SANGAMO THERAPEUTICS, INC
Form 8-K
April 03, 2019

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, DC 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d)

of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): April 3, 2019

SANGAMO THERAPEUTICS, INC.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**000-30171**	**68-0359556**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

501 Canal Blvd., Richmond, California 94804

(Address of Principal Executive Offices) (Zip Code)

(510) 970-6000

(Registrant s telephone number, including area code)

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (*see* General Instruction A.2. below):

Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))
Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

In this Current Report on Form 8-K, Sangamo, the Company, we, us, and our refer to Sangamo Therapeu Inc. and its consolidated subsidiaries.

Item 8.01 Other Events.

Business Update

Sangamo is filing information for the purpose of supplementing and updating certain aspects of the description of its business from that described under the heading, Item 1. Business in Sangamo s Annual Report on Form 10-K for the year ended December 31, 2018, filed with the U.S. Securities and Exchange Commission, or SEC, on March 1, 2019. The updated disclosure is set forth below:

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 (b^0/b^0) and for the two years prior to treatment in the study, received packed red blood cell, or PRBC, transfusions every other week.

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.

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 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.

Forward-Looking Statements

Item 8.01 of this Current Report on Form 8-K contains forward-looking statements, including, without limitation, statements relating to: the potential therapeutic applications for SB-525, ST-400, SB-913, SB-318 and SB-FIX and for Sangamo s ZFP-TF platform technology, and their potential benefits; the anticipated initiation, enrollment, scope and rate of progress of, and data availability and other next steps related to, Sangamo s preclinical studies and clinical

trials, as well as the anticipated timing thereof; statements related to the anticipated benefits to Sangamo of its option agreement with Brammer Bio; the anticipated operational status of Sangamo s planned manufacturing facility and the timing thereof; and other statements that are not historical fact. These forward-looking statements are based upon Sangamo s current expectations. Actual results could differ materially from these forward-looking statements as a result of certain factors, including, without limitation, risks and uncertainties related to: the lengthy and uncertain research and development process; early, preliminary or interim data, including the possibility of unfavorable new clinical data and further analyses of existing clinical data that could materially change Sangamo s conclusions with respect to such early, preliminary or interim data; whether the final results from clinical trials conducted by Sangamo will validate and

support any early, preliminary or interim data reported to date and/or the overall safety and efficacy of Sangamo s product candidates; Sangamo s dependence on the success of its clinical trials; the initiation, enrollment and completion of clinical trials; whether Sangamo will be able to effectively deliver its ZFNs to produce a beneficial therapeutic effect, including the risks that the second-generation ZFNs may not be successfully integrated into Sangamo s product candidates and even if successfully integrated, the second-generation ZFNs may not have any advantages over Sangamo s first-generation ZFNs; whether Sangamo s ZFNs and/or ZFP-TF technology will produce any beneficial therapeutic effect; the lengthy and uncertain regulatory approval process, including whether regulatory authorities will be satisfied with the design of and results from Sangamo s clinical trials and those of its collaborators; Sangamo s ability to maintain its collaborative relationships and Sangamo s reliance on collaborators and other third parties, including Brammer Bio, to meet their respective obligations; the complex and difficult nature of manufacturing biological components and Sangamo s lack of experience as a company in manufacturing biologic products; Sangamo s ability to obtain or protect intellectual property rights related to its product candidates; technological challenges Sangamo may encounter; and other risks and uncertainties affecting Sangamo and its development programs. Further, there can be no assurance that the necessary regulatory approvals for SB-525, ST-400, SB-913, SB-318, SB-FIX or any other product candidates will be obtained or that Sangamo and its collaborators will be able to develop commercially viable product candidates for the treatment of hemophilia A, beta-thalassemia, MPS II and other diseases. These risks and uncertainties are described more fully in Sangamo s Annual Report on Form 10-K for the year ended December 31, 2018, filed with the SEC on March 1, 2019. Forward-looking statements contained in this Current Report on Form 8-K are made as of the date of this Current Report on Form 8-K, and Sangamo undertakes no duty to update such information except as required under applicable law.

Item 9.01 Financial Statements and Exhibits.

(b) Pro Forma Financial Information

TxCell Acquisition Pro Forma Financial Information

As previously reported, in the fourth quarter of 2018, Sangamo acquired 98.2% of the outstanding share capital and voting rights of TxCell S.A., or the TxCell Acquisition. The Company has previously included in filings with the SEC pro forma financial information giving effect to the TxCell Acquisition as of and for the nine months ended September 30, 2018 and for the year ended December 31, 2017. The Company is now filing with this Current Report on Form 8-K the unaudited pro forma condensed combined statement of operations for the year ended December 31, 2018 giving effect to the TxCell Acquisition (and the notes related thereto). This pro forma financial information is attached as Exhibit 99.1 and incorporated herein by reference.

(d) Exhibits

Exhibit No.	Description
99.1	TxCell Acquisition: Unaudited pro forma condensed combined statement of operations for the year ended December 31, 2018, and the notes related thereto.

Signature

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

SANGAMO THERAPEUTICS, INC.

By:

/s/ KATHY Y. YI
Name: Kathy Y. Yi
Title: Executive Vice President and Chief Financial Officer

Dated: April 3, 2019