SANGAMO THERAPEUTICS, INC
Form 424B5
April 03, 2019
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 3, 2019

Preliminary Prospectus Supplement

(To Prospectus dated April 24, 2018)

Shares

Common Stock

We are offering shares of our common stock.

Our common stock is listed on The Nasdaq Global Select Market under the symbol SGMO. On April 2, 2019, the last reported sale price of our common stock as reported on The Nasdaq Global Select Market was $12.29 per share.

	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 additional shares of our common stock.

Investing in our common stock involves a high degree of risk. See Risk Factors on page S-7 of this prospectus supplement and in our Annual Report on Form 10-K for the year ended December 31, 2018, which is 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.

The underwriters expect to deliver the shares to purchasers on or about April , 2019.

Joint Book-Running Managers

Cowen **Wells Fargo Securities** **Barclays**

April , 2019

Table of Contents

TABLE OF CONTENTS

Prospectus Supplement

Prospectus

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 on page S-7 of this prospectus supplement and in our Annual Report on Form 10-K for the year ended December 31, 2018 filed with the SEC on March 1, 2019, which is 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 medicines with the potential to transform patients lives using our platform technologies in gene therapy, *ex vivo* gene-edited cell therapy, *in vivo* genome editing, and gene regulation.

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 gene therapy and genome editing products by forward integrating into manufacturing, development and commercial operations. In other therapeutic areas we intend to partner with biopharmaceutical companies to develop products as appropriate. Decisions to partner product candidates or not will be based on the best way to bring new medicines to patients and on an evaluation of our capacity to bring such products to commercial stage rapidly and efficiently on our own. For our proprietary clinical development programs, we are focused on three therapeutic areas: inherited metabolic diseases, central nervous system diseases and inflammatory and autoimmune diseases.

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 development 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.

In the fourth quarter of 2018, we completed our acquisition of 98.2% of the outstanding share capital and voting rights of TxCell S.A., or TxCell, which we refer to as the TxCell Acquisition. With the TxCell Acquisition, we believe we can now accelerate our research and development of innovative, personalized T-cell immunotherapies for the treatment of inflammatory and autoimmune diseases with high unmet medical need. In this regard, we expect the TxCell Acquisition will accelerate our entry into the clinic with a CAR-Treg (which is a regulatory T-cell, or Treg, genetically modified with a chimeric antigen receptor, or CAR) therapy. We are evaluating the potential of the TxCell platform in solid organ transplantation as well as a range of autoimmune diseases, such as multiple sclerosis, rheumatoid arthritis, inflammatory bowel diseases and inflammatory skin diseases. In addition, we intend to use our ZFN gene editing technology to potentially develop next-generation autologous and allogeneic CAR-Treg cell therapies for use in treating autoimmune diseases.

We have a substantial intellectual property position including the design, selection, manufacture, composition and use of engineered ZFPs, CAR-Tregs and cell therapies to support our research and development

Table of Contents

activities. We continue to license and file new patent applications that strengthen our patent portfolio. We believe that our intellectual property position is a critical element in our ability to research, develop, manufacture and commercialize products and services based on genome editing, gene therapy, gene regulation and cell therapy.

Recent Developments

Clinical Updates

SB-525 Gene Therapy for the Treatment of Hemophilia A

We are conducting the Phase 1/2 Alta study, an open-label, ascending-dose clinical trial to evaluate investigational SB-525 gene therapy for severe hemophilia A, under global collaboration with Pfizer Inc., or Pfizer. In April 2019, we and Pfizer announced interim data that indicate that SB-525 was generally well-tolerated and demonstrated a dose-dependent increase in Factor VIII, or FVIII, levels across the four dosage cohorts. Based on these interim results, the Safety Monitoring Committee, or SMC, recommended cohort expansion at the 3e13 vg/kg dose.

The Phase 1/2 interim data include eight patients treated across four ascending dosage cohorts, with two patients per cohort. Patients demonstrated a dose-dependent increase in FVIII levels, achieving clinically relevant increases in FVIII activity in the higher dosage cohorts and normal FVIII levels in the highest 3e13 vg/kg dose cohort (normal range: 50-150%). At week six post infusion, the two cohort patients dosed at the 3e13 vg/kg level reached 140% and 94% of normal (as measured by one-stage clotting assay) and 93% and 65% (as measured by chromogenic assay). A dose-dependent reduction in the use of FVIII replacement therapy was also observed, with patients in the highest dose cohort not requiring factor replacement therapy after initial use of prophylactic factor and experiencing no bleeding events to date.

No treatment-related serious adverse events and no alanine transaminase, or ALT, elevations requiring more than seven days of corticosteroid treatment were observed in the first three cohorts. Patients in the Alta study were not treated with prophylactic steroids. One patient in the fourth cohort experienced an ALT elevation (>1.5x upper limit of normal) at week four that required a tapering course of oral steroids. The patient did not have any associated loss of FVIII activity or ALT elevations seven weeks following initiation of the steroid therapy (five weeks post vector infusion). The same patient in the fourth cohort experienced a treatment-related infusion reaction, classified as a serious adverse event, and was discharged the following day according to the protocol-specified timeline.

We expect to present longer-term follow-up data at an upcoming scientific meeting. Per the SMC recommendation and study protocol, we are in the process of expanding the fourth cohort by up to five patients and patient enrollment is underway.

ST-400 ex vivo Gene-Edited Cell Therapy for Beta Thalassemia

We are conducting the Phase 1/2 THALES study, an open-label, single arm clinical trial to evaluate the safety and efficacy of ST-400 in up to six subjects with beta thalassemia. ST-400 is an *ex vivo* gene-edited beta thalassemia cell therapy developed in partnership with Sanofi, that involves gene editing of a patient s own hematopoietic stem progenitor cells using non-viral delivery of ZFN technology.

In April 2019, we announced early preliminary data from the first patient treated with ST-400 in the THALES study. This patient has the most severe form of transfusion-dependent beta thalassemia (ß°/ß°) and for the two years prior to treatment in the study, received packed red blood cell, or PRBC, transfusions every other week.

Table of Contents

During the ST-400 infusion, the patient experienced a serious adverse event, a transient allergic reaction considered related to the cryoprotectant present in the product. Thereafter, the post-transplant clinical course was routine.

The patient demonstrated neutrophil and platelet recovery, within two and four weeks of infusion, respectively, indicating that ST-400 successfully reconstituted hematopoiesis following conditioning. Indels (small insertions or deletions generated at the targeted DNA sequence) have been detected in circulating white blood cells, indicating successful editing of the *BCL11A* gene and disruption of the *BCL11A* erythroid specific enhancer, which is intended to upregulate endogenous fetal hemoglobin production in red blood cells.

At seven weeks post ST-400 infusion, total hemoglobin levels remained stable (~9 g/dL), and levels of fetal hemoglobin have continued to rise from approximately 1% of total hemoglobin at the time of infusion to 31% as of the most recent measurement.

The patient received several PRBC transfusions for approximately two weeks after the ST-400 infusion. During the subsequent five weeks, the most recent data available, no further PRBC transfusions have been required.

We caution that these data regarding ST-400 are very early, represent only the first patient dosed, and will require confirmation in additional patients as well as longer follow-up to draw any clinical conclusion. In addition, these very early data should not be viewed as an indication, belief or guarantee that future dosed patients in the THALES study will achieve similar results or that the early results from the first patient dosed will be maintained. For more information about the risks of early clinical data, including the risk that the very early data from the first patient dosed in the THALES study to date may not be maintained or replicated in that patient or in any other dosed patients, see the risk factor entitled *Success in preclinical studies or early clinical trials may not be indicative of results obtained in later trials. Likewise, preliminary data from clinical trials should be considered carefully and with caution since the final data may be materially different from the preliminary data, particularly as more patient data become available* found in Part I, Item 1A of our Annual Report on Form 10-K for the year ended December 31, 2018, filed with the SEC on March 1, 2019, which is incorporated by reference into this prospectus supplement and the accompanying prospectus.

Enrollment in the THALES study is ongoing. We expect to present longer-term ST-400 data in the fourth quarter of 2019, including results from additional patients. Until that time, we are not planning to report additional clinical data from the program.

In vivo Genome Editing Programs

In April 2019, we provided an update on our *in vivo* genome editing programs: the ongoing Phase 1/2 clinical trials evaluating SB-913 (mucopolysaccharidosis type II, or MPS II), SB-318 (MPS I), and SB-FIX (hemophilia B).

We announced that data will continue to accumulate throughout 2019, including in the recently treated expansion cohort patients in the CHAMPIONS study (SB-913), and further updates on all three studies are expected later this year. We expect that no additional patients will be treated at this time with first-generation ZFNs given that clinical benefit has not been demonstrated in analyses conducted to date in ongoing clinical trials and the expected near-term clinical development of second-generation ZFNs.

We are planning a new clinical trial to evaluate second-generation ZFNs for SB-913 to treat MPS II. *In vitro* preclinical data presented last year showed three potential advantages of second-generation ZFNs for use in the clinic: (1) improvements in efficiency and potency due to structural modifications to the ZFN architecture and

Table of Contents

expression vector; (2) the ability to function equally well in the patients with a single nucleotide polymorphism, or SNP, in the target locus in the albumin gene (~20% of the population); and (3) improvements in specificity. The clinical trial of SB-913 using second-generation ZFNs is planned to begin in the second half of 2019. We expect to use data from this study to make a Phase III decision for the SB-913 program in 2020 and to define the next steps for the SB-318 and SB-FIX programs.

Zinc Finger Protein Transcription Factor for Treatment of Tauopathies

In March 2019, we presented new preclinical data describing the effects of tau-targeted ZFP-TFs, delivered with adeno-associated viruses, or AAVs, in the mouse and nonhuman primate, or NHP, brain. The data demonstrate significant (>80%) reduction of tau expression in the NHP brain following administration of ZFP-TFs.

Our ZFP-TF technology acts at the DNA level to selectively repress or activate the expression of specific genes to achieve a desired therapeutic effect. Gene regulation differs from other genome editing approaches as it is designed to enable precise, robust, and long-term repression of a selected gene following a single administration of AAV and does not cut or modify the target DNA.

Tau pathology is strongly linked to the progression of several neurodegenerative diseases, called tauopathies, including Alzheimer s disease. Tauopathies are characterized by the accumulation of toxic tau protein in the brain that leads to widespread neuronal dysfunction and loss. Reducing the total amount of tau expressed within neurons has been shown to provide benefit in animal models of tauopathies.

The new preclinical data demonstrate that ZFP-TFs selectively reduced mouse and human tau by up to 98% *in vitro* in both primary mouse and induced pluripotent stem cell-derived human neurons. Intrahippocampal ZFP-TF delivery to adult mice resulted in more than 80% tau reduction, and intravenous ZFP-TF administration reduced tau levels by 50-70% across the entire mouse brain. ZFP-TF expression and mouse tau reduction were sustained for at least six months following a single administration. Furthermore, in APP/PS1 mice, tau-targeted ZFP-TFs reduced dystrophic neurites by approximately 50% across the cerebral cortex.

AAV ZFP-TFs targeting tau were administered to the adult NHP hippocampus using real-time MRI-guided stereotaxic infusion. ZFP-TF treatment resulted in more than 80% lowering of tau in the hippocampus and entorhinal cortex, and transgene expression levels were strongly correlated with tau reduction. The treatment was well tolerated for the duration of the study. We believe that together, these preclinical data from mice and NHPs highlight the potential for a single administration of ZFP-TF to lower tau as a treatment for tauopathies, including Alzheimer s disease.

We are continuing preclinical development of tau-targeted ZFP-TFs, and plan to present additional data at a future scientific meeting.

Manufacturing Update

In April 2019, we announced that we had signed an option agreement with Brammer Bio MA, LLC, or Brammer Bio, a gene therapy contract development and manufacturing organization, to secure access to large-scale AAV manufacturing. Additionally, at our new facilities in Brisbane, California, construction is underway of a Phase 1/2 cGMP manufacturing facility, which we expect to be operational in 2020.

The option agreement with Brammer Bio enables us to secure access to dedicated AAV manufacturing capacity up to 2000-L bioreactor scale capable of handling large-scale commercial grade runs for products such as ST-920, our gene

therapy product candidate for Fabry disease.

Table of Contents

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. 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 102,187,471 shares of common stock outstanding as of December 31, 2018 and excludes:

- 8,726,092 shares of our common stock issuable upon the exercise of options outstanding as of December 31, 2018, having a weighted-average exercise price of $11.23 per share;
- 322,701 shares of our common stock issuable upon the vesting of restricted stock units outstanding as of December 31, 2018;
- 9,491,418 shares of our common stock reserved for future issuance under our 2018 Stock Incentive Plan, or the 2018 Plan, as of December 31, 2018; and
- 3,006,964 additional shares of our common stock reserved for future issuance under our 2010 Employee Stock Purchase Plan, or the ESPP, as of December 31, 2018.

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, 2018 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.

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

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 Annual Report on Form 10-K for the year ended December 31, 2018 filed with the SEC on March 1, 2019 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

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, 2018, 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.

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.

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 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;

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 ability to realize the anticipated benefits of the TxCell Acquisition, including our ability to develop a CAR-Treg therapy that can be used in patients;

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, continues, could, estimates, expects, intends, may, plans, seeks, should, will and similar expressions intended to identify forward-looking statements. These statements reflect our current views with

Table of Contents

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 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 Annual Report on Form 10-K for the year ended December 31, 2018 filed with the SEC on March 1, 2019, which is 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.

Table of Contents

USE OF PROCEEDS

We estimate that the net proceeds we will receive from the sale of shares of our common stock that we are offering will be approximately $ million (or approximately $ million if the underwriters exercise in full their option to purchase up to an additional $ of shares of our common stock), 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, 2018 was $272.3 million, or approximately $2.67 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, 2018.

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, 2018 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, 2018	$ 2.67	
Increase in net tangible book value per share attributable to this offering		
As adjusted net tangible book value per share as of December 31, 2018 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 102,187,471 shares of common stock issued and outstanding as of December 31, 2018 and exclude:

- 8,726,092 shares of our common stock issuable upon the exercise of options outstanding as of December 31, 2018, having a weighted-average exercise price of $11.23 per share;
- 322,701 shares of our common stock issuable upon the vesting of restricted stock units outstanding as of December 31, 2018;

- 9,491,418 shares of our common stock reserved for future issuance under the 2018 Plan as of December 31, 2018; and

- 3,006,964 additional shares of our common stock reserved for future issuance under the ESPP as of December 31, 2018.

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, 2018 pursuant to the ATM Agreement with Cowen.

Table of Contents

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.

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 U.S. income taxpayers for U.S. federal tax purposes, persons that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or integrated investment or ot 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 United States, 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 United States 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.

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

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 5% 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.

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 United States), 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 United States 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 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

Table of Contents

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 were scheduled to apply to payments of gross proceeds from a sale or other disposition of common stock on or after January 1, 2019. The U.S. Treasury Department recently released proposed regulations that, if finalized in their present form, would eliminate the federal withholding tax of 30% applicable to the gross proceeds of a disposition of our common stock. In its preamble to such proposed regulations, the U.S. Treasury Department stated that taxpayers may generally rely on the proposed regulations until final regulations are issued.

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

Cowen and Company, LLC, Wells Fargo Securities, LLC and Barclays Capital Inc. 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.

Underwriter	Number of Shares
Cowen and Company, LLC	
Wells Fargo Securities, LLC	
Barclays Capital Inc.	
Total	

Subject to the terms and conditions set forth in the underwriting agreement, the underwriters have agreed, severally and not jo