable to a particular series of warrants that we or selling securityholders may offer under this prospectus. We urge you to read the applicable prospectus supplement related to the particular series of warrants that we or selling securityholders may offer under this prospectus, as well as any related free writing prospectus, and the complete form of warrant and/or the warrant agreement and warrant certificate, as applicable, and any supplemental agreements, that contain the terms of the warrants.

General

We will describe in the applicable prospectus supplement the terms of the series of warrants being offered, including:

the offering price and aggregate number of warrants offered;

the currency for which the warrants may be purchased;

if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;

in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at, and currency in which, this principal amount of debt securities may be purchased upon such exercise;

in the case of warrants to purchase common stock or preferred stock, the number of shares of common stock or preferred stock, as the case may be, purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;

the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreements and the warrants;

the terms of any rights to redeem or call the warrants;

any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;

the dates on which the right to exercise the warrants will commence and expire;

Table of Contents

the manner in which the warrant agreements and warrants may be modified;

a discussion of material or special U.S. federal income tax considerations, if any, of holding or exercising the warrants;

the terms of the securities issuable upon exercise of the warrants; and

any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

Before exercising their warrants, holders of warrants will not have any of the rights of holders of the securities purchasable upon such exercise, including:

in the case of warrants to purchase debt securities, the right to receive payments of principal of, or premium, if any, or interest on, the debt securities purchasable upon exercise or to enforce covenants in the applicable indenture; or

in the case of warrants to purchase common stock or preferred stock, the right to receive dividends, if any, or payments upon our liquidation, dissolution or winding up or to exercise voting rights, if any.

Exercise of Warrants

Each warrant will entitle the holder to purchase the securities that we specify in the applicable prospectus supplement at the exercise price that we describe in the applicable prospectus supplement. The warrants may be exercised as set forth in the prospectus supplement relating to the warrants offered. Unless we otherwise specify in the applicable prospectus supplement, warrants may be exercised at any time up to the close of business on the expiration date set forth in the prospectus supplement relating to the warrants offered thereby. After the close of business on the expiration date, unexercised warrants will become void.

Upon receipt of payment and the warrant or warrant certificate, as applicable, properly completed and duly executed at the corporate trust office of the warrant agent, if any, or any other office, including ours, indicated in the prospectus supplement, we will, as soon as practicable, issue and deliver the securities purchasable upon such exercise. If less than all of the warrants (or the warrants represented by such warrant certificate) are exercised, a new warrant or a new warrant certificate, as applicable, will be issued for the remaining warrants.

Governing Law

Unless we provide otherwise in the applicable prospectus supplement, the warrants and any warrant agreements will be governed by and construed in accordance with the internal laws of the State of New York.

Enforceability of Rights by Holders of Warrants

Each warrant agent, if any, will act solely as our agent under the applicable warrant agreement and will not assume any obligation or relationship of agency or trust with any holder of any warrant. A single bank or trust company may act as warrant agent for more than one issue of warrants. A warrant agent will have no duty or responsibility in case of

any default by us under the applicable warrant agreement or warrant, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a warrant may, without the consent of the related warrant agent or the holder of any other warrant, enforce by appropriate legal action its right to exercise, and receive the securities purchasable upon exercise of, its warrants.

Table of Contents

LEGAL OWNERSHIP OF SECURITIES

We may issue securities in registered form or in the form of one or more global securities. We describe global securities in greater detail below. We refer to those persons who have securities registered in their own names on the books that we or any applicable trustee, depositary or warrant agent maintain for this purpose as the holders of those securities. These persons are the legal holders of the securities. We refer to those persons who, indirectly through others, own beneficial interests in securities that are not registered in their own names, as indirect holders of those securities. As we discuss below, indirect holders are not legal holders, and investors in securities issued in book-entry form or in street name will be indirect holders.

Book-Entry Holders

We may issue securities in book-entry form only, as we will specify in the applicable prospectus supplement. This means securities may be represented by one or more global securities registered in the name of a financial institution that holds them as depositary on behalf of other financial institutions that participate in the depositary's book-entry system. These participating institutions, which are referred to as participants, in turn, hold beneficial interests in the securities on behalf of themselves or their customers.

Only the person in whose name a security is registered is recognized as the holder of that security. Securities issued in global form will be registered in the name of the depositary or its participants. Consequently, for securities issued in global form, we will recognize only the depositary as the holder of the securities, and we will make all payments on the securities to the depositary. The depositary passes along the payments it receives to its participants, which in turn pass the payments along to their customers who are the beneficial owners. The depositary and its participants do so under agreements they have made with one another or with their customers; they are not obligated to do so under the terms of the securities.

As a result, investors in a book-entry security will not own securities directly. Instead, they will own beneficial interests in a global security, through a bank, broker or other financial institution that participates in the depositary's book-entry system or holds an interest through a participant. As long as the securities are issued in global form, investors will be indirect holders, and not holders, of the securities.

Street Name Holders

We may terminate a global security or issue securities in non-global form. In these cases, investors may choose to hold their securities in their own names or in street name. Securities held by an investor in street name would be registered in the name of a bank, broker or other financial institution that the investor chooses, and the investor would hold only a beneficial interest in those securities through an account he or she maintains at that institution.

For securities held in street name, we will recognize only the intermediary banks, brokers and other financial institutions in whose names the securities are registered as the holders of those securities, and we will make all payments on those securities to them. These institutions pass along the payments they receive to their customers who are the beneficial owners, but only because they agree to do so in their customer agreements or because they are legally required to do so. Investors who hold securities in street name will be indirect holders, not holders, of those securities.

Legal Holders

Our obligations, as well as the obligations of any applicable trustee and of any third parties employed by us or a trustee, run only to the legal holders of the securities. We do not have obligations to investors who hold beneficial interests in global securities, in street name or by any other indirect means. This will be the case whether an investor chooses to be an indirect holder of a security or has no choice because we are issuing the securities only in global form.

Table of Contents

For example, once we make a payment or give a notice to the holder, we have no further responsibility for the payment or notice even if that holder is required, under agreements with depositary participants or customers or by law, to pass it along to the indirect holders but does not do so. Similarly, we may want to obtain the approval of the holders to amend an indenture, to relieve us of the consequences of a default or of our obligation to comply with a particular provision of the indenture or for other purposes. In such an event, we would seek approval only from the holders, and not the indirect holders, of the securities. Whether and how the holders contact the indirect holders is up to the holders.

Special Considerations for Indirect Holders

If you hold securities through a bank, broker or other financial institution, either in book-entry form or in street name, you should check with your own institution to find out:

the performance of third-party service providers;

how it handles securities payments and notices;

whether it imposes fees or charges;

how it would handle a request for the holders' consent, if ever required;

whether and how you can instruct it to send you securities registered in your own name so you can be a holder, if that is permitted in the future;

how it would exercise rights under the securities if there were a default or other event triggering the need for holders to act to protect their interests; and

if the securities are in book-entry form, how the depositary's rules and procedures will affect these matters.

Global Securities

A global security is a security that represents one or any other number of individual securities held by a depositary. Generally, all securities represented by the same global securities will have the same terms.

Each security issued in book-entry form will be represented by a global security that we deposit with and register in the name of a financial institution or its nominee that we select. The financial institution that we select for this purpose is called the depositary. Unless we specify otherwise in the applicable prospectus supplement, DTC will be the depositary for all securities issued in book-entry form.

A global security may not be transferred to or registered in the name of anyone other than the depositary, its nominee or a successor depositary, unless special termination situations arise. We describe those situations below under the

section entitled "Special Situations When a Global Security Will Be Terminated" in this prospectus. As a result of these arrangements, the depositary, or its nominee, will be the sole registered owner and holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by means of an account with a broker, bank or other financial institution that in turn has an account with the depositary or with another institution that does. Thus, an investor whose security is represented by a global security will not be a holder of the security, but only an indirect holder of a beneficial interest in the global security.

If the prospectus supplement for a particular security indicates that the security will be issued in global form only, then the security will be represented by a global security at all times unless and until the global security is terminated. If termination occurs, we may issue the securities through another book-entry clearing system or decide that the securities may no longer be held through any book-entry clearing system.

Table of Contents

Special Considerations for Global Securities

The rights of an indirect holder relating to a global security will be governed by the account rules of the investor's financial institution and of the depository, as well as general laws relating to securities transfers. We do not recognize an indirect holder as a holder of securities and instead deal only with the depository that holds the global security.

If securities are issued only in the form of a global security, an investor should be aware of the following:

an investor cannot cause the securities to be registered in his or her name, and cannot obtain non-global certificates for his or her interest in the securities, except in the special situations we describe below;

an investor will be an indirect holder and must look to his or her own bank or broker for payments on the securities and protection of his or her legal rights relating to the securities, as we describe above;

an investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form;

an investor may not be able to pledge his or her interest in a global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective;

the depository's policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor's interest in a global security;

we and any applicable trustee have no responsibility for any aspect of the depository's actions or for its records of ownership interests in a global security, nor do we or any applicable trustee supervise the depository in any way;

the depository may, and we understand that DTC will, require that those who purchase and sell interests in a global security within its book-entry system use immediately available funds, and your broker or bank may require you to do so as well; and

financial institutions that participate in the depository's book-entry system, and through which an investor holds its interest in a global security, may also have their own policies affecting payments, notices and other matters relating to the securities.

There may be more than one financial intermediary in the chain of ownership for an investor. We do not monitor and are not responsible for the actions of any of those intermediaries.

Special Situations When a Global Security Will Be Terminated

In a few special situations described below, the global security will terminate and interests in it will be exchanged for physical certificates representing those interests. After that exchange, the choice of whether to hold securities directly or in street name will be up to the investor. Investors must consult their own banks or brokers to find out how to have their interests in securities transferred to their own name, so that they will be direct holders. We have described the rights of holders and street name investors above.

Unless we provide otherwise in the applicable prospectus supplement, the global security will terminate when the following special situations occur:

if the depositary notifies us that it is unwilling, unable or no longer qualified to continue as depositary for that global security and we do not appoint another institution to act as depositary within 90 days;

if we notify any applicable trustee that we wish to terminate that global security; or

if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived.

Table of Contents

The applicable prospectus supplement may also list additional situations for terminating a global security that would apply only to the particular series of securities covered by the applicable prospectus supplement. When a global security terminates, the depository, and not we or any applicable trustee, is responsible for deciding the names of the institutions that will be the initial direct holders.

Table of Contents

SELLING SECURITYHOLDERS

Selling securityholders are persons or entities that, directly or indirectly, have acquired or will from time to time acquire from us, our securities. If the registration statement of which this prospectus forms a part is used by selling securityholders for the resale of any securities registered thereunder pursuant to a registration rights agreement between us and such selling securityholders or otherwise, information about such selling securityholders, their beneficial ownership of our securities and their relationship with us will be set forth in a prospectus supplement.

Table of Contents

PLAN OF DISTRIBUTION

We or selling securityholders may sell the securities from time to time pursuant to underwritten public offerings, at-the-market offerings, negotiated transactions, block trades or a combination of these methods. We or selling securityholders may sell the securities to or through one or more underwriters or dealers (acting as principal or agent), through agents, or directly to one or more purchasers. We or selling securityholders may distribute securities 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.

A prospectus supplement or supplements (and any related free writing prospectus that we may authorize to be provided to you) will describe the terms of the offering of the securities, including, to the extent applicable:

the name or names of the underwriters, dealers or agents, if any;

the name or names of the selling securityholders, if any;

the purchase price of the securities or other consideration therefor, and the proceeds, if any, we will receive from the sale;

any over-allotment or other options under which underwriters may purchase additional securities from us or any selling securityholders;

any agency fees or underwriting discounts and other items constituting agents or underwriters compensation;

any public offering price;

any discounts or concessions allowed or reallocated or paid to dealers; and

any securities exchange or market on which the securities may be listed.

Only underwriters named in the prospectus supplement will be underwriters of the securities offered by the prospectus supplement. Dealers and agents participating in the distribution of the securities may be deemed to be underwriters, and compensation received by them on resale of the securities may be deemed to be underwriting discounts. If such dealers or agents were deemed to be underwriters, they may be subject to statutory liabilities under the Securities Act.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We or selling securityholders may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement, other than securities covered by any over-allotment option. If a dealer is used in the sale of securities, we, a selling stockholder, or an underwriter will sell the securities to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale. To the extent required, we will set forth in the prospectus supplement the name of the dealer and the terms of the transaction. Any public offering price and any discounts or concessions allowed or reallocated or paid to dealers may change from time to time.

We or selling securityholders may use underwriters, dealers or agents with whom we have a material relationship. We will describe in the prospectus supplement, naming the underwriter, dealer or agent, the nature of any such relationship.

Table of Contents

We or selling securityholders may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities and we will describe any commissions payable to the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, the agent will act on a best-efforts basis for the period of its appointment.

We may provide agents, underwriters and dealers with indemnification against civil liabilities, including liabilities under the Securities Act, or contribution with respect to payments that the agents, underwriters or dealers may make with respect to these liabilities. Agents, underwriters and dealers, or their affiliates, may engage in transactions with, or perform services for, us in the ordinary course of business.

Selling securityholders may be deemed to be underwriters under the Securities Act in connection with the securities they resell and any profits on the sales may be deemed to be underwriting discounts and commissions under the Securities Act.

All securities we may offer, other than common stock, will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities.

Any underwriter may engage in over-allotment, stabilizing transactions, short-covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Over-allotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum price. Syndicate-covering or other short-covering transactions involve purchases of the securities, either through exercise of the over-allotment option or in the open market after the distribution is completed, to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a stabilizing or covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

Any underwriters that are qualified market makers on The Nasdaq Global Select Market may engage in passive market making transactions in the common stock on The Nasdaq Global Select Market in accordance with Regulation M under the Exchange Act, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the common stock. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded. Passive market making may stabilize the market price of the securities at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

In compliance with guidelines of the Financial Industry Regulatory Authority, or FINRA, the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus and the applicable prospectus supplement.

Table of Contents

LEGAL MATTERS

Unless otherwise indicated in the applicable prospectus supplement, the validity of the securities offered by this prospectus, and any supplement thereto, will be passed upon for us by Cooley LLP, San Francisco, California.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2017, and the effectiveness of our internal control over financial reporting as of December 31, 2017, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of the registration statement on Form S-3 we filed with the SEC under the Securities Act and does not contain all the information set forth or incorporated by reference in the registration statement. Whenever a reference is made in this prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference into this prospectus for a copy of such contract, agreement or other document. Because we are subject to the information and reporting requirements of the Exchange Act, we file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at <http://www.sec.gov>. You may also read and copy any document we file at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference information from other documents that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus, while information that we file later with the SEC will automatically update and supersede the information in this prospectus. We incorporate by reference into this prospectus and the registration statement of which this prospectus is a part the information or documents listed below that we have filed with the SEC (Commission File No. 000-30171):

our annual report on Form 10-K for the year ended December 31, 2017, which was filed with the SEC on March 1, 2018, as amended by Form 10-K/A, which was filed with the SEC on April 24, 2018;

the information specifically incorporated by reference into our annual report on Form 10-K for the year ended December 31, 2017 from our revised definitive proxy statement relating to our 2018 annual meeting of stockholders, which was filed with the SEC on April 24, 2018;

our current reports on Form 8-K, which were filed with the SEC on January 3, 2018, February 22, 2018 (except for the information furnished under Item 2.02 thereof and the accompanying exhibit 99.1), March 23, 2018 and April 17, 2018; and

Table of Contents

the description of our common stock in our registration statement on Form 8-A, which was filed with the SEC on March 31, 2000, including all amendments and reports filed for the purpose of updating such description.

We also incorporate by reference any future filings (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items unless such Form 8-K expressly provides to the contrary) made with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act until we file a post-effective amendment that indicates the termination of the offering of the securities made by this prospectus and will become a part of this prospectus from the date that such documents are filed with the SEC. Information in such future filings updates and supplements the information provided in this prospectus. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

We will furnish without charge to each person, including any beneficial owner, to whom a prospectus is delivered, upon written or oral request, a copy of any or all of the documents incorporated by reference, including exhibits to these documents. Any such request may be made by writing or telephoning us at the following address or phone number:

Sangamo Therapeutics, Inc.

501 Canal Boulevard

Richmond, California 94804

(510) 970-6000

Attention: Investor Relations

Table of Contents

\$200,000,000

Common Stock

PRELIMINARY PROSPECTUS SUPPLEMENT

April , 2018

Joint Book-Running Managers

BofA Merrill Lynch

J.P. Morgan

Cowen