SANGAMO THERAPEUTICS, INC
Form 10-K
March 01, 2019

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2018

or

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the transition period from to

Commission file number: 000-30171

SANGAMO THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	68-0359556
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
501 Canal Boulevard,	
Richmond, California	94804
(Address of principal executive offices)	(Zip Code)

(510) 970-6000

(Registrant's telephone number, including area code)

None

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	Name of Each Exchange on Which Registered
Common Stock, $0.01 par value per share	Nasdaq Global Select Market

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. Yes No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes No

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or emerging growth company. See the definition of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	Accelerated filer
Non-accelerated filer	Smaller reporting company
	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.

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes No

The aggregate market value of the voting stock held by non-affiliates of the registrant based upon the closing sale price of the common stock on June 30, 2018 (the last business day of the registrant's most recently completed second fiscal quarter), as reported on the Nasdaq Global Select Market was $1,442,357,545. For purposes of this calculation, directors and executive officers of the registrant have been deemed affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

As of February 15, 2019, a total of 102,273,353 shares of common stock $0.01 par value per share were outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Certain information required by Part III, Items 10-14 of this Form 10-K is incorporated by reference to the registrant's definitive Proxy Statement for the 2019 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission pursuant to Regulation 14A not later than 120 days after the end of the fiscal year covered by this Form 10-K, provided that if such Proxy Statement is not filed within such period, such information will be included in an amendment to this Form 10-K to be filed within such 120-day period.

TABLE OF CONTENTS

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Some statements contained in this report are “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; 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” and “will.” These forward-looking statements reflect our c views with respect to future events and are based on assumptions and involve known and unknown risks, uncertainties and other factors which 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. Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. We discuss many of these risks in greater detail under the headings “Risk Factors” and “Management’s Discussion and Analysis of Financial Results of Operations” in this Form 10-K. Accordingly, the forward-looking statements, speak only as of the date of this Form 10-K. Except as required by law, we undertake no obligation to update or publicly release any revisions to forward-looking statements to reflect events or circumstances arising after the date of this report.

PART I

ITEM 1 – BUSINESS

OVERVIEW

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 genome editing, gene therapy, gene regulation and cell therapy. We are focused on three therapeutic areas: inherited metabolic diseases, or IMDs, 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.

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 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.

In August 2018, we announced positive preliminary data from the Alta Study, a Phase 1/2 clinical trial evaluating SB-525, a complementary DNA, or cDNA, gene therapy candidate for hemophilia A. SB-525 is being developed as part of a global collaboration between us and Pfizer Inc., or Pfizer, for the development and commercialization of potential gene therapy programs for hemophilia A. In October 2018, the independent safety monitoring committee, or SMC, of the Alta Study reviewed accumulated safety and efficacy data from the six patients enrolled in three dose cohorts. The SMC recommended that the study continue with escalation to an additional dose. We plan to present safety and efficacy data from the Alta Study in 2019 after dose escalation is complete and the clinical trial has progressed to the cohort expansion phase.

In September 2018 we announced preliminary safety and efficacy data from the Phase 1/2 clinical trial evaluating SB-913 for the treatment of MPS II, or the CHAMPIONS Study. In October 2018, the SMC of the CHAMPIONS Study reviewed accumulated safety and efficacy data from all three cohorts. In February 2019, we announced interim results from the CHAMPIONS Study. SB-913 showed preliminary evidence of in vivo genome editing in patients with MPS II and was generally well-tolerated with no treatment-related serious adverse events.

We have an ongoing Phase 1/2 clinical trial evaluating SB-318 for the treatment of MPS I, or the EMPOWERS Study. In October 2018, the SMC reviewed accumulated safety and efficacy data from the EMPOWERS Study. In accordance with the recommendation of the SMC, the second patient enrolled in the EMPOWERS Study received the 5e13 vg/kg dose, or the highest dose. In February 2019, we announced interim results from the EMPOWERS Study. SB-318 demonstrated a dose-dependent increase in leukocyte alpha-L-iduronidase, or IDUA, enzyme activity in patients with MPS I and was generally well-tolerated with no treatment related serious adverse events.

We are also evaluating SB-FIX in a Phase 1/2 open-label, ascending dose clinical trial which is designed to assess the safety, tolerability and preliminary efficacy of SB-FIX in adults with severe hemophilia B. The study is currently screening subjects in the United States and the United Kingdom. Recently, we announced the treatment of the first patient in this trial and expect to announce preliminary safety and efficacy data in 2019.

We are evaluating ST-400 in a Phase 1/2 open-label, single arm clinical trial to evaluate the safety and efficacy in up to six adult subjects with beta-thalassemia. Our IND submitted to the U.S. Food and Drug Administration, or the FDA, for ST-400 became effective in September 2017. The clinical trial was initiated in March 2018 and the first patient was enrolled in August 2018 and dosed in January 2019.

In the fourth quarter of 2018, we acquired 98.2% of the outstanding share capital and voting rights of TxCell S.A., or TxCell, which we refer to in this report as the TxCell Acquisition, for aggregate purchase consideration of approximately $80.4 million. As of December 31, 2018 the fair value of the remaining outstanding free shares was approximately $1.3 million. The total fair value of the net assets acquired was approximately $81.7 million (see Note 6 to our consolidated financial statements – Acquisition of TxCell, S.A.).

With the TxCell Acquisition, 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 that 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 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.

INTRODUCTION TO TECHNOLOGY

ZFPs are Naturally Occurring Transcription Factors in Humans

A transcription factor recognizes and binds to a specific DNA sequence within or near a particular gene and causes expression of that gene to be “turned on” (activated) or “turned off” (repressed). ZFPs are the most common class of naturally occurring transcription factors in organisms from yeast to humans. To these naturally occurring transcription factors, we have added functional domains which enable genome editing at the site determined by the ZFP DNA-binding domain.

Figure 1:

Schematic of the two-domain structure of a ZFP and its therapeutic functional domain

ZFNs can be designed for genome editing and ZFP TFs can be designed for gene regulation

Consistent with the modular structure of natural ZFPs, we take a modular approach to the design of the proteins that we engineer. The ZFP portion of our engineered proteins, the DNA-recognition domain, is typically composed of four to six zinc fingers. Each individual finger recognizes and binds to a three or four base pair sequence of DNA and multiple fingers can be linked together to recognize longer stretches of DNA, thereby improving specificity. By modifying the amino acid sequence of a ZFP, we can engineer novel ZFPs capable of recognizing the DNA sequences of a chosen genomic target. We use the engineered ZFP DNA-binding domain to link to a functional domain. The ZFP DNA-binding domain brings the functional domain to the target of interest. Our ability to use our highly specific ZFP technology to precisely target a DNA sequence in a gene of interest provides us with a range of genome editing and gene regulation functions that we believe can be applied in many different cell types.

Our engineered ZFPs can be attached to a cleavage domain of a restriction endonuclease, an enzyme that cuts DNA, creating a ZFN. When a pair of ZFNs is bound to the DNA in the correct orientation and spacing, the DNA sequence is cut between the ZFP binding sites. DNA binding by both ZFNs is necessary for cleavage, and both nuclease of the restriction endonuclease must be present in the correct orientation to interact with each other, in order to mediate DNA cleavage. This break in the DNA triggers a natural process of DNA repair in the cell. The repair process can be harnessed to achieve one of several outcomes that may be therapeutically useful (Figure 2). If cells are simply treated with ZFNs alone, the repair process joins the two ends of the broken DNA together and frequently results in the loss or addition of a small amount of genetic material at the site of the break. This disrupts the original DNA sequence and can result in the expression of a truncated or non-functional protein from the targeted gene, effectively “knocking out” the gene function. ZFN-mediated genome editing can be used to disrupt genes that are involved in disease pathology. We are using ZFN-mediated genome editing of the BCL11A erythroid enhancer in hematopoietic stem progenitor cells, or HSPCs, which is designed to be a single long-lasting treatment for beta-thalassemia (ST-400) and sickle cell disease, or SCD (BIVV-003).

Figure 2:

Schematic of ZFP genome editing and gene regulation

In contrast, if cells with a mutation in a particular gene are treated not only with ZFNs, but also with a DNA sequence that encodes the correct gene sequence (referred to as a “donor” DNA) and with ZFNs that recognize and bind to sequences flanking the mutation, the cell’s repair machinery can use the donor as a template to correct the mutated gene. This ZFN-mediated gene correction enables the corrected gene to be expressed in its natural chromosomal context and may provide a novel approach for the precise repair of DNA sequence mutations responsible for certain monogenic diseases. In addition to providing a donor sequence that encodes a complete gene, a new copy of a gene can also be precisely added into the genome at a specific location. The ability to precisely place a gene-sized segment of DNA specifically into a pre-determined location in the genome broadens the range of mutations of a gene that can be corrected in a single step. It also reduces the insertional mutagenesis concerns associated with traditional integrating gene replacement approaches such as lentiviruses, in which the insertion of a new corrective copy of the gene typically occurs at random locations in the genome. Our ZFN technology is used to insert a gene encoding a therapeutic protein into a location such as the Albumin gene, is an approach that we are investigating for the treatment of hemophilia B (SB-FIX) and MPS I and MPS II (SB-318 and SB-913), which we believe may potentially provide a single and potentially curative treatment for these diseases.

We are also evaluating ZFP TFs with the potential to control or regulate the expression of a target gene in the desired manner (Figure 2). For instance, attaching an activation domain to a ZFP will cause a target gene to be expressed at enhanced levels, relative to expression in an untreated cell. Alternatively, a repression domain causes the gene to be downregulated or completely turned off. Pursuant to a collaboration agreement with Shire International GmbH, or Shire, a wholly owned subsidiary of Takeda Pharmaceutical Company Limited, or Takeda, we have a preclinical program for Huntington's disease in which we are evaluating a ZFP TF designed to differentially down regulate the mutated disease-causing Huntingtin, or HTT, gene, while leaving expression of the normal gene unchanged.

ZFPs provide the Opportunity to Develop a New Class of Human Therapeutics

We believe that our ZFP technology provides a unique and proprietary basis for a broad new class of drugs that have differential technical advantages over small-molecule drugs, protein pharmaceuticals, RNA-based therapeutics, conventional gene therapy approaches and other genome editing platforms, potentially enabling us to develop therapies for a broad range of unmet medical needs.

We can generate highly specific ZFNs for genome editing and ZFP TFs for gene regulation and have developed multiple delivery strategies to administer these therapeutics, including using mRNA, AAV, adenovirus, plasmid, and lipid nanoparticles. As more genes and DNA sequences are linked to specific diseases, we believe that the clinical breadth and scope of our ZFP applications will continue to expand.

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 Fok1 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.

In February 2019, we announced our development of second generation, potentially more potent ZFN constructs designed to increase editing efficiency. In vitro data of these second-generation ZFNs were reviewed by the FDA. The in vitro data showed three potential advantages for use in the clinic: (1) a five to thirty-fold improvement in efficiency and potency due to structural changes; (2) the ability to function equally well in the patients who have a single nucleotide polymorphism in the target locus in the albumin gene (approximately 20% of the population); (3) improvements in specificity. The second-generation ZFNs are being manufactured and we expect to have them available for use in the clinic later this year. Additional data from our in vivo genome editing programs will be assessed before potential integration plans for the second-generation ZFNs are finalized.

Advancements in T Cell Editing Capabilities

In May 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.

TxCell - Regulatory T Cells

With the TxCell Acquisition, we can now accelerate our research and development of platforms for innovative, personalized T-cell immunotherapies for the treatment of inflammatory and autoimmune diseases with high unmet medical need. Through our

subsidiary, TxCell, we believe we will accelerate our entry into the clinic with a CAR-Treg. 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.

Our CAR Tregs are composed of Tregs engineered with a CAR. The antigen specificity comes from the CAR receptor as shown below.

After their isolation from the blood of patients, Tregs are genetically modified by transduction with CAR. The CAR introduced into Tregs is designed to allow Treg activation and immuno-modulation through in vivo recognition of a protein present in inflamed areas in patients suffering from autoimmune and chronic inflammatory diseases.

THERAPEUTIC PRODUCT DEVELOPMENT

Our Product Development Programs

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, as part of a global collaboration between us and Pfizer for the development and commercialization of potential gene therapy programs for hemophilia A (See "—Collaborations—Pfizer Inc.").

In 2017, we initiated 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 clinical trial to evaluate the safety and efficacy of SB-525 in up to 20 adults with severe hemophilia A. In August 2017, we announced that the first subject was treated in our Alta Study. In August 2018, we announced positive preliminary data from the Alta Study. In October 2018, the SMC of the Alta Study reviewed accumulated safety and efficacy data from the six patients enrolled in three dose cohorts. As of that review, SB-525 exhibited dose dependent efficacy on serum factor levels and was generally well-tolerated with no treatment-related serious adverse events and no use of tapering courses of oral steroids. The SMC recommended that the study continue with escalation to an additional dose. We plan to present safety and efficacy data from the Alta Study in 2019 after dose escalation is complete and the clinical trial has progressed to the cohort expansion phase.

SB-525 has been granted Orphan Drug and Fast Track designations by the 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 potentially 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.

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 FIXtendz Study. The CTA permits evaluation of SB-FIX in adults. Recently, we announced the treatment of the first adult patient in this study and expect to announce safety and efficacy data in 2019.

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

Inherited Metabolic Diseases, or IMDs

IMDs 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.

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 heparan 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 Organization for Rare Disorders, one in 500,000 births in the United States will result in Scheie syndrome, one in 115,000 births will result in Hurler/Scheie, and one in 100,000 births will result 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 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, approximately one in 100,000 to one in 170,000 births, primarily 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, or NIH, 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 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 approved treatment options for MPS II and Fabry disease, respectively. Because of the availability of few approved treatment options that effectively and safely treat these diseases, there remains significant unmet medical need.

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 potentially reducing or eliminating the need for chronic ERT infusions.

In 2017, we initiated 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.

In October 2018, the SMC reviewed accumulated safety and efficacy data from the EMPOWERS Study. In accordance with the recommendation of the SMC, the second patient enrolled in the EMPOWERS Study received the 5e13 vg/kg dose, the highest dose.

In February 2019, we announced the interim results of the EMPOWERS Study. SB-318 demonstrated increased leukocyte IDUA activity in patients with MPS I. One patient has been dosed with 1e13 vector genomes per kilogram body weight (vg/kg) of SB-318 and two patients have been dosed with 5e13 vg/kg of SB-318. The interim results suggest a dose-dependent increase in leukocyte IDUA activity, with activity levels rising above baseline and in the normal range (normal range is 6.0-71.4 nmol/hr/mg). However, plasma IDUA activity was unchanged from baseline in all three patients. Baseline urine GAG measurements for the three patients in the EMPOWERS Study were in a range considered to be at or slightly above normal. Urine GAG measurements showed no meaningful change at the time of the announcement. Safety data were collected and analyzed for the three patients. Administration of SB-318 was generally well-tolerated. No treatment related serious adverse events have been reported. Of the six total adverse events reported, all were mild or moderate and consistent with ongoing MPS I disease, and none were considered related to SB-318 treatment. The clinical relevance of the biochemical changes observed following administration of SB-318 will be assessed as clinical data and patient outcomes are analyzed following a trial of withdrawal from ERT. ERT withdrawal is expected for these patients later in 2019. We expect to report analyses of liver biopsies later in 2019.

We have developed second generation albumin locus ZFN constructs for potential use in the ongoing in vivo genome editing development programs. We plan to initiate a clinical trial this year using these second-generation ZFNs that should enable a Phase 3 decision for the MPS II program in 2020.

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.

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.

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. Two patients are currently enrolled in each of cohort 1 (low-dose), cohort 2 (mid-dose) and cohort 3 (high-dose), along with an additional three patients, all of which have received the high dose, in an expanded cohort.

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. In September 2018 we announced updated preliminary safety and efficacy data from the CHAMPIONS Study. In cohort 2 of the CHAMPIONS study, at 16 weeks post-dosing, mean reductions were observed in total urinary GAGs (which is a key biomarker of MPS II disease pathophysiology), dermatan sulfate, and heparan sulfate of 51%, 32%, and 61%, respectively. In October 2018, the SMC of the CHAMPIONS Study reviewed accumulated safety and efficacy data from all three cohorts and made the following three recommendations: 1) proceed to the cohort expansion phase of the clinical trial with the dose used at the third dose cohort (5e13 vg/kg); 2) initiate screening and enrollment of adolescent subjects (12 to 17 years of age); and 3) initiate the withdrawal of ERT when appropriate.

In February 2019, we announced interim study results from the CHAMPIONS Study. SB-913 showed preliminary evidence of in vivo genome editing in patients with MPS II. Small increases in IDS enzyme activity compared to baseline were recorded in one patient in cohort 1 (low-dose) and two patients in cohort 2 (mid-dose) of the CHAMPIONS Study. At 24 weeks these measurements remained within the expected range for baseline values (less than 10 nmol/hour/mL, as compared to the normal range which is estimated at greater than 82 nmol/hour/mL). A more substantial increase in plasma IDS activity was measured in the second patient in cohort 3 (high-dose), with levels rising to approximately 50 nmol/hour/mL by week 6 following SB-913 administration. The plasma IDS activity levels subsequently decreased in the context of the development of a mild transaminitis – a known risk of AAV-based therapies – due to a suspected immune response. Grade 1 elevations in liver function tests were measured at Day 62, 111 and 128. The patent was hospitalized on Day 121 for an incarcerated umbilical hernia considered unrelated to the SB-913. As of the date of our February 2019 announcement, the patent's plasma IDS activity measured 14 nmol/hour/mL, above the baseline value but below the normal range. Baseline GAG measurements for all six patients were in a range considered at or slightly above normal, except for heparan sulfate which was elevated in all patients at baseline. At 24 weeks post-dosing, urine GAG results did not show a meaningful change. Safety data on eight patients were collected and analyzed. Administration of SB-913 was generally well-tolerated in all eight patients. Of the 18

total adverse events reported as related to SB-913, 16 were mild (Grade 1), two were moderate (Grade 2) and all adverse events resolved. There were no treatment-related serious adverse events reported. The clinical relevance of the biochemical changes observed following administration of SB-913 will be assessed as clinical data and patient outcomes are analyzed following a trial of withdrawal from ERT. Two mid-dose and one high-dose patients have initiated ERT withdrawal. One mid-dose patient was recommended to resume ERT approximately three months after initiation of ERT withdrawal due to fatigue and increasing GAG measurements. Analyses from these withdrawals will be available later this year.

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.

ST-920 — Fabry Disease

We are developing ST-920 for Fabry disease, 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. Our IND submitted to the FDA for ST-920 became effective in January 2019 and we expect to initiate a Phase 1/2 clinical trial in 2019.

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 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 decreases 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, Inc., or Bioverativ, a wholly owned subsidiary of Sanofi Genzyme Corporation, or Sanofi Genzyme, 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, 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 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 (>10^8 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. Preclinical 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 submitted to the FDA for ST-400 became effective 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. This trial was initiated in February 2018 and the first patient was enrolled in June 2018 and dosed in January 2019.

Bioverativ is our partner for ST-400 and is responsible for the clinical development of BIVV-003 for sickle cell disease, or SCD. The Phase 1/2 clinical trial to evaluate the safety and efficacy of BIVV-003 in up to eight adult subjects with SCD was initiated in August 2018 and patients are currently being screened in the United States. For more information relating to our collaboration with Bioverativ, see "—Collaborations—Bioverativ, Inc."

CAR-Treg

With the TxCell Acquisition, 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

that 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 plan to initiate a Phase 1/2 clinical trial of for TX-200, our first CAR-Treg investigational product candidate for solid organ transplant, in 2019.

Engineered Cell Therapies

In February 2018, we entered into a worldwide collaboration with Kite Pharma, Inc., or Kite, a wholly owned subsidiary of Gilead Sciences, Inc., or Gilead, using our ZFN technology platform for the development of next-generation ex vivo cell therapies in oncology.

Central Nervous System

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 central nervous system, or 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 FTLD linked to mutations of the C9ORF72 gene. ALS and FTLD 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 FTLD. Currently, there are no cures to halt or reverse the progression of ALS or FTLD. 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.

We also have research stage programs in other monogenic diseases, immunology and cancer immunotherapy. See "—Collaborations—Pfizer Inc." for more information relating to this agreement.

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. For more information on our collaboration with Shire, see "—Collaborations—Shire International GmbH."

Legacy Clinical Research Programs

Human Immunodeficiency Virus, or HIV, and Acquired Immunodeficiency Syndrome, or AIDS

HIV infection results in the death of immune system cells, particularly CD4+ T-cells, and thus leads to AIDS, a condition in which the body's immune system is depleted to such a degree that the patient is unable to fight off common infections. Ultimately, these patients succumb to opportunistic infections or cancers.

Current Treatments and Unmet Medical Need

Currently, there are over 30 antiretroviral drugs approved by the FDA to treat people infected with HIV. While these drugs can suppress virus in the blood to undetectable levels, they cannot eliminate the reservoir of cells containing genomically-integrated HIV from the body. Hence, individuals infected with HIV need to take antiretroviral drugs continuously. The drugs are expensive and can have significant side effects over time. There is no therapeutic approach available that protects CD4+ T-cells, suppresses viral load, reduces the viral reservoir and does not require daily dosing.

SB-728 – HIV/AIDS

SB-728 uses our ZFN-mediated genome editing technology to disrupt the CCR5 gene in cells of a patient's immune system to make these cells permanently resistant to HIV infection. CCR5 is a co-receptor for HIV entry into T-cells and if CCR5 is not expressed on the cell surface HIV cannot infect them or infects them with lower efficiency. The aim of this approach is to provide the patient with a population of HIV-resistant cells that can fight HIV and opportunistic infections, by mimicking the naturally occurring CCR5 delta-32 mutation that renders a population of individuals largely resistant to infection by the most common strains of HIV. We are evaluating this genome editing approach to disrupt the CCR5 gene in both T cells and HSPCs as two potential therapeutic candidates, SB-728-T and SB-728-HSPC, respectively.

We have conducted several clinical trials with SB-728-T, which were designed to evaluate safety and tolerability of SB-728-T, as well as the effect of SB-728-T on subjects' CD4 T-cell counts, levels of CCR5-modified T-cells, viral burden during a treatment interruption (TI) from anti-retroviral therapy, or ART, and measure of the viral reservoir. The data to date have demonstrated an ability to efficiently knock out the CCR5 gene in T-cells by ZFN-driven genome editing and grow the cells ex vivo, that a single infusion of SB-728-T led to proven engraftment, expansion and persistence of T-cells in vivo, sustained increases in CD4 T-cell counts, a significant and continuous decay of the HIV reservoir and the ability of certain subjects to control their viral loads for prolonged periods in the absence of ART. Over 100 subjects have been treated to date and the treatment appears to be well-tolerated.

In addition, we have an ongoing investigator-sponsored Phase 1/2 clinical trial (SB-728mR-HSPC) to investigate SB-728-HSPC as a self-renewable and potentially lifelong source of HIV-resistant immune cells.

We plan to advance the SB-728 program through potential future externally-funded collaborations.

COLLABORATIONS

We have established collaborative and strategic partnerships for several of our therapeutic programs and also for several non-therapeutic applications of our technology. We will continue to pursue further partnerships when appropriate with selected pharmaceutical and biotechnology companies to fund internal research and development activities and to assist in product development and commercialization. Our partnering decisions 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. We are applying our ZFN technology platform to several commercial applications in which our products provide us and our strategic partners and collaborators with potential technical, competitive and economic advantages.

Kite Pharma, Inc.

In February 2018, we entered into a collaboration and license agreement with Kite, a wholly-owned subsidiary of Gilead, for the research, development and commercialization of potential engineered cell therapies for cancer. Kite will be responsible for all

clinical development and commercialization of any resulting products. The Kite agreement became effective on April 5, 2018, when the waiting periods under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, and other customary closing conditions were completed.

Subject to the terms of this agreement, we granted Kite an exclusive, royalty-bearing, worldwide, sublicensable license, under our relevant patents and know-how, to develop, manufacture and commercialize, for the purpose of treating cancer, specific cell therapy products that may result from the research program and that are engineered ex vivo using selected ZFNs and AAVs developed under the research program, to express CARs, TCRs or NKRs directed to candidate targets.

During the research program term and subject to certain exceptions, except pursuant to this agreement, we will be prohibited from researching, developing, manufacturing and commercializing, for the purpose of treating cancer, any cell therapy product that, as a result of ex vivo genome editing, expresses a CAR, TCR or NKR that is directed to a target expressed on or in a human cancer cell. After the research program term concludes and subject to certain exceptions, except pursuant to this agreement, we will be prohibited from developing, manufacturing and commercializing, for the purpose of treating cancer, any cell therapy product that, as a result of ex vivo genome editing, expresses a CAR, TCR or NKR that is directed to a candidate target.

We received a $150 million upfront payment from Kite when the Kite agreement became effective in April 2018. In addition, Kite will reimburse our direct costs to conduct the joint research program, and Kite will be responsible for all subsequent development, manufacturing and commercialization of any licensed products. We are also eligible to receive contingent development- and sales-based milestone payments that could total up to $3.01 billion if all the specified milestones set forth in this agreement are achieved. Of this amount, approximately $1.26 billion relates to the achievement of specified research, clinical development, regulatory and first commercial sale milestones, and approximately $1.75 billion relates to the achievement of specified sales-based milestones if annual worldwide net sales of licensed products reach specified levels. Each development- and sales-based milestone payment is payable (i) only once for each licensed product, regardless of the number of times that the associated milestone event is achieved by such licensed product, and (ii) only for the first ten times that the associated milestone event is achieved, regardless of the number of licensed products that may achieve such milestone event. In addition, we will be entitled to receive escalating, tiered royalty payments with a percentage in the single digits based on potential future annual worldwide net sales of licensed products. These royalty payments will be subject to reduction due to patent expiration, entry of biosimilar products to the market and payments made under certain licenses for third-party intellectual property.

Kite has the right to terminate this agreement, in its entirety or on a per licensed product or per candidate target basis, for any reason after a specified notice period. Each party has the right to terminate this agreement on account of the other party’s bankruptcy or material, uncured breach.

Pfizer Inc.

We have two separate collaboration agreements with Pfizer. In May 2017, we entered into an exclusive, global collaboration and license agreement with Pfizer, pursuant to which we established a collaboration 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 may also collaborate in the research and development of additional AAV-based gene therapy products for hemophilia A.

We received an upfront fee of $70.0 million and are eligible to receive development milestone payments contingent on the achievement of specified clinical development, intellectual property, regulatory and first commercial sale milestones for SB-525 and potentially other products. The total amount of potential clinical development, intellectual property, regulatory, and first commercial sale milestone payments, assuming the achievement of all specified milestones in this agreement, is $475.0 million, which includes up to $300.0 million for SB-525 and up to $175.0 million for other products that may be developed under the agreement, subject to reduction on account of payments made under certain licenses for third party intellectual property. In addition, Pfizer agreed to pay us royalties for each potential licensed product developed under the agreement that are an escalating tiered, double-digit percentage of the annual net sales of such product and are subject to reduction due to patent expiration, entry of biosimilar products to the market and payment made under certain licenses for third party intellectual property.

Subject to the terms of the agreement, we granted Pfizer an exclusive, worldwide, royalty-bearing license, with the right to grant sublicenses, to use certain technology controlled by us for the purpose of developing, manufacturing and commercializing SB-525 and related products. Pfizer granted us a non-exclusive, worldwide, royalty free, fully paid license, with the right to grant sublicenses, to use certain manufacturing technology developed under the agreement and controlled by Pfizer to manufacture our products that utilize the AAV delivery system. During a specified period, neither we nor Pfizer will be permitted to clinically develop or commercialize, outside of the collaboration, certain AAV-based gene therapy products for hemophilia A.

Unless earlier terminated, the agreement has a term that continues, on a per product and per country basis, until the later of (i) the expiration of patent claims that cover the product in a country, (ii) the expiration of regulatory exclusivity for a product in a country, and (iii) fifteen years after the first commercial sale of a product in a country. Pfizer has the right to terminate the agreement without cause in its entirety or on a per product or per country basis. The agreement may also be terminated by either party based on an uncured material breach by the other party or the bankruptcy of the other party. Upon termination for any reason, the license granted by us to Pfizer to develop, manufacture and commercialize SB-525 and related products will automatically terminate. Upon termination by us for cause or by Pfizer any country or countries, Pfizer will automatically grant us an exclusive, royalty-bearing license under certain technology controlled by Pfizer to develop, manufacture and commercialize SB-525 in the terminated country or countries.

In December 2017, we entered into a separate exclusive, global collaboration and license agreement with Pfizer for the development and commercialization of potential gene therapy products that use ZFP-TFs to treat ALS and FTLD linked to mutations of the C9ORF72 gene. Pursuant to this agreement, we agreed to work with Pfizer on a research program to identify, characterize and preclinically develop ZFP-TFs that bind to and specifically reduce expression of the mutant form of the C9ORF72 gene.

We received a $12.0 million upfront payment from Pfizer and are eligible to receive up to $60.0 million in development milestone payments from Pfizer contingent on the achievement of specified preclinical development, clinical development and first commercial sale milestones, and up to $90.0 million commercial milestone payments if annual worldwide net sales of the licensed products reach specified levels. In addition, Pfizer will pay us royalties based on an escalating tiered, mid- to high-single digit percentage of the annual worldwide net sales of the licensed products. These royalty payments are subject to reduction due to patent expiration, entry of biosimilar products to the market and payments made under certain licenses for third party intellectual property. Each party will be responsible for the cost of its performance of the research program. Pfizer will be operationally and financially responsible for subsequent development, manufacturing and commercialization of the licensed products.

Subject to the terms of the agreement, we granted Pfizer an exclusive, royalty-bearing, worldwide, license under our relevant patents and know-how to develop, manufacture and commercialize gene therapy products that use resulting ZFP-TFs that satisfy pre-agreed criteria. During a specified period, neither our company nor Pfizer will be permitted to research, develop, manufacture or commercialize outside of the collaboration any ZFPs that specifically bind to the C9ORF72 gene.

Unless earlier terminated, the agreement has a term that continues, on a per licensed product and per country basis, until the later of (i) the expiration of patent claims that cover the licensed product in a country, (ii) the expiration of regulatory exclusivity for a licensed product in a country, and (iii) fifteen years after the first commercial sale of a licensed product in a major market country. Pfizer has the right to terminate the agreement without cause in its entirety or on a per product or per country basis. The agreement may also be terminated by either party based on an uncured material breach by the other party or the bankruptcy of the other party. The agreement will also terminate if we are unable to identify any lead candidates for development within a specified period of time or if Pfizer elects not to advance a lead candidate beyond a certain development milestone within a specified period of time. Upon termination for any reason, the license granted by us to Pfizer to develop, manufacture and commercialize licensed products under the agreement will automatically terminate. Upon termination by us for cause or by Pfizer without cause for any licensed product or licensed products in any country or countries, we will have the right to negotiate with Pfizer to obtain a non-exclusive, royalty-bearing license under certain technology controlled by Pfizer to develop, manufacture and commercialize the licensed product or licensed products in the terminated country or countries.

Following termination by us for Pfizer’s material breach, Pfizer will not be permitted to research, develop, manufacture or commercialize ZFPs that specifically bind to the C9ORF72 gene for a period of time. Following termination by Pfizer for our material breach, we will not be permitted to research, develop, manufacture or commercialize ZFPs that specifically bind to the C9ORF72 gene for a period of time.

Bioverativ Inc.

In January 2014, we entered into an exclusive worldwide collaboration and license agreement with Bioverativ, a wholly-owned subsidiary of Sanofi Genzyme, to develop therapeutics for hemoglobinopathies, focused on beta-thalassemia and SCD. Under the agreement, we are jointly conducting two research programs: the beta-thalassemia program and the SCD program. In the beta-thalassemia program, we are responsible for all discovery, research and development activities through the first human clinical trial. In the SCD program, both parties are responsible for research and development activities through the submission of an IND application for ZFP therapeutics intended to treat SCD. Bioverativ reimburses us for agreed upon internal and external program-related costs.

Under both programs, Bioverativ is responsible for subsequent worldwide clinical development, manufacturing and commercialization of licensed products developed under the agreement. At the end of the specified research terms for each program or under certain specified circumstances, Bioverativ has the right to step in and take over any of our remaining activities. Furthermore, we have an option to co-promote in the United States any licensed products to treat beta-thalassemia and SCD developed under the agreement, and Bioverativ will compensate us for such co-promotion activities. Subject to the terms of the agreement, we have

granted Bioverativ an exclusive, royalty-bearing license, with the right to grant sublicenses, to use certain ZFP and other technology controlled by us for the purpose of researching, developing, manufacturing and commercializing licensed products developed under the agreement. We have also granted Bioverativ a non-exclusive, worldwide, royalty-free, fully paid license, with the right to grant sublicenses, under our interest in certain other intellectual property developed pursuant to the agreement. During the term of the agreement, we are not permitted to research, develop, manufacture or commercialize, outside of the agreement, certain gene therapy products that target genes relevant to the licensed products.

Under the agreement, we received an upfront license fee of $20.0 million and are eligible to receive development and sales milestone payments upon the achievement of specified regulatory, clinical development and sales milestones. The total amount of potential regulatory, clinical development, and sales milestone payments, assuming the achievement of all specified milestones in the agreement, is $276.3 million. In addition, we will receive royalty payments for each licensed product that are a tiered double-digit percentage of annual net sales of each product.

The agreement may be terminated by (i) us or Bioverativ for the uncured material breach of the other party, (ii) us or Bioverativ for the bankruptcy or other insolvency proceeding of the other party; (iii) Bioverativ, upon 180 days' advance written notice to us and (iv) Bioverativ, for certain safety reasons upon written notice to, and after consultation with, us. As a result, actual future milestone payments could be lower than the amounts stated above.

Shire International GmbH

In January 2012, we entered into a collaboration and license agreement with Shire, a wholly-owned subsidiary of Takeda, to research, develop and commercialize human therapeutics and diagnostics for monogenic diseases based on our ZFP technology. We received an upfront license fee of $13.0 million in 2012 and recognized a $1.0 million milestone payment in 2014. In September 2015, we amended and restated our agreement with Shire. Pursuant to the amended and restated agreement, Shire retained its exclusive, worldwide license to ZFP therapeutics for treating Huntington's disease and returned to us the worldwide, exclusive rights to gene targets for the development and commercialization of ZFP therapeutics for hemophilia A and B.

Under the amended and restated agreement, Shire has full control over, and full responsibility for the costs of, the Huntington's disease program retained by Shire, subject to certain obligations, including the obligation to retain us to perform ZFP design, optimization and assessment services and to reimburse us for the costs of such services. Shire does not have any milestone payment obligations but is required to pay single digit percentage royalties to us, up to a specified maximum cap, on the commercial sales of ZFP therapeutic products for Huntington's disease. During the term of the amended and restated agreement, we are not permitted to research, develop or commercialize, outside of the agreement, certain products that target the HTT gene.

Under the amended and restated agreement, we have full control over, and full responsibility for the costs of, the hemophilia A and B programs returned to us by Shire, subject to certain diligence obligations. We also granted Shire a right of first negotiation to obtain a license to such programs under certain circumstances. We are required to pay single digit percentage royalties to Shire, up to a specified maximum cap, on commercial sales of therapeutic products from the programs returned to us by Shire.

The amended and restated agreement may be terminated by (i) us or Shire, in whole or in part, for the uncured material breach of the other party, (ii) us or Shire for the bankruptcy or other insolvency proceeding of the other party and (iii) Shire, in its entirety, effective upon at least 90 days' advance written notice.

Other Partnerships

In addition to our partnerships for the development of human therapeutic applications, we have also licensed our technology in several other areas, such as plant agriculture and research reagents, including the production of

transgenic animals and cell-line engineering. These license partners include Dow AgroSciences LLC, Sigma-Aldrich Corporation, Genentech, Inc., Open Monoclonal Technology, Inc. and F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc.

INTELLECTUAL PROPERTY

Patents and licenses are important to our business. Our strategy is to file or license patent applications to protect technology, inventions and improvements to inventions that we consider important for the development of our genome editing and gene regulation technology. We seek patent protection and licenses that relate to our technology and candidates in our pipeline and/or may be important to our future. We have filed numerous patents and patent applications with the United States Patent and Trademark Office, or U.S. PTO, and foreign jurisdictions. This proprietary intellectual property includes methods relating to the design of zinc finger, Transcription Activator-Like Effector, or TALE, proteins and Clustered Regularly Interspaced Short Palindromic Repeats, or CRISPR/Cas editing systems, therapeutic applications of genome editing technology, enabling technologies related to our platform and the use of genome editing across a variety of applications. We rely on a combination of patent, copyright, trademark, proprietary

know–how, continuing technological innovations, trade secret laws, as well as confidentiality agreements, materials transfer agreements, research agreements and licensing agreements, to establish and protect our proprietary rights.

In-Licensed Technology

We have exclusively licensed intellectual property directed to the design, selection, and use of ZFPs, ZFNs and ZFP TFs for genome editing and gene regulation from the California Institute of Technology, or Cal Tech, and the University of Utah, or Utah. These licenses grant us exclusive rights to make, use and sell ZFPs, ZFNs and ZFP TFs under three families of patent filings. As of February 15, 2019, these patent filings have resulted in over nine issued U.S. patents and over 26 granted foreign patents and are still active, with one pending U.S. patent application and 2 pending applications in foreign patent offices.

Our license agreement with CalTech granted us a worldwide exclusive license to certain patents related to chimeric nucleases for genome targeting for all fields of use, which expire in September 2023. Our license agreement with Utah granted us a worldwide exclusive license to technology and patents relating to the use of ZFNs for all fields of use, which expires in May 2025.

We have also entered into licenses potentially useful for specific therapeutic uses of our genome editing technologies with the Regents of the University of California or UC, and the Children's Medical Center Corporation or CMCC. The patents included in these licenses relate to CNS disorders and hemoglobinopathies, respectively. These licenses include three patent families, including three issued U.S. patents, 12 allowed or granted foreign patents, over 25 pending foreign patent applications and three pending U.S. patent applications. The UC patents expire in May of 2021, the first CMCC family expires in September 2029, and the second expires in November 2033.

Our subsidiary, TxCell has a license agreement with the University of British Columbia pursuant to which it exclusively licensed the right to the CAR for use in TX-200. This license includes one patent family which expires in September 2038.

Our Intellectual Property

In addition to our in-licensed patent portfolio, we have numerous issued patents and pending patent filings directed to the design, composition and use of ZFPs, ZFNs, ZFP TFs, TALE proteins and CRISPR/Cas systems and other technology related to our program.

Some of the earliest zinc finger patents in our portfolio began expiring in 2015, with the average expiration of our currently issued patents expiring being late-2026. However, we have continued to build on this patent portfolio and have been issued additional patents and have applications pending that provide protection for our ZFP technology. These patents in our portfolio may be subject to Patent Term Adjustment (due to delays in patent prosecution by the USPTO), Patent Term Extension (due to review of a patented product by a regulatory agency) or terminal disclaimer. Additionally, patents that may be issued from our pending applications will extend the patent exclusivity of our patent estate.

We believe that our licensed patents and patent applications, as well as our issued patents and pending patent applications, in the aggregate, will provide us with a substantial intellectual property position in our commercial development of our genome editing, gene therapy, cell therapy and gene regulation programs. In this regard, patents issued to us, applied for by us, or exclusively and non-exclusively licensed to us, cover the following types of inventions, processes and products:

- ZFP and ZFN design, engineered nucleases, and compositions (four patents issued with expiration dates ranging from 2029 to 2036): includes DNA target site selection, zinc finger binding domain design, nuclease domain design, linker design, DNA nickases, ZFP libraries databases and methods of construction, as well as methods to increase

zinc finger binding specificity (see, e.g., US9982245, US10066242, US10113207);

- ZFP Therapeutics (three patents issued with expiration dates ranging from 2028 to 2031): Methods relating to activation and inhibition of endogenous genes, identification of accessible regions within chromatin, including treatment of Huntington's disease, HIV, cancer therapeutics, modulation of cardiac contractility and methods to regulate the glucocorticoid receptor (see, e.g., US9943565);
- Nuclease Therapeutics (12 patents issued with expiration dates ranging from 2031 to 2036): Treatments for HIV, beta-thalassemia and SCD, hemophilia IMDs, genome editing, Parkinson's Disease, regulation of the expression of PD1; Immunomodulatory therapeutics; Cystic Fibrosis; CNS disease; Severe combined immunodeficiency, Modified T cells, including HLA knock out and methods of editing stem cells (see, e.g., US9877988, US9963715, US10072066, US10081661, US10143760); and
- Non-Therapeutic Applications of ZFPs and Nucleases (seven patents issued with expiration dates ranging from 2028 to 2035): Identification of regulatory sequences, analysis of gene regulation, structure and biological function, methods of agricultural biotechnology, methods of altering cellular differentiation state, development of cell lines for improved protein

production, methods of transgenic animal development, engineering of stem cells, methods of genome editing (see, e.g., US9890395).

The patent positions of pharmaceutical and biotechnology firms, including our patent position, are uncertain and involve complex legal and factual questions for which important legal tenets are largely unresolved and are subject to interpretation and refinement by the court system. Patent applications may not result in the issuance of patents and the coverage claimed in a patent application may be significantly reduced before a patent is issued. Although we have filed for patents on some aspects of our technology, we cannot provide assurances that patents will be issued as a result of these pending applications or that any patent that has been or may be issued will be upheld. The laws of some foreign countries may not protect our proprietary rights to the same extent as do the laws of the United States. For example, our issued European patents EP2171052 and EP2527435 have been opposed in Europe. Our EP2281050 case was revoked during Opposition in November 2016. EP2126054, which is exclusively licensed to TxCell, was revoked during Opposition in November 2018. Similarly, EP2171052 and EP2527435 underwent Opposition hearings in early 2017. Although these cases emerged from the Opposition hearings, the opponent filed appeals that are currently underway, and we do not know what the outcome of these procedures will be. The claims of these patents may be amended such that claim scope is reduced or the patents may be revoked as a result of these procedures.

In the future, third parties may assert patent, copyright trademark, and other intellectual property rights to technologies that are important to our business. For example, TxCell has exclusively licensed the rights to technology related to redirected Treg cells from the Yeda Research and Development Company, or Yeda. A patent included in this exclusive license agreement with Yeda was granted in Europe in July 2016. Subsequent to this grant, the patent was opposed by several parties in May 2017 and revoked in November 2018. The outcome following legal assertions of invalidity and unenforceability is unpredictable. Any claims asserting that our products infringe or may infringe proprietary rights of third parties, if determined adversely to us, could significantly harm our business. See “Risk Factors—Risks Relating to Our Intellectual Property”.

COMPETITION

We, and our licensed partners, are the leaders in the research, development, and commercialization of DNA binding proteins for genome editing and regulation of gene expression. We are aware of several companies focused on other methods for editing genes and regulating gene expression and a limited number of commercial and academic groups pursuing the development of ZFP gene regulation and genome editing technology. The field of applied gene regulation and genome editing is highly competitive and we expect competition to persist and intensify in the future from a number of different sources, including pharmaceutical and biotechnology companies; academic and research institutions; and government agencies that will seek to develop ZFPs as well as technologies that will compete with our ZFP technology platform, such as TALE proteins and the CRISPR/Cas9 system.

Accordingly, our competitors may succeed in obtaining patent protection, receiving FDA approval, or commercializing competitive products before us. If we commence commercial product sales, we may be competing against companies with greater marketing, sales, distribution and manufacturing capabilities, areas in which we have limited or no experience. In addition, any product candidate that we successfully develop may compete with existing products that have long histories of safe and effective use.

Although we are in the clinical development phase of operations and have no current therapeutic product sales, we believe the following companies, products and/or technologies may potentially be competitive with our technology or our product candidates under development:

- Protein pharmaceuticals under development at pharmaceutical and biotechnology companies such as Pfizer, Bayer AG, Novo Nordisk A/S, Genzyme Corp., Shire, BioMarin Pharmaceutical Inc., Biogen Inc., Acceleron Pharma Inc., ArmaGen, Inc., Protalix Biotherapeutics, Inc., F. Hoffman-LaRoche Ltd., Novartis AG, or Novartis, and numerous other pharmaceutical and biotechnology firms.
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Gene therapy companies developing gene-based products in clinical trials. Orchard Therapeutics plc's Strimvelis™ (acquired from GlaxoSmithKline plc, or GSK) is approved in Europe and Spark Therapeutics, Inc.'s LUXTURNA™ is approved in the United States and Europe. Other competitors in this category may include, but not be limited to, uniQure N.V., BioMarin Pharmaceutical Inc., bluebird bio, Inc., REGENXBIO Inc., Ultragenyx Pharmaceutical Inc., Voyager Therapeutics, Inc., Shire, Pfizer, Freeline Therapeutics and Novartis.

- Cell therapy companies developing cell-based products. Novartis' Kymriah™ and Gilead's Yescarta™, two gene-modified cell-based therapies, are approved in both the United States and Europe. Other competitors in this category may include, but not be limited to, Adaptimmune Therapeutics PLC, bluebird bio, Inc., Cellectis S.A., Juno Therapeutics, Inc., Kite / Gilead, AvroBio, Inc., Medeor Therapeutics, Inc., CRISPR Therapeutics AG, Intellia Therapeutics, Inc., Casebia Therapeutics, Targazyme, Inc., ZIOPHARM Oncology, Inc., Tmunity Therapeutics, Inc., Caladrius Biosciences, Inc., TRACT Therapeutics, Inc., Cellenkos™, Inc., Regcell Co., Ltd. and Celgene Corporation, or Celgene.

- Nuclease technologies under development for therapeutic applications of genome modification including companies such as Editas Medicine, Inc., CRISPR Therapeutics AG, Caribou Biosciences, Inc. and Intellia Therapeutics, Inc. developing the CRISPR/Cas9 system, Cellectis S.A. developing TALE nucleases and meganucleases, bluebird bio, Inc. developing Homing Endonucleases and MegaTALs and Precision BioSciences, Inc. developing meganucleases.
- Antisense therapeutics and RNA interference technology, including RNAi and microRNA, which are technologies that may compete with us in the development of novel therapeutic products acting through the regulation of gene expression. These technologies are being developed by several companies including Alnylam Pharmaceuticals, Inc., Ionis Pharmaceuticals, Inc., Sanofi Genzyme and Regulus Therapeutics Inc.
- Small molecules in development from both in-house drug discovery programs of pharmaceutical companies such as Pfizer, GSK, Novartis AG and Merck & Co., Inc., as well as from biotechnology companies with expertise and capabilities in small molecule discovery and development such as Gilead, Sanofi Genzyme, Celgene and Global Blood Therapeutics, Inc., which has a small molecule product in development for SCD.
- Monoclonal antibody companies and product candidates from certain biotechnology firms such as Genentech, Inc. and Amgen Inc.

We expect to face intense competition from other companies for collaborative arrangements with pharmaceutical and biotechnology companies for establishing relationships with academic and research institutions, for licenses to proprietary technology and for subjects in our clinical trials of treatments for rare diseases. These competitors, either alone or with their collaborative partners, may succeed in developing technologies or products that are more effective or less costly than ours.

Our ability to compete successfully will depend, in part, on our ability to:

- develop safe, efficacious and commercially attractive proprietary products;
- obtain access to gene transfer technology on commercially reasonable terms;
- obtain required regulatory approvals;
- obtain reimbursement for our products in approved indications;
- attract and retain qualified scientific and product development personnel;
- enter into collaborative and strategic partnerships with others, including our competitors, to develop our technology and product candidates;
- obtain and enforce patents, licenses or other proprietary protection for our products and technologies;
- formulate, manufacture, market and sell any product that we develop;
- develop and maintain products that reach the market first and are technologically superior to or are of lower cost than other products in the market; and
- recruit subjects into our clinical trials in a timely fashion.

MANUFACTURING

We rely on contract manufacturing organizations, or CMOs, to produce our preclinical and clinical product candidates in accordance with FDA and EMA mandated regulations, also known as current good manufacturing practices, or cGMPs. We employ a technical operations staff in the areas of process development, analytical development, quality control, quality assurance, project management, and manufacturing to facilitate appropriate oversight of our CMOs, support of our regulatory filings and execution of clinical trials. In 2017, we expanded our services agreement with Brammer Bio MA, LLC to provide dedicated capacity to supply our preclinical and clinical programs. Additionally, we plan to build a cGMP manufacturing facility in our new building in Brisbane, CA for which we are currently occupying the 2nd and 3rd floors. This facility will be designed to manufacture Phase 1/2 clinical trial supplies for our pipeline programs. We believe this balanced approach to manufacturing, investing in internal capacity/capabilities while strengthening our commitment to external capacity, will enable us to meet our anticipated pipeline needs.

We currently leverage three distinct manufacturing platforms: AAV vector production for our genome editing and gene therapy product candidates, HSPC modification for our cell therapy product candidates and engineered T cell

therapies. We use a commercial scale baculovirus manufacturing platform to manufacture AAV vectors for genome editing and gene therapy, with each AAV vector packaging a different transgene specific to the target indication or ZFN. The manufacturing process for our HSPC cell therapy product candidates utilizes the patient's own HSPCs. These HSPCs are transfected using mRNA to produce ZFNs that target specific DNA sites, resulting in modified HSPCs. The third platform utilizes our ZFN technology to transform CAR-Tregs for autologous and

allogeneic cell therapies. With the acquisition of TxCell, we also added capabilities to manufacture regulator T-cells in therapeutic quantities to be used to treat auto-immune disorders.

GOVERNMENT REGULATION

We operate within the heavily regulated pharmaceutical framework and much of our operations, including nonclinical and clinical trials, development, manufacturing, commercialization, marketing and reimbursement are subject to regulatory approvals. Relevant regulatory authorities include, but are not limited to, the FDA, the EMA, Commission of the European Union, or EU member state agencies, including the UK Medicines and Healthcare Products Regulatory Agency, or MHRA.

In the United States, the FDA regulates biologic products including gene therapy and human cellular therapy products under the Federal Food, Drug, and Cosmetic Act, or the FDCA, the Public Health Service Act, or the PHSA, and regulations and guidance implementing these laws. The FDCA, PHSA and their corresponding regulations govern, among other things, the testing, manufacturing, safety, efficacy, labeling, packaging, storage, record keeping, distribution, reporting, advertising and other promotional practices involving biologic products. Applications to the FDA are required before conducting human clinical testing of biologic products and in the European Union approval must be obtained from the EMA. FDA approval also must be obtained before marketing of biologic products. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources and we may not be able to obtain the required regulatory approvals.

Accelerated Assessment

A number of agencies, including the FDA and the EMA, have accelerated approval programs, including for innovative products and in areas of high unmet medical need, such as PRIME in the EU. These programs require a certain level of evidence demonstrating safety and efficacy in patients from early stage clinical trials. Entry into one of these accelerated schemes may result in assistance with the scientific opinion and faster approval timelines. Some of these programs may offer joint approval and reimbursement advice. It is noted that even applications in an accelerated assessment scheme may be assessed under standard timelines, where the regulatory authority deems it necessary to address more questions.

U.S. Biologic Products Development Process

Our product candidates must be approved by the FDA before they may be legally marketed in the United States. The process required by the FDA before a biologic product candidate may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests and in vivo studies in accordance with the FDA's current Good Laboratory Practice, or GLP, regulations and applicable requirements for the humane use of laboratory animals or other applicable regulations;
- submission to the FDA of an application for an IND exemption, which allows human clinical trials to begin unless FDA objects within 30 days;
- approval by an independent institutional review board, or IRB, reviewing each clinical site before each clinical trial may be initiated;
- performance of adequate and well controlled human clinical trials according to the FDA's GCP regulations, and any additional requirements for the protection of human research subjects and their health information, to establish the safety and efficacy of the proposed biologic product candidate for its intended use;
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preparation and submission to the FDA of a biologics license application, or BLA, for marketing approval that includes substantial evidence of safety, purity and potency from results of nonclinical testing and clinical trials;

- review of the product by an FDA advisory committee, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the biologic product candidate is produced to assess compliance with cGMP requirements and to assure that the facilities, methods and controls are adequate to preserve the biologic product candidate's identity, safety, strength, quality, potency and purity;
- potential FDA audit of the nonclinical and clinical trial sites that generated the data in support of the BLA; and

- payment of user fees and FDA review and approval, or licensure, of the BLA.

Before testing any biologic product candidate in humans, including a gene therapy product candidate, the product candidate must undergo preclinical testing. Preclinical tests, also referred to as nonclinical studies, include laboratory evaluations of product chemistry, toxicity and formulation, as well as in vivo studies to assess the potential safety and activity of the product candidate and to establish a rationale for therapeutic use. The conduct of the preclinical tests must comply with federal regulations and requirements including GLPs.

Concurrent with clinical trials, companies usually must complete some long term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the drug in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final drug product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

Human gene transfer protocols are subject to the FDA's oversight and other clinical trial regulations, and oversight at the local level as set forth in NIH Guidelines. Specifically, under the NIH Guidelines, supervision of human gene transfer trials includes evaluation and assessment by an institutional biosafety committee, or IBC, a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment, and such review may result in some delay before initiation of a clinical trial. Compliance with the NIH Guidelines is mandatory for investigators at institutions receiving NIH funds for research involving recombinant DNA. However, many companies and other institutions, not otherwise subject to the NIH Guidelines, voluntarily follow them.

The clinical trial sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA also may impose clinical holds on a biologic product candidate at any time before or during clinical trials due to safety concerns or non compliance. If the FDA imposes a clinical hold, trials may not recommence without FDA authorization and then only under terms authorized by the FDA. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical studies to begin, or that, once begun, issues will not arise that suspend or terminate such studies.

EU Drug Development Process

Similar to the United States, the EU regulatory framework sets both EU-wide and national, Member State-specific requirements for the development and approval of medicinal products. Article 8(3) of Directive 2001/83/EC sets out the contents of a marketing authorization, or MA, application and all the information that must be submitted for the evaluation of a medicinal product. Certain preclinical (also termed "non-clinical") data is required in order to enable clinical trials and later be used in dossier for a marketing authorization application. All studies should take place in accordance with GLP and all applicable EMA, Commission and European Pharmacopoeia guidelines on preclinical studies, including guidance on quality, non-clinical and clinical aspects of medicinal products containing genetically modified cells.

The requisite amount of preclinical data enables the design of a clinical trial, from Phase I (first-in-human clinical trials) through to Phases II and III, which are safety and efficacy and dosing studies and similar restrictions and requirements apply as in the US regarding preclinical data, approvals for trials using vectors. The preclinical tests

should establish parameters such as toxicity, pharmacodynamics and pharmacokinetic properties, the quality of gene transfer medicinal products. Due to the particular nature of gene therapy medicinal products, it is recognized that that it may not always be possible for the non-clinical safety studies to be in conformity with the principles of GLP and a proper justification should be submitted where a pivotal non-clinical safety study has not been conducted under GLP rules.

Clinical studies are crucial to obtaining the required data and the requirements governing the conduct of clinical trials are further analyzed below.

All medicinal products and advanced therapy medicinal products, or ATMPs, must be manufactured in accordance with the guidelines on GMP, and in a GMP licensed facility, which can be subject to GMP inspections.

Human Clinical Trials Under an IND

Clinical trials involve the administration of the biologic product candidate to healthy volunteers or patients under the supervision of qualified investigators which generally are physicians not employed by, or under, the control of the trial sponsor. Clinical trials are conducted under written study protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters to be used to monitor subject safety, including stopping rules that assure a clinical trial will be stopped if certain adverse events should occur. Each protocol and any amendments to the protocol must be submitted to the FDA as part of the IND. Clinical trials must be conducted and monitored in accordance with the FDA's regulations comprising the GCP requirements, including the requirement that all research subjects provide informed consent.

Further, each clinical trial must be reviewed and approved by an IRB at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers items such as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the form and content of the informed consent that must be signed by each clinical trial subject, or their legal representative, reviews and approves the study protocol, and must monitor the clinical trial until completed.

Human clinical trials typically are conducted in three sequential phases that may overlap or be combined:

- Phase 1. The biologic product candidate initially is introduced into a small number of human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early understanding of its effectiveness. Phase 1 clinical trials of gene therapies are typically conducted in patients rather than healthy volunteers.
- Phase 2. The biologic product candidate is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product candidate for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule.
- Phase 3. Phase 3 clinical trials are commonly referred to as "pivotal" studies, which typically denotes a study which presents the data that the FDA or other relevant regulatory agency will use to determine whether or not to approve a biologic product. In Phase 3 studies, the biologic product candidate is administered to an expanded patient population, generally at multiple geographically dispersed clinical trial sites in adequate and well controlled clinical trials to generate sufficient data to statistically confirm the potency and safety of the product for approval. These clinical trials are intended to establish the overall risk/benefit ratio of the product candidate and provide an adequate basis for product labeling.

Post approval clinical trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial approval. These clinical trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication, particularly for long term safety follow up. Sometimes approval for a product is conditional upon the completion of post-marketing clinical studies.

During all phases of clinical development, regulatory agencies (such as the FDA, the EMA and other comparable regulatory agencies) require extensive monitoring and auditing of all clinical activities, clinical data and clinical trial investigators. Annual progress reports detailing the results of the clinical trials must be submitted to the FDA.

Written IND safety reports must be promptly submitted to the FDA, the NIH and the investigators for: serious and unexpected adverse events; any findings from other trials, in vivo laboratory tests or in vitro testing that suggest a significant risk for human subjects; or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information.

The FDA or the sponsor or its data safety monitoring board may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the biologic product candidate has been associated with unexpected serious harm to patients.

The FDA usually recommends that sponsors observe subjects for potential gene therapy related delayed adverse events for a 15 year period, including a minimum of five years of annual examinations followed by 10 years of annual queries, either in person or by questionnaire.

In the EU, clinical trials almost always require approval from a national competent authority of the relevant Member State and an approval from an Ethics Committee. If the medicinal product is considered to be a genetically modified organism, or GMO, then GMO approval must also be obtained. There is no harmonization between Member States regarding the approach to and timelines of GMO approval, which results in significant challenges and time restrictions.

The conduct of clinical trials should follow the approved clinical trial protocol and be in accordance with the principles of GCP. Gene therapy medicinal products are in addition subject to the rules of GCP for ATMPs (currently in draft form), which outline specific additional safeguards and requirements. Record retention requirements are increased for ATMPs and there are relevant long-term follow up and human safety and traceability requirements.

Compliance with cGMP Requirements

Manufacturers of biologics must comply with applicable cGMP regulations, including quality control and quality assurance and maintenance of records and documentation. Manufacturers and others involved in the manufacture and distribution of such products also must register their establishments with the FDA and certain state agencies. Both domestic and foreign manufacturing establishments must register and provide additional information to the FDA upon their initial participation in the manufacturing process. Any material changes to the manufacturing equipment, process or location of the approved manufacturing site must be reported to the relevant agency/authority. Establishments may be subject to periodic, unannounced inspections by government authorities (including regulatory agencies) to ensure compliance with cGMP requirements and other laws. Discovery of problems may result in a government entity placing restrictions on a product, manufacturer or holder of an approved BLA, and may extend to requiring withdrawal of the product from the market, issue warning or similar letters or seeking civil, criminal or administrative sanctions against the company. The FDA will not approve a BLA unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specification.

Concurrent with clinical trials, companies usually complete additional preclinical studies and must also develop additional information about the physical characteristics of the biologic product candidate as well as finalize a process for manufacturing the product candidate in commercial quantities in accordance with cGMP requirements. To help reduce the risk of the introduction of adventitious agents or of causing other adverse events with the use of biologic products, the PHSA emphasizes the importance of manufacturing control for products whose attributes cannot be precisely defined. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other requirements, the sponsor must develop methods for testing the identity, strength, quality, potency and purity of the final biologic product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the biologic product candidate does not undergo unacceptable deterioration over its shelf life.

U.S. Review and Approval Processes

The results of the preclinical tests and clinical trials, together with detailed information relating to the product’s CMC and proposed labeling, among other things, are submitted to the FDA as part of a BLA requesting approval to market the product for one or more indications.

Under the Prescription Drug User Fee Act, or PDUFA, as amended, each BLA must be accompanied by a significant user fee. The FDA adjusts the PDUFA user fees on an annual basis. The PDUFA also imposes an annual program fee for approved biologics. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business.

The FDA reviews a BLA within 60 days of submission to determine if it is substantially complete before the agency accepts it for filing. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the

time of submission and may request additional information. In that event, the BLA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in depth, substantive review of the BLA.

The FDA reviews the BLA to determine, among other things, whether the proposed product candidate is safe and potent, or effective, for its intended use, has an acceptable purity profile and whether the product candidate is being manufactured in accordance with cGMP to assure and preserve the product candidate's identity, safety, strength, quality, potency and purity. The FDA may refer applications for novel biologic products or biologic products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. During the product approval process, the FDA also will determine whether a risk evaluation and mitigation strategy, or REMS, is necessary to assure the safe use of the product candidate. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the

potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events, and whether the product is a new molecular entity. A REMS could include medication guides, physician communication plans and elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. If the FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS; the FDA will not approve the BLA without a REMS, if required.

Before approving a BLA, the FDA will inspect the facilities at which the product candidate is manufactured. The FDA will not approve the product candidate unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product candidate within required specifications. Additionally, before approving a BLA, the FDA typically will inspect one or more clinical sites to assure that the clinical trials were conducted in compliance with IND trial requirements and GCP requirements.

On the basis of the BLA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the biologic product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the BLA, the FDA will issue an approval letter.

If a product candidate receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. The FDA may impose restrictions and conditions on product distribution, prescribing or dispensing in the form of a REMS, or otherwise limit the scope of any approval. In addition, the FDA may require post marketing clinical trials, sometimes referred to as Phase 4 clinical trials, designed to further assess a biologic product's safety and effectiveness, and testing and surveillance programs to monitor the safety of approved products that have been commercialized.

The FDA has agreed to specified performance goals in the review of BLAs under the PDUFA. One such goal is to review standard BLAs in 10 months after the FDA accepts the BLA for filing, and priority BLAs in six months, whereupon a review decision is to be made. The FDA does not always meet its PDUFA goal dates for standard and priority BLAs and its review goals are subject to change from time to time. The review process and the PDUFA goal date may be extended by three months if the FDA requests or the BLA sponsor otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

EU Review and Approval Process

Before a medicinal product can be placed on the market in the EU, it must have received an MA. This could either be at national or EU level under a mutual recognition, decentralized or centralized procedure. Our product candidates are innovative treatments, which will bear the classification of ATMP and/or orphan status. As such, the appropriate authorization procedure is the centralized procedure, which involves an MA being granted by the European Commission following a positive opinion by the EMA. A centralized MA is simultaneously valid in all EU Member States and the European Economic Area, or EEA, (Iceland, Liechtenstein and Norway). A centralized MA also results in a single set of product information (patient information leaflet, labelling and summary of product characteristics) for all EU Member States.

The timeline for the grant of a centralized MA since the time of the application is 210 days for the assessment of the application (including "clock stops" for the applicant to prepare answers to the questions from the EMA). The Committee for Medicinal Products for Human Use, or the CHMP, may either provide a positive or negative opinion.

Following a positive opinion, the European Commission will usually issue its legally binding MA after 67 days. A negative opinion may be appealed by the applicant who must submit a request for re-examination within 60 days. There is the possibility for accelerated timelines of drug applications for eligible applicants, which can reduce the timeline to 150 days, if the applicant can produce sufficient justification.

If the MA application contains less comprehensive than the required standard as at the time of the application, when there are public health grounds and often in the case of orphan medicinal products, the EMA may recommend to the European Commission that it issues a different type of an MA, as follows: (a) a Conditional MA (valid for one year and renewable), when the medicinal product shows a positive benefit-risk balance and targets an unmet medical need and it is expected that the applicant will be able to provide comprehensive data in due course; or (b) an MA under ‘exceptional circumstances’, when it is not expected that the applicant will be able to provide comprehensive efficacy and safety data (often for very rare indications).

Post approval Requirements

Rigorous and extensive FDA regulation of biologic products continues after approval, particularly with respect to cGMP requirements. Manufacturers are required to comply with applicable requirements in the cGMP regulations, including quality control and quality assurance and maintenance of records and documentation. Other post approval requirements applicable to biologic products include reporting of cGMP deviations that may affect the identity, potency, purity and overall safety of a distributed product, record keeping requirements, reporting of adverse effects, reporting updated safety and efficacy information and complying with electronic record and signature requirements. After a BLA is approved, the product also may be subject to official lot release. If the product is subject to official release by the FDA, the manufacturer submits samples of each lot of product to the FDA, together with a release protocol, showing a summary of the history of manufacture of the lot and the results of all tests performed on the lot. The FDA also may perform certain confirmatory tests on lots of some products before releasing the lots for distribution. In addition, the FDA conducts laboratory research related to the regulatory standards on the safety, purity, potency and effectiveness of biologic products.

A sponsor also must comply with the FDA's or appropriate national authority's advertising and promotion requirements, such as the prohibition on promoting products for uses or in patient populations that are not described in the product's approved labeling (known as "off label use"). Discovery of previously unknown problems or the failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product or withdrawal of the product from the market as well as possible civil or criminal sanctions. In addition, changes to the manufacturing process or facility generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

Orphan designation

We maintain product candidates that have obtained FDA and EU orphan designation (see "Therapeutic Product Development" section above). These products are intended for treating rare conditions that affect fewer than 200,000 people in the U.S., or that affect more than 200,000 persons but are not expected to recover the costs of developing and marketing a treatment drug. In the EU, these rare conditions are defined as having a prevalence of no more than five in every 10,000 people in the EU. Once a medicinal product with orphan designation obtains a marketing approval, it can benefit from a marketing exclusivity period in respect of the specific orphan indication for which the drug has been approved for a period of seven years in the U.S. and for up to ten years in the EU. This measure is intended at incentivizing the development of medicines for rare diseases. The product must be able to maintain its orphan designation, by reference to the criteria of (a) prevalence of the condition and (b) significant benefit of the product over competing products. If the manufacturer is no longer able to assert that the product meets the orphan designation criteria or is not able to provide sufficient quantities, it may lose the orphan market exclusivity.

Clinical Trial Data Disclosure

Many jurisdictions have mandatory clinical trial information obligations on sponsors. In the EU this is under the Transparency Regulation No. 1049/ 2001, EMA Policy 0043, EMA Policy 0070, as well as the new Clinical Trials Regulation No. 536/2014, all of which impose on sponsors the obligation to make publicly available certain information stemming from clinical studies. In the EU, the transparency framework provides for a wide right for (EU-based at the moment) interested parties to submit an access to documents request to the EMA for information included in the marketing authorization application dossier for approved medicinal products. Only very limited information is exempted from disclosure, i.e. commercially confidential information (which is construed increasingly narrowly) and protected personal data. It is possible for competitors to access and use this data in their own research and development programs anywhere in the world, once this data is in the public domain.

Additional Regulation

Although we currently do not have any products on the market, we may be subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which we conduct our business. Such laws include, without limitation, state and federal anti-kickback, fraud, anti-bribery and abuse, false claims, privacy and security and physician transparency laws and regulations, many of which may become more applicable if our product candidates are approved and we begin commercialization. If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs, individual imprisonment, suspension or withdrawal of our marketing and commercialization in respect of our commercially approved products, and additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, any of which could adversely affect our ability to operate our business and our financial results. See “Risk Factors—Our relationships with customers and third-party payors will be subject to applicable anti-

kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings."

The United States and some foreign jurisdictions are considering enacting or have enacted a number of additional legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our product candidates profitably, if approved. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts, which include major legislative initiatives, such as the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, to reduce the cost of care through changes in the healthcare system, including limits on the pricing, coverage, and reimbursement of pharmaceutical and biopharmaceutical products, especially under government-funded health care programs, and increased governmental control of drug pricing. See "Risk Factors—Recently enacted and future legislation, including potentially unfavorable pricing regulations or other healthcare reform initiatives, may increase the difficulty and cost for us to obtain regulatory approval of and commercialize our product candidates and affect the prices we may obtain."

Pricing and reimbursement of a therapeutic product will largely determine the affordability of the product, and whether the product is prescribed and supplied to patients and private insurance companies may take into account government reimbursement methodologies. Due to these proposed and enacted laws, as well as other actions, significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we obtain regulatory approval, particularly for novel products. In both domestic and foreign markets, sales and reimbursement of any approved products will depend, in part, on the extent to which third-party payors, such as government health programs, commercial insurance and managed healthcare organizations provide coverage, and establish adequate reimbursement levels, for such products. Third-party payors are increasingly challenging the prices charged for medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the FDA-approved products for a particular indication. Additionally, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost-effectiveness of our products. If third-party payors do not consider our products to be cost-effective compared to other therapies, these payors may not cover our products after approved as a benefit under their plans or, if they do, the level of reimbursement may not be sufficient to allow us to sell our products on a profitable basis. See "Risk Factors—Even if we are able to commercialize our product candidates, the products may not receive coverage and adequate reimbursement from third-party payors in the United States and in other countries in which we seek to commercialize our products, which could harm our business."

In the EU, pricing and reimbursement are the prerogative of Member States. Therefore, the requirements around reimbursement of medicinal products can vary widely. Each Member State can follow its own approach, subject to common rules of transparency, competition, and freedom of trade and movement in the EU. Many Member States, including France, Germany and the United Kingdom, follow a health technology assessment, or HTA, procedure for medicinal products in order to assess the cost-effectiveness of a product which could then be recommended for reimbursement under the national health services. There is increasingly exchange of information concerning HTAs on a voluntary basis among EU Member States. In the United Kingdom, the National Institute for Health and Care Excellence is the body which conducts HTAs and issues guidance to be followed by the regional health bodies called clinical commissioning groups.

EMPLOYEES

As of February 15, 2019, we had 302 full-time employees. Approximately 247 of these employees are located in California, six of these employees are located in London, UK and the remaining employees are located in France. None of our employees located in California or London are represented by a collective bargaining organization or covered by a collective bargaining agreement, nor have we experienced work stoppages. Our employees located in France are represented by the Confédération Française de l'Encadrement - Confédération Générale des Cadres. We

believe that our relations with our employees are good.

AVAILABLE INFORMATION

Our website is located at www.sangamo.com. This Annual Report on Form 10-K, our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act, are available (free of charge) on our website as soon as reasonably practicable after we electronically file this material with, or furnish it to, the SEC. Information found on, or accessible through, our website is not a part of, and is not incorporated into, this Annual Report on Form 10-K.

ITEM 1A – RISK FACTORS

An investment in our common stock involves significant risk. This Form 10-K contains forward-looking information based on our current expectations. Because our actual results may differ materially from any forward-looking statements made by or on our behalf, this section includes a discussion of important factors that could affect our actual future results, including, but not limited to, our revenues, expenses, net loss and net loss per share. You should carefully consider the information described in the following risk factors, together with the other information appearing elsewhere in this report, before making an investment decision regarding our common stock. Unless otherwise indicated or the context suggests otherwise, references in this Annual Report on Form 10-K to "Sangamo," "we," "us," and "our" refer to Sangamo Therapeutics, Inc. and our consolidated subsidiaries, including TxCell S.A., or TxCell

Risks Relating to Development, Commercialization and Regulatory Approval of our Products and Technology

Our success depends substantially on the results of clinical trials of our lead therapeutic programs, and we may not be able to demonstrate safety and efficacy of our product candidates.

We do not have any products that have gained regulatory approval. Our failure to enroll sufficient patients to conduct the trials, demonstrate safety or obtain positive clinical trial results, or our inability to meet the expected timeline of clinical trials or release of data for these programs, would have a material adverse effect on our business operations and financial conditions, which may cause a significant decline in our stock price.

Our ability to conduct clinical trials successfully and on a timely basis for these programs is subject to a number of additional risks, including but are not limited to the following:

•disagreement with the design or implementation of our clinical trials;

•the ability to identify and recruit sufficient number of acceptable patients to complete enrollment of trials;

•failure to demonstrate that a product candidate is safe and effective for its proposed indication;

•the occurrence of unexpected adverse events or toxicity;

•disagreement with the U.S. Food and Drug Administration, or FDA, or foreign regulatory authorities, on the interpretation of data from preclinical studies or our clinical trial results;

•failure of clinical trials to meet the level of statistical significance required for approval;

•the insufficiency of data collected from clinical trials of our product candidates to support the submission and filing of a biologics license application, or BLA, or other submission or to obtain regulatory approval;

•changes in the approval policies or regulations that render our preclinical and clinical data insufficient for approval;

•failure to obtain approval of our manufacturing processes or facilities of third-party manufacturers with whom we contract for clinical and commercial supplies or our own manufacturing facility;

•defects in the preparation and manufacturing of our product candidates;

•failure by third parties, including vendors, manufacturers and clinical trial organizations, to provide timely and adequate supplies and services;

•development of similar gene therapies by our competitors;

•unexpected costs and expenses and lack of sufficient funding for these programs; and

•loss of licenses to critical intellectual properties.

We have ongoing Phase 1/2 clinical trials evaluating product candidates for the treatment of hemophilia A (SB-525), hemophilia B (SB-FIX), MPS I (SB-318), MPS II (SB-913), and beta-thalassemia (ST-400). We also plan to initiate a Phase 1/2 clinical trial of TxCell's first CAR-Treg (which is a regulatory T cell, or Treg, genetically modified with a chimeric antigen receptor, or CAR) investigational product candidate for solid organ transplant, or TX-200, in 2019.

Even if we are able to complete our Phase 1/2 clinical trials for these programs successfully, we will be required to conduct additional clinical trials with larger patient populations, before obtaining the necessary regulatory approval to commercialize any products, which involves significantly greater resources, commitments and expertise. We also have limited experience in conducting later stage clinical trials and may not possess the necessary resources and expertise to complete such trials. Therefore, we may be required to scale up our operations and enter into collaborative relationships with pharmaceutical companies that could assume responsibility for late-stage development and commercialization. In this regard, while we have entered into collaborative agreements to provide funding and assistance in the development of certain product candidates through the clinical trial process, there is no guarantee that we will be able to enter into future collaborative relationships with third parties that can provide us with the funding and expertise for later stage trials. In addition, there is no guarantee that any positive results achieved in our Phase 1/2 clinical trials will be indicative of long-term efficacy and safety in later stage clinical trials. If a larger patient population does not demonstrate an acceptable safety and efficacy profile, or if any positive results in our Phase 1/2 clinical trials are not reproducible, our products may not receive approval from the FDA or foreign regulatory authorities, which could have a material adverse effect on our business that would cause our stock price to decline significantly.

In addition, we have not yet reached agreement with regulatory authorities on the development pathway for our product candidates. As a result, we have not yet determined what endpoints would support approval for certain of our programs. Due to the novelty of certain programs, such as SB-913 and SB-318, the endpoints needed to support regulatory approvals may be different than originally anticipated. For example, in order to support regulatory approval for SB-913 and SB-318, we may be required to detect certain levels of enzymes in patients. In this regard, in September 2018, we announced preliminary safety and efficacy data from the Phase 1/2 clinical trial evaluating SB-913, or the CHAMPIONS study. In cohort 2 of the CHAMPIONS study, at 16 weeks post-dosing, mean reductions were observed in total urinary glycosaminoglycans, or GAGs (which is a key biomarker of MPS II disease pathophysiology), dermatan sulfate, and heparan sulfate of 51%, 32%, and 61%, respectively. Due to the sensitivity of the assay we used to measure plasma iduronate-2-sulfatase, or IDS, enzyme levels, we were unable to detect IDS in any of the patients over the 16 weeks following treatment with SB-913. In February 2019, we announced interim results of the CHAMPIONS Study. A newly developed sensitive quantitative assay (lower limit of quantification of 0.78 nmol/hour/mL) was used to measure plasma IDS activity for these interim results. Small increases in IDS enzyme activity compared to baseline were recorded in the two patients receiving the mid-dose and in one patient receiving the high-dose. At 24 weeks post-dosing, these measurements remained within the expected range for baseline values (less than 10 nmol/hour/mL, as compared to the normal range, which is estimated at greater than 82 nmol/hour/mL). While the newly developed, more sensitive assay was able to detect IDS at lower levels, there can be no guarantee that we will be able to continue to be able to detect IDS in patients or otherwise show direct evidence of efficacy or gene editing. Moreover, we also may never see a clinical benefit to patients from SB-913. This may delay or preclude any regulatory approvals for SB-913.

Even if a product candidate were to successfully obtain approval from the FDA and comparable foreign regulatory authorities, any approval might contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications, or may be subject to burdensome post-approval study or risk management requirements. If we are unable to obtain regulatory approval for one of our product candidates in one or more jurisdictions, or any approval contains significant limitations, we may not be able to obtain sufficient funding to continue the development of that product or generate revenues attributable to that product candidate. Also, any regulatory approval of our current or future product candidates, once obtained, may be withdrawn.

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.

Results from preclinical studies or previous clinical trials are not necessarily predictive of future clinical trial results, and interim results of a clinical trial are not necessarily indicative of final results. Our product candidates may fail to

show the desired safety and efficacy in clinical development despite demonstrating positive results in preclinical studies or having successfully advanced through initial clinical trials or preliminary stages of clinical trials. In addition, from time to time, we have and may in the future publish or report interim or preliminary data from our clinical trials, such as the preliminary data we announced from the CHAMPIONS study and the Phase 1/2 clinical trial evaluating SB-525, or the Alta Study, as well as the interim data recently announced for the CHAMPIONS study and the Phase 1/2 clinical trial evaluating SB-318, or the EMPOWERS Study. Interim or preliminary data from clinical trials that we may conduct may not be indicative of the final results of the trial and are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and/or more patient data become available. Interim or preliminary data also remain subject to audit and verification procedures that may result in the final data being materially different from the interim or preliminary data. As a result, interim or preliminary data should be considered carefully and with caution until the final data are available.

We have ongoing Phase 1/2 clinical trials evaluating product candidates for the treatment of hemophilia A (SB-525), hemophilia B (SB-FIX), MPS I (SB-318), MPS II (SB-913), and beta-thalassemia (ST-400), and there is no guarantee that we can achieve positive final safety and efficacy results in our Phase 1/2 clinical trials for these product candidates. Moreover, the interim results recently announced for SB-913 and SB318 casts doubt with regard to whether there will be evidence of a clinical benefit of

either product candidate. Furthermore, these programs (other than TX-200 that we acquired through the TxCell Acquisition) are novel in-vivo gene therapy or genome editing therapies that utilize adeno-associated viral, or AAV, vector to deliver therapeutic levels of zinc finger nuclease, or ZFN, into the patient's blood stream. The AAV delivery system has not been validated in human clinical trials previously, and if such delivery system does not meet the safety criteria or cannot produce the desirable efficacy results we expect, we may be forced to suspend or terminate the affected program.

There is a high failure rate for drugs, biologic products and cell therapies proceeding through clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in preclinical testing and earlier-stage clinical trials. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, we may experience regulatory delays or rejections as a result of many factors, including due to changes in regulatory policy during the period of our product candidate development. Any such delays could materially and adversely affect our business, financial condition, results of operations and prospects.

Our potential products are subject to a lengthy and uncertain regulatory approval process in each jurisdiction where approval is sought.

A regulatory authority such as the FDA or the European Medicines Agency, or EMA, must approve any human therapeutic product before it can be marketed in such jurisdiction. The process for receiving regulatory approval is long and uncertain, and a potential product may not withstand the rigors of testing under the regulatory approval processes.

Before commencing clinical trials in humans, we must submit an Investigational New Drug application, or IND, to the FDA. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like the IND prior to the commencement of human clinical trials. In the European Union, for example, a clinical trial authorization application, or CTA, must be submitted for each clinical protocol to each country's national health authority and an independent ethics committee. Only after an IND becomes effective and/or the applicable CTA has been accepted may clinical trials begin. While we have stated our intention to submit additional IND and CTA applications in the future, this is only a statement of intent, and we may not be able to do so because the associated product candidates may not meet the necessary preclinical requirements. In addition, there can be no assurance that, once submitted, an IND or CTA will result in the actual initiation of clinical trials or that we will be able to meet our targeted timeline for the initiation of clinical trials. Clinical trials are subject to oversight by institutional review boards, or IRBs, and the applicable regulatory authority. In addition, our proposed clinical studies in the United States may require review from the Recombinant DNA Advisory Committee, or RAC, which is the advisory board to the NIH focusing on clinical trials involving gene transfer.

Clinical trials:

•must be conducted in conformance with the FDA's good clinical practices, within the guidelines of the International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, or ICH, and other applicable regulations;

•must meet requirements for IRB oversight;

•must follow Institutional Biosafety Committee, or IBC, and NIH RAC guidelines where applicable;

•must meet requirements for informed consent;

•are subject to continuing FDA or similar foreign government oversight;

•may require oversight by a Data Monitoring Committee, or DMC;

•may require large numbers of test subjects; and

•may be suspended by a commercial partner, the FDA, applicable foreign regulatory authorities or us at any time if it is believed that the subjects participating in these trials are being exposed to unacceptable health risks or if the FDA or applicable foreign regulatory authorities find deficiencies in our INDs or their foreign equivalents or the conduct of these trials.

If we are not able to obtain the necessary regulatory approval to commercialize our products or if such approval is delayed or suspended, it would have a material adverse effect on our business operations and trading price of our common stock.

We may encounter difficulties that may delay, suspend or scale back our efforts to advance additional early research programs through preclinical development, IND and foreign equivalent submissions and into clinical development.

We intend to advance early research programs through preclinical development and to submit new INDs, CTAs and equivalent filings in foreign regulatory jurisdictions necessary to commence and conduct human clinical trials evaluating the preclinical candidates in our pipeline. The preparation and submission of INDs and their foreign equivalents requires us to conduct rigorous and time-consuming preclinical testing, studies, and prepare documentation relating to, among other things, the toxicity, safety, manufacturing, chemistry and clinical protocol of our product candidates. We may experience unforeseen difficulties that could delay or otherwise prevent us from executing this strategy successfully. For example, we may encounter problems in the manufacturing of our products and fail to demonstrate consistency in the formulation of the drug. Our preclinical tests may produce negative or inconclusive results, which may lead us to decide, or regulators may require us, to conduct additional preclinical testing. If we cannot obtain positive results in preclinical testing, we may decide to abandon the projects altogether. In addition, our ability to complete and submit certain IND applications and foreign equivalent filings depends on the support of our partners and the timely performance of their obligations under relevant collaboration agreements. If our partners are not able to perform such obligations or if they choose to slow down or delay the progress, we may not be able to prepare and submit the intended INDs or their foreign equivalents on a timely basis or at all. Furthermore, the submission of several INDs and their foreign equivalents involves significant cost and labor, and we may not have sufficient resources and personnel to complete the filing of all intended INDs and their foreign equivalents, which may force us to scale back the number of INDs and their foreign equivalents or forego potential INDs and foreign equivalents that we believe are promising. Any delay, suspension or reduction of our efforts to pursue our preclinical and IND strategy could have a material adverse effect on our business and cause our stock price to decline.

We may not successfully identify, acquire, develop or commercialize new potential product candidates.

Part of our business strategy is to expand our product candidate pipeline by identifying and validating new product candidates, which we may develop ourselves, in-license or otherwise acquire from others. For example, through the TxCell Acquisition, we recently acquired the rights among others to TxCell's first CAR-Treg product candidate, TX-200, and its CAR-Treg technology and know-how. In this regard, 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, and expect that the TxCell Acquisition will accelerate our entry into the clinic with a CAR-Treg therapy. However, we are new to the field of immunology and to the use of CARs with Tregs, and we may not be successful at developing a CAR-Treg therapy that can be used in patients. Moreover, we may not achieve the expected accelerated development timeline. If we are unable to successfully develop and obtain regulatory approval for TX-200 or other CAR-Treg therapies and effectively commercialize them, or if we are unable to achieve the expected accelerated development timeline, we may not realize the anticipated benefits from the TxCell Acquisition, resulting in possible impairments or other charges or losses which may materially and adversely affect our results of operations and financial condition.

In addition, in the event that our existing product candidates do not receive regulatory approval or are not successfully commercialized, then the success of our business will depend on our ability to continue to expand our product pipeline through in-licensing or other acquisitions. We may be unable to identify relevant product candidates. If we do identify such product candidates, we may be unable to reach acceptable terms with any third party from which we desire to in-license or acquire them. Even if we are able to successfully identify and acquire such product candidates, we may not be able to successfully manage the risks associated with integrating acquired or in-licensed product candidates or technologies or the risks arising from anticipated and unanticipated problems in connection with an acquisition or in-licensing transaction. Further, while we seek to mitigate risks and liabilities of potential acquisitions and in-licensing transactions through, among other things, due diligence, there may be risks and liabilities that such due diligence efforts fail to discover, that are not disclosed to us, or that we inadequately assess. Any failure in identifying and managing these risks and uncertainties effectively, including in connection with the TxCell Acquisition, would have a material adverse effect on our business. Additionally, we may not realize the anticipated benefits of such transactions for a variety of reasons, including the possibility that acquired product candidates, such as TX-200, prove not to be safe or effective in clinical trials, the integration of an acquired product candidate, technology or business gives rise to unforeseen difficulties and expenditures, or that the expected benefits will not otherwise be realized or

will not be realized within the expected timeframe.

We may encounter substantial delays in our clinical trials or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates. Clinical testing is expensive, time consuming and uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. A failure of one or more clinical trials can occur at any stage of testing. Events that may prevent successful or timely completion of clinical development include:

•delays in reaching a consensus with regulatory authorities on trial design;

•delays in reaching agreement on acceptable terms with prospective CROs and clinical trial sites;

•delays in opening clinical trial sites or obtaining required IRB or independent ethics committee approval at each clinical trial site;

•delays in recruiting suitable subjects to participate in our clinical trials;

•imposition of a clinical hold by regulatory authorities as a result of a serious adverse event or after an inspection of our clinical trial operations or trial sites;

•failure by us, any CROs we engage or any other third parties to adhere to clinical trial requirements;

•failure to perform in accordance with FDA good clinical practices, or GCP, or applicable regulatory guidelines in the European Union and other countries;

•delays in the testing, validation, manufacturing and delivery of our product candidates to the clinical sites, including delays by third parties with whom we have contracted to perform certain of those functions;

•delays in having subjects complete participation in a trial or return for post-treatment follow-up;

•clinical trial sites or subjects dropping out of a trial;

•selection of clinical endpoints that require prolonged periods of clinical observation or analysis of the resulting data;

•occurrence of serious adverse events associated with the product candidate that are viewed to outweigh its potential benefits;

•occurrence of serious adverse events in trials of the same class of agents conducted by other sponsors; or

•changes in regulatory requirements and guidance that require amending or submitting new clinical protocols.

Any inability to successfully complete preclinical and clinical development could result in additional costs to us or impair our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties. In addition, if we make manufacturing or formulation changes to our product candidates, we may need to conduct additional studies to bridge our modified product candidates to earlier versions. Clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business, financial condition, results of operations and prospects.

Additionally, if the results of our clinical trials are inconclusive or if there are safety concerns or serious adverse events associated with our product candidates, we may:

•be delayed in obtaining marketing approval for our product candidates, if at all;

•obtain approval for indications or patient populations that are not as broad as intended or desired;

•obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;

•be subject to changes in the way the product is administered;

•be required to perform additional clinical trials to support approval or be subject to additional post-marketing testing requirements;

•have regulatory authorities withdraw, or suspend, their approval of the product or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation strategy;

•be subject to the addition of labeling statements, such as warnings or contraindications;

•be sued; or

•experience damage to our reputation.

We may not be able to find acceptable patients or may experience delays in enrolling patients for our clinical trials, which could delay or prevent us from proceeding with clinical trials of our product candidates.

Identifying and qualifying patients to participate in clinical trials of our product candidates is critical to our success. The timing of our clinical trials depends on our ability to recruit patients to participate as well as completion of required follow-up periods. For example, hemophilia trials often take longer to enroll due to the availability of existing treatments. We have only recently begun to enroll patients into the Phase 1/2 clinical trials evaluating SB-FIX for the treatment of hemophilia B, SB-318 for the treatment of MPS I and ST-400 for the treatment of beta-thalassemia. If we are not able to enroll the necessary number of patients in a timely manner, we may not be able to complete the clinical trial. We may face similar challenges or delays in our other or potential future clinical trials. If patients are unwilling to participate in our gene therapy studies because of negative publicity from adverse events related to the biotechnology or gene therapy fields, competitive clinical trials for similar patient populations or for other reasons, the timeline for

recruiting patients, conducting studies and obtaining regulatory approval of our product candidates may be delayed. These delays could result in increased costs, delays in advancing our product candidates, delays in testing the effectiveness of our product candidates or termination of the clinical trials altogether.

We may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics, to complete our clinical trials in a timely manner. Patient enrollment and trial completion is affected by factors including:

•size of the patient population and process for identifying subjects;

•design of the trial protocol;

•eligibility and exclusion criteria;

•perceived risks and benefits of the product candidate under study;

•perceived risks and benefits of gene therapy-based approaches to treatment of diseases;

•availability of competing therapies and clinical trials;

•severity of the disease under investigation;

•availability of genetic testing for potential patients;

•proximity and availability of clinical trial sites for prospective subjects;

•ability to obtain and maintain subject consent;

•risk that enrolled subjects will drop out before completion of the trial;

•patient referral practices of physicians; and

•ability to monitor subjects adequately during and after treatment.

Our current product candidates are being developed to treat rare conditions. We may not be able to initiate or continue clinical trials if we cannot enroll a sufficient number of eligible patients to participate in the clinical trials required by regulatory authorities. We may need to expand the conduct of our clinical trials to foreign countries so that we may be better able to access and enroll subjects. Our ability to successfully initiate, enroll and complete a clinical trial in any foreign country is subject to numerous risks unique to conducting business in foreign countries, including:

•difficulty in establishing or managing relationships with contract research organizations, or CROs, and physicians;

•different standards for the conduct of clinical trials;

•absence in some countries of established groups with sufficient regulatory expertise for review of gene therapy protocols;

•our inability to locate qualified local consultants, physicians and partners; and

•the potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatment.

If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit or terminate ongoing or planned clinical trials, any of which would have an adverse effect on our business, financial condition, results of operations and prospects.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial potential or result in significant negative consequences following any potential marketing approval.

During the conduct of clinical trials, patients report changes in their health, including illnesses, injuries and discomforts, to their study doctor. Often, it is not possible to determine whether or not the product candidate being studied caused these conditions, particularly as many of the diseases we are studying have complex comorbidities. If clinical experience indicates that our product candidates have side effects or cause serious or life-threatening side effects, the development of the product candidate may fail or be delayed, or, if the product candidate has received regulatory approval, such approval may be revoked, which would severely harm our business, prospects, operating results and financial condition.

There have been several significant adverse side effects in gene therapy treatments in the past, including reported cases of leukemia and death seen in other trials using other genomic therapies. Gene therapy is still a relatively new approach to disease treatment and additional adverse side effects could develop. There also is the potential risk of significantly delayed adverse events following exposure to gene therapy products due to persistent biologic activity of the genetic material or other components of products used to carry the genetic material. Possible adverse side effects that could occur with treatment with gene therapy products include an immunologic reaction early after administration that, while not necessarily adverse to the patient's health, could substantially limit the effectiveness of the treatment.

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

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

We may be unable to obtain additional orphan drug designations or orphan drug exclusivity for any product. If our competitors are able to obtain orphan drug exclusivity for products that constitute the same drug and treat the same indications as our product candidates, we may not be able to have competing products approved by the applicable regulatory authority for a significant period of time.

Regulatory authorities in some jurisdictions, including the United States and the European Union, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act of 1983, the FDA may designate a product candidate as an Orphan Drug if it is intended to treat a rare disease or condition, which is generally defined as having a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the European Union, the European Medicines Agency's Committee for Orphan Medicinal Products grants such designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the European Union. Additionally, orphan designation is granted for products intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the European Union would be sufficient to justify the necessary investment in developing the drug or biologic product.

Our four most advanced product candidates, SB-525, SB-FIX, SB-318 and SB-913 have all been granted Orphan Drug Designation by the FDA, and SB-525 and SB-318 and SB-913 have also been designated Orphan Medicinal Products by the European Medicines Agency, or EMA. If we request such designation for our other current or future product candidates, there can be no assurances that the FDA or the EMA will grant any of our product candidates such designation. Additionally, such designation does not guarantee that any regulatory agency will accelerate regulatory review of, or ultimately approve, that product candidate, nor does it limit the ability of any regulatory agency to grant such designation to product candidates of other companies that treat the same indications as our product candidates prior to our product candidates receiving exclusive marketing approval.

Generally, if a product candidate with an orphan drug designation receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for a product that constitutes the same

drug treating the same indication for that marketing exclusivity period, except in limited circumstances. If another sponsor receives such approval before we do (regardless of our orphan drug designation), we will be precluded from receiving marketing approval for our product for the applicable exclusivity period. The applicable period is seven years in the United States and 10 years in the European Union. The exclusivity period in the United States can be extended by six months if the BLA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The exclusivity period in the European Union can be reduced to six years if a product no longer meets the criteria for orphan drug designation or if the product is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be revoked if any regulatory agency determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition.

Even if we obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the product candidate from competition because different drugs can be approved for the same condition. In the United States, even after an orphan drug is approved, the FDA may subsequently approve another drug for the same condition if the FDA concludes that the latter drug is

not the same drug or is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. In the European Union, marketing authorization may be granted to a similar medicinal product for the same orphan indication if:

•the second applicant can establish in its application that its medicinal product, although similar to the orphan medicinal product already authorized, is safer, more effective or otherwise clinically superior;

•the holder of the marketing authorization for the original orphan medicinal product consents to a second orphan medicinal product application; or

•the holder of the marketing authorization for the original orphan medicinal product cannot supply sufficient quantities of orphan medicinal product.

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

We expect to rely, to some extent, on our strategic partners to provide funding in support of our research and to perform independent research and preclinical and clinical testing. Our technology is broad-based, and we do not currently possess the resources necessary to fully develop and commercialize potential products that may result from our technologies or the resources or capabilities to complete the lengthy marketing approval processes that may be required for the products. Therefore, we plan to rely on strategic partnerships to help us develop and commercialize our products. We have entered into collaborative agreements to provide funding and assistance in the development of certain product candidates through the clinical trial process. For example, we have an agreement with Kite for potential engineered cell therapies for cancer, two separate agreements with Pfizer, one for SB-525 for hemophilia A, and another for amyotrophic lateral sclerosis and frontotemporal lobar degeneration linked to mutations of the C9ORF72 gene, and an agreement with Bioverativ for our beta-thalassemia and sickle cell disease product candidates.

If we are unable to find additional partners or if the partners we are unable or unwilling to advance our programs, or if they do not diligently pursue product approval, this may slow our progress and adversely affect our ability to generate revenues. In addition, our partners may sublicense or abandon development programs or we may have disagreements or disputes with our partners, which would cause associated product development to slow or cease. In addition, the business or operations of our partners may change significantly through restructuring, acquisition or other strategic transactions or decisions that may negatively impact their ability to advance our programs.

There can be no assurance that we will be able to establish further strategic collaborations for our products. We may require significant time to secure collaborations or partners because we need to effectively market the benefits of our technology to these future collaborators and partners, which may direct the attention and resources of our research and development personnel and management away from our primary business operations. Further, each collaboration or partnering arrangement will involve the negotiation of terms that may be unique to each collaborator or partner. These business development efforts may not result in a collaboration or partnership.

The loss of partnering agreements may delay or terminate the potential development or commercialization of products we may derive from our technologies, but it may also delay or terminate our ability to test our product candidates. If any partner fails to conduct the collaborative activities successfully or in a timely manner, the preclinical or clinical development or commercialization of the affected product candidates or research programs could be delayed or terminated.

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

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

In order to regulate or modify a gene in a cell, the zinc finger protein, or ZFP, must be efficiently delivered to the cell. We have licensed certain gene transfer technologies for our ZFP in research including AAV and mRNA technology. We are evaluating these systems and other technologies that may need to be used in the delivery of ZFP into cells for in vitro and in vivo applications. However, we may not be able to license the gene transfer technologies required to develop and commercialize our product candidates. We have not developed our own gene transfer technologies, and we rely on our ability to enter into license agreements to provide us with rights to the necessary gene transfer technology. Our approach has been to license appropriate technology as required. The inability to obtain a license to use gene transfer technologies with entities which own such technology on reasonable commercial

terms, if at all, could delay or prevent the preclinical evaluation, drug development collaborations, clinical testing, and/or commercialization of our therapeutic product candidates.

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

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

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

Effective delivery of ZFNs and ZFP TFs into the appropriate target cells and tissues is critical to the success of the therapeutic applications of our ZFP technology. In order to have a meaningful therapeutic effect, product candidates based must be delivered to sufficient numbers of cells in the targeted tissue. The ZFN or ZFP TF must be present in that tissue for sufficient time to effect either modification of a therapeutically relevant gene or regulation of its expression. In our current clinical and preclinical programs, we administer these product candidates as a nucleic acid that encodes the ZFN or ZFP TF. We use different formulations to deliver the ZFN or ZFP TF depending on the required duration of expression, the targeted tissue and the indication that we intend to treat, including our proprietary AAV delivery system. However, there can be no assurances that we will be able to effectively deliver our ZFNs and ZFP TFs to produce a beneficial therapeutic effect.

In February 2019, we announced our development of second generation, potentially more potent ZFN constructs designed to increase editing efficiency. In vitro data of these second-generation ZFNs were reviewed by FDA. The in vitro data showed three potential advantages for use in the clinic: (1) a five to thirty-fold improvement in efficiency and potency due to structural changes; (2) the ability to function equally well in the patients who have a single nucleotide polymorphism in the target locus in the albumin gene (approximately 20% of the population); (3) improvements in specificity. The second generation ZFNs already being manufactured and we expect to be ready to use them in the clinic later this year; however, there can be no assurances that we will be able to effectively deliver this second-generation ZFN to produce a beneficial therapeutic effect. Additional data from our in vivo genome editing programs will be assessed before potential integration plans for the second-generation ZFNs are finalized.

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

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

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

Even if we, our collaborators or strategic partners are successful in using our ZFP technology in drug discovery, protein production, therapeutic development or other areas in which we have licensed our technology, such as plant agriculture, they may not be able to commercialize the resulting products or may decide to use other methods competitive with this technology. To date, no

company has received marketing approval or has developed or commercialized any therapeutic or agricultural products based on our ZFP technology. Should our technology fail to provide safe, effective, useful or commercially viable approaches to the discovery and development of these product candidates, this would significantly limit our business and future growth and would adversely affect our value.

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

Even if we obtain regulatory approval for any of our product candidates that we may develop or acquire in the future, the applicable product may not gain market acceptance among physicians, healthcare payors, patients or the medical community. Market acceptance of any of our product candidates for which we receive approval depends on a number of factors, including:

•the efficacy and safety of such product candidates as demonstrated in clinical trials;

•the clinical indications and patient populations for which the product candidate is approved;

•acceptance by physicians, major cancer treatment centers and patients of the drug as a safe and effective treatment;

•the adoption of novel gene therapies by physicians, hospitals and third-party payors;

•the potential and perceived advantages of product candidates over alternative treatments;

•the safety of product candidates seen in a broader patient group, including its use outside the approved indications;

•any restrictions on use together with other medications;

•the prevalence and severity of any side effects;

•product labeling or product insert requirements of the FDA or other regulatory authorities;

•the timing of market introduction of our products as well as competitive products;

•the development of manufacturing and distribution processes for our product candidates;

•the cost of treatment in relation to alternative treatments;

•the availability of coverage and adequate reimbursement and the willingness of patients to pay out-of-pocket in the absence of coverage or inadequacy of reimbursement by third-party payors and government authorities;

•relative convenience and ease of administration; and

•the effectiveness of our sales and marketing efforts and those of our collaborators.

If any of our product candidates are approved but fail to achieve market acceptance among physicians, patients, healthcare payors or treatment centers, we will not be able to generate significant revenues, which would compromise our ability to become profitable.

Even if we are able to commercialize our product candidates, the products may not receive coverage and adequate reimbursement from third-party payors in the United States and in other countries in which we seek to commercialize our products, which could harm our business.

Our ability to commercialize any product successfully will depend, in part, on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations.

Government authorities and third-party payors, such as private health insurers and health maintenance organizations, determine which medications they will cover and establish reimbursement levels. A primary trend in the healthcare industry is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Third-party payors may also seek additional clinical evidence, beyond the data required to obtain regulatory approval, demonstrating clinical benefits and value in specific patient populations before covering our products for those patients. We cannot be sure that coverage and adequate reimbursement will be available for any product that we commercialize and, if reimbursement is available, what the level of reimbursement will be. Coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we obtain regulatory approval. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize any product candidate for which we obtain regulatory approval.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for coverage and reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may only be temporary. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors in the United States often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies, but also have their own methods and approval process apart from Medicare determinations. Our inability to promptly obtain coverage and profitable reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Recently enacted and future legislation, including potentially unfavorable pricing regulations or other healthcare reform initiatives, may increase the difficulty and cost for us to obtain regulatory approval of and commercialize our product candidates and affect the prices we may obtain.

The regulations that govern, among other things, regulatory approvals, coverage, pricing and reimbursement for new drug products vary widely from country to country. In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay regulatory approval of our product candidates, restrict or regulate post-approval activities and affect our ability to successfully sell any product candidates for which we obtain regulatory approval. In particular, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively, the Affordable Care Act, was enacted, which substantially changes the way healthcare is financed by both governmental and private insurers, and significantly impacts the U.S. pharmaceutical industry. The Affordable Care Act and its implementing regulations, among other things, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for certain drugs and biologics, including products similar to our product candidates, that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program, extended the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations, subjected manufacturers to new annual fees and taxes for certain branded prescription drugs, created a new Patient Centered Outcomes Research Institute, which provides incentives to programs that increase the federal government’s comparative effectiveness research, established a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (and 70% commencing January 1, 2019) point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer’s outpatient drugs to be covered under Medicare Part D, and created a licensure framework for follow-on biologic products.

Some of the provisions of the Affordable Care Act have yet to be fully implemented, and there have been legal and political challenges to certain aspects of the Affordable Care Act. Since January 2017, President Trump has signed two executive orders and other directives designed to delay, circumvent, or loosen certain requirements mandated by the Affordable Care Act. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the Affordable Care Act. While Congress has not passed repeal legislation, two bills affecting the implementation of certain taxes under the Affordable Care Act have been signed into law. The Tax Cuts and Jobs Act of 2017 includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the Affordable Care Act on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the “individual mandate”. Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of

certain Affordable Care Act-mandated fees. Further, the Bipartisan Budget Act of 2018, among other things, amends the Affordable Care Act, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole". More recently, in July 2018, the Centers for Medicare & Medicaid Services, or CMS, published a final rule permitting further collections and payments to and from certain Affordable Care Act qualified health plans and health insurance issuers under the Affordable Care Act risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. Congress may consider other legislation to repeal, or repeal and replace, other elements of the Affordable Care Act.

Other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013, and, due to subsequent legislative amendments to the statute, including the Bipartisan Budget Act of 2018, will remain in effect through 2027 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American

Taxpayer Relief Act of 2012, or the ATRA, which, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Also, there has been heightened governmental scrutiny recently over pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for pharmaceutical products, some of which are included in the Trump administration's budget proposal for fiscal year 2019. Additionally, the Trump administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. The U.S. Department of Health and Human Services has begun the process of soliciting feedback on some of these measures and, at the same, is immediately implementing others under its existing authority. Although a number of these, and other potential, proposed measures will require authorization through additional legislation to become effective. Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, have been designed to encourage importation from other countries and bulk purchasing.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls may adversely affect:

•the demand for our product candidates, if we obtain regulatory approval;

•our ability to set a price that we believe is fair for our products;

•our ability to generate revenue and achieve or maintain profitability;

•the level of taxes that we are required to pay; and

•the availability of capital.

Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors, which may adversely affect our future profitability.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the regulatory approvals of our product candidates, if any, may be.

In the United States, the European Union and other potentially significant markets for our product candidates, government authorities and third-party payors are increasingly attempting to limit or regulate the price of medical products and services, particularly for new and innovative products and therapies, which has resulted in lower average selling prices. Furthermore, the increased emphasis on managed healthcare in the United States and on country and

regional pricing and reimbursement controls in the European Union will put additional pressure on product pricing, reimbursement and usage, which may adversely affect our future product sales and results of operations. These pressures can arise from rules and practices of managed care groups, judicial decisions and governmental laws and regulations related to Medicare, Medicaid and healthcare reform, pharmaceutical reimbursement policies and pricing in general.

Price controls may be imposed in foreign markets, which may adversely affect our future profitability.

In some countries, particularly member states of the European Union, the pricing of prescription drugs is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after receipt of regulatory approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we, or our collaborators, may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product candidates to other available therapies in order to obtain or maintain reimbursement or

pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be adversely affected.

Even if we complete the necessary preclinical and clinical studies, we cannot predict when or if we will obtain regulatory approval to commercialize a product candidate or the approval may be for a more narrow indication than we expect.

We cannot commercialize a product until the appropriate regulatory authorities have reviewed and approved the product candidate. Even if our product candidates demonstrate safety and efficacy in clinical studies, the regulatory agencies may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA Advisory Committee or other regulatory advisory group or authority recommends non-approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical studies and the review process. Regulatory agencies also may approve a treatment candidate for fewer or more limited indications than requested or may grant approval subject to the performance of post-marketing studies. In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our treatment candidates. For example, the development of certain product candidates for pediatric use is an important part of our current business strategy, and if we are unable to obtain regulatory approval for the desired age ranges, our business may suffer.

Even if we obtain regulatory approval for a product candidate, our products will remain subject to regulatory scrutiny.

Even if we obtain regulatory approval in a jurisdiction, the regulatory authority may still impose significant restrictions on the indicated uses or marketing of our product candidates, or impose ongoing requirements for potentially costly post-approval studies, post-market surveillance or patient or drug restrictions. For example, the FDA typically advises that patients treated with gene therapy undergo follow-up observations for potential adverse events for a 15-year period. Additionally, the holder of an approved BLA is obligated to monitor and report adverse events and any failure of a product to meet the specifications in the BLA. The holder of an approved BLA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws.

In addition, products are subject to payment of annual program user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with good manufacturing practices, or GMP, and adherence to commitments made in the BLA. If we or a regulatory agency discovers previously unknown problems with a product such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions relative to that product or the manufacturing facility, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

Moreover, if any of our product candidates is approved, our product labeling, advertising and promotion will be subject to regulatory requirements and continuing regulatory review. The FDA and foreign regulatory authorities strictly regulate the promotional claims that may be made about drug and biologic products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product’s approved labeling.

If we fail to comply with applicable regulatory requirements following approval of any of our product candidates, a regulatory agency may:

•issue a warning letter asserting that we are in violation of the law;

•seek an injunction or impose civil or criminal penalties or monetary fines;

•suspend or withdraw regulatory approval;

•suspend any ongoing clinical studies;

•refuse to approve a pending marketing application, such as a BLA or supplements to a BLA submitted by us;

•seize product; or

•refuse to allow us to enter into supply contracts, including government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenues.

Failure to obtain regulatory approval in international jurisdictions would prevent our product candidates from being marketed abroad.

In addition to regulations in the United States, to market and sell our products in the European Union, many Asian countries and other jurisdictions, we must obtain separate regulatory approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. Clinical trials accepted in one country may not be accepted by regulatory authorities in other countries. In addition, many countries outside the United States require that a product be approved for reimbursement before it can be approved for sale in that country. A product candidate that has been approved for sale in a particular country may not receive reimbursement approval in that country. We may not be able to obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for regulatory approvals and may not receive necessary approvals to commercialize our products in any market. If we are unable to obtain approval of any of our product candidates by the FDA or regulatory authorities in the European Union, Asia or elsewhere, the commercial prospects of that product candidate may be significantly diminished, our business prospects could decline and this could materially adversely affect our business, results of operations and financial condition.

Our current and future relationships with healthcare providers, customers and third-party payors subject us to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations. If we fail to comply with federal, state and foreign laws and regulations, including healthcare, privacy and data security laws and regulations, we could face substantial penalties and our business, results of operations, financial condition and prospects could be adversely affected.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any product candidates for which we obtain regulatory approval. Our current and future arrangements with healthcare providers, third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we would market, sell and distribute our products. As a biotechnology company, even though we will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are and will be applicable to our business. Restrictions under applicable federal and state healthcare laws and regulations that may affect our ability to operate include the following:

•the federal healthcare Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;

•federal civil and criminal false claims laws and civil monetary penalty laws, including the federal False Claims Act, which can be enforced through civil whistleblower or qui tam actions, prohibits, among other things, individuals or entities from knowingly presenting, or causing to be presented, to the federal government, including the Medicare and Medicaid programs, claims for payment or approval that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;

•the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also created federal criminal laws that prohibit, among other things, knowingly and willfully falsifying, concealing or covering up a material fact or making

any materially false statements in connection with the delivery of or payment for healthcare benefits, items or services;

•HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations, impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information held by certain healthcare providers, health plans and healthcare clearinghouses, known as covered entities, and individuals and entities that perform services for them that involve individually identifiable health information, known as business associates;

•the federal Physician Payments Sunshine Act created under the Affordable Care Act requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the CMS information related to payments and other transfers of value to physicians and teaching hospitals, and ownership and investment interests held by physicians and their immediate family members;

•analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; some state laws require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal

government, require drug manufacturers to report information related to payments and other transfers of value to other healthcare providers and healthcare entities, or marketing expenditures; and/or ensure the registration and compliance of sales and medical personnel; and

•state and foreign laws govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies, healthcare providers and other third parties, including charitable foundations, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. Responding to investigations can be time-and resource-consuming and can divert management's attention from the business. Any such investigation or settlement could increase our costs or otherwise have an adverse effect on our business.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, personal imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations. If any physicians or other healthcare providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusion from government funded healthcare programs.

In addition, the provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the European Union. The provision of benefits or advantages to physicians is governed by the national anti-bribery laws of European Union Member States, such as the U.K. Bribery Act. Infringement of these laws could result in substantial fines and imprisonment. Moreover, payments made to physicians in certain European Union Member States must be publicly disclosed. Agreements with physicians often must also be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual European Union Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the European Union, including personal health data, is subject to the EU General Data Protection Regulation, or the GDPR, which became effective on May 25, 2018. The GDPR, which is wide-ranging in scope, imposes several requirements relating to the control over personal data by individuals to whom the personal data relates, the information provided to the individuals, the documentation we must maintain, the security and confidentiality of the personal data, data breach notification and the use of third party processors in connection with the processing of personal data. The GDPR also imposes strict rules on the transfer of personal data out of the European Union, provides an enforcement authority and authorizes the imposition of large penalties for noncompliance, including the potential for fines of up to €20 million or 4% of the annual global revenues of the non-compliant company, whichever is greater. The GDPR requirements apply not only to third-party transactions, but also to transfers of information between us and our subsidiaries such as TxCell, including employee information. The GDPR has increased our responsibility and potential liability in relation to personal data that we process compared to prior European Union law, particularly in light of the TxCell

Acquisition, and we may be required to put in place additional mechanisms to ensure compliance with the GDPR, which could divert management's attention and increase our cost of doing business. However, despite our ongoing efforts to bring our practices into compliance with the GDPR, we may not be successful either due to various factors within our control or other factors outside our control. It is also possible that local data protection authorities may have different interpretations of the GDPR, leading to potential inconsistencies amongst various European Union Member States. Any failure or alleged failure (including as a result of deficiencies in our policies, procedures or measures relating to privacy, data security, marketing or communications) by us to comply with laws, regulations, policies, legal or contractual obligations, industry standards or regulatory guidance relating to privacy or data security, may result in governmental investigations and enforcement actions, litigation, fines and penalties or adverse publicity. In addition, new regulation, legislative actions or changes in interpretation of existing laws or regulations regarding data privacy and security (together with applicable industry standards) may increase our costs of doing business. In this regard, we expect that there will continue to be new proposed laws, regulations and industry standards relating to privacy and data protection in the United States, the European Union and other jurisdictions, such as the California Consumer Privacy Act of 2018 that will go into effect beginning January 1, 2020, and we cannot determine the impact such future laws, regulations and standards will have on our business.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of employee fraud or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant civil, criminal and administrative penalties, damages, fines, disgorgement, personal imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations..

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any products that we may develop. Product liability claims may be brought against us by subjects enrolled in our clinical trials, patients, healthcare providers or others using, administering or selling our products. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

•decreased demand for any product candidates or products that we may develop;

•termination of clinical trial sites or entire trial programs;

•injury to our reputation and significant negative media attention;

•withdrawal of clinical trial participants;

•significant costs to defend the related litigation;

•substantial monetary awards to trial subjects or patients;

•loss of revenue;

•diversion of management and scientific resources from our business operations; and

•the inability to commercialize any products that we may develop.

We currently hold product liability insurance coverage at a level that we believe is customary for similarly situated companies and adequate to provide us with insurance coverage for foreseeable risks, but which may not be adequate to cover all liabilities that we may incur. Insurance coverage is increasingly expensive. We may not be able to

maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. We intend to expand our insurance coverage for products to include the sale of commercial products if we obtain regulatory approval for our product candidates in development, but we may be unable to obtain commercially reasonable product liability insurance for any products that receive regulatory approval. Large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. A successful product liability claim or series of claims brought against us, particularly if judgments exceed our insurance coverage, could decrease our cash and adversely affect our business.

We currently rely on third parties to conduct some or all aspects of manufacturing of our product candidates for preclinical and clinical development. If one of our third-party manufacturers fails to perform adequately or fulfill our needs, we may be required to incur significant costs and devote significant efforts, to find new suppliers or manufacturers.

We currently have limited experience in clinical-scale manufacturing of our product candidates and we rely upon third-party contract manufacturing organizations to manufacture and supply drug product for our preclinical and clinical studies. The manufacture of pharmaceutical products in compliance with the FDA’s current good manufacturing practices, or cGMP, requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls.

Manufacturers of pharmaceutical products often encounter difficulties in production, including difficulties with production costs and yields, quality control, including stability of the product candidate and quality assurance testing, shortages of qualified personnel, as well as compliance with strictly enforced cGMP requirements, other federal and state regulatory requirements and foreign regulations. If our manufacturers were to encounter any of these difficulties or otherwise fail to comply with their obligations to us or under applicable regulations, our ability to provide study biologics in our clinical studies would be jeopardized. Any delay or interruption in the supply of clinical study materials could delay the completion of our clinical studies, increase the costs associated with maintaining our clinical study programs and, depending upon the period of delay, require us to commence new studies at significant additional expense or terminate the studies completely.

All manufacturers of our product candidates must comply with cGMP requirements enforced by the FDA through its facilities inspection program. These requirements include, among other things, quality control, quality assurance and the maintenance of records and documentation. Manufacturers of our product candidates may be unable to comply with these cGMP requirements and with other FDA, state and foreign regulatory requirements. The FDA or similar foreign regulatory agencies may also implement new standards at any time, or change their interpretation and enforcement of existing standards for manufacture, packaging or testing of products. We have limited control over our manufacturers' compliance with these regulations and standards. Failure to comply with these requirements may result in fines and civil penalties, suspension of production, suspension or delay in product approval, product seizure or recall or withdrawal of product approval. If the safety of any product supplied is compromised due to our manufacturers' failure to adhere to applicable laws or for other reasons, we may not be able to obtain regulatory approval for or successfully commercialize our products and we may be held liable for any injuries sustained as a result. Any of these factors could cause a delay of clinical studies, regulatory submissions, approvals or commercialization of our product candidates, entail higher costs or impair our reputation.

Our current agreements with our suppliers do not provide for the entire supply of the drug product necessary for all anticipated clinical studies or for full scale commercialization. If we and our suppliers cannot agree to the terms and conditions for them to provide the drug product necessary for our clinical and commercial supply needs, we may not be able to manufacture the product candidate until a qualified alternative supplier is identified, which could also delay the development of, and impair our ability to commercialize, our product candidates.

The number of third-party suppliers with the necessary manufacturing and regulatory expertise and facilities is limited, and it could be expensive and take a significant amount of time to arrange for alternative suppliers, which could have a material adverse effect on our business. New suppliers of any product candidate would be required to qualify under applicable regulatory requirements and would need to have sufficient rights under applicable intellectual property laws to the method of manufacturing the product candidate. Obtaining the necessary FDA approvals or other qualifications under applicable regulatory requirements and ensuring non-infringement of third-party intellectual property rights could result in a significant interruption of supply and could require the new manufacturer to bear significant additional costs which may be passed on to us.

We are building a manufacturing facility that could support future clinical production of our product candidates. We have no experience as a company manufacturing pharmaceutical products, and there can be no assurance that we will be able to build a compliant manufacturing facility or, if built, we will be able to successfully manufacture any of our product candidates.

We expect to utilize both contract manufacturing organizations, or CMOs, and our own facility to meet our projected needs for clinical supply. We intend to expand our manufacturing capacity by designing and building a manufacturing facility that we plan to initially use to support our clinical supply needs. To meet these objectives we will need to transition manufacturing processes and know-how of our product candidates to our own facility. Transferring manufacturing processes and know-how is complex and involves review and incorporation of both documented and undocumented processes that may have evolved over time. In addition, transferring production to different facilities may require utilization of new or different processes to meet the specific requirements of a given facility. Additional

studies may also need to be conducted to support the transfer of certain manufacturing processes and process improvements. We cannot be certain that all relevant know-how and data has been adequately incorporated into the manufacturing process until the completion of studies (and the related evaluations) intended to demonstrate the comparability of material previously produced with that generated by our CMOs. Although some of our employees have experience in the manufacturing of pharmaceutical products from prior employment at other companies, we, as a company, have no prior experience in pharmaceutical product manufacturing, and operating this facility would require us to comply with complex regulations and to continue to hire and retain experienced scientific, quality control, quality assurance and manufacturing personnel. Designing and building a manufacturing facility has been and will continue to be time-consuming and expensive, and we may experience delays or cost overruns. In addition, government approvals would be required for us to operate a manufacturing facility and can be time-consuming to obtain. As a manufacturer of pharmaceutical products, we also would be required to demonstrate and maintain cGMP compliance. These requirements include, among other things, quality control, quality assurance and the maintenance of records and documentation. Furthermore, establishing manufacturing operations may require a reallocation of other resources, particularly the time and attention of our senior management. Even if we are able to establish our own manufacturing capabilities, we could encounter challenges in operating the manufacturing facility in compliance with cGMP, regulatory or other applicable requirements, resulting in potential negative consequences, including regulatory actions, which could undermine our ability to utilize this facility for our own

manufacturing needs. Any failure or delay in the development of our manufacturing capabilities could adversely impact the development of our product candidates.

There are risks associated with manufacturing for clinical and commercial use. Manufacturing biological components at the appropriate scale and quality is complex and difficult.

There are risks associated with manufacturing our product candidates including, among others, cGMP compliance, cost overruns, technical problems with process scale-up, process reproducibility, stability issues, lot consistency, yields and timely availability of raw materials. Even if efficacy and safety data from our clinical trials would otherwise support regulatory approval for a product candidate, there is no assurance that we or any third-party manufacturer will be able to manufacture our product candidates to specifications at levels necessary to support or maintain regulatory approval by the FDA or other regulatory authorities. In addition, we may not be able to manufacture our product candidates in sufficient quantities to meet the requirements for a potential launch or to meet potential future demand. If we or our third-party manufacturers are unable to produce sufficient quantities of the approved product for commercialization, either on a timely basis or at all, our commercialization efforts would be impaired, which would have a material adverse effect on our business, financial condition, results of operations and growth prospects.

We face uncertainties and risks associated with the manufacture of our product candidates. Our product candidates are biologics and their manufacture involves complex processes, including the development of cell lines or cell systems to produce the biologic, with the challenge of significant variability. Further, there are difficulties in growing large quantities of such cells, consistently and sufficiently isolating certain types of cells and harvesting and purifying the biologic produced by them. The cost to manufacture biologics is generally far higher than traditional small molecule chemical compounds, and the manufacturing process can be difficult to reproduce. There is no guarantee we will be successful in establishing a larger-scale commercial manufacturing process for our pipeline product candidates or obtaining the needed manufacturing capacity. Due to the high cost to manufacture, inherent uncertainty related to manufacturing costs, and uncertainty in our patient population, there is risk that some of our product candidates may not be commercially viable.

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

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

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to generate any revenue.

We do not currently have an organization for the sale, marketing and distribution of pharmaceutical products and the cost of establishing and maintaining such an organization may exceed the cost-effectiveness of doing so. In order to market any products that may be approved by the FDA and comparable foreign regulatory authorities, we must build our sales, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. There are significant risks involved in building and managing a sales organization, including our ability to hire, retain and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would

adversely impact the commercialization of any approved products. If we are unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, we may not be able to generate product revenues and may not become profitable. We will be competing with many companies that currently have extensive and well-funded sales and marketing operations. Without an internal commercial organization or the support of a third party to perform sales and marketing functions, we may be unable to compete successfully against these more established companies. If we are not successful in commercializing our current or future product candidates either on our own or through collaborations with one or more third parties, our future product revenue will suffer and we would incur significant additional losses.

We will need to grow the size of our organization, and we may experience difficulties in managing this growth.

As of February 15, 2019, we had 302 full-time employees. We need to grow the size of our organization in order to support our continued development and potential commercialization of our product candidates. In particular, we will need to add substantial numbers of additional personnel and other resources to support our development and potential commercialization of our product candidates. In addition, we may not be able to attract or retain employees with the appropriate levels of experience and to skills to accomplish our objectives. As our development and commercialization plans and strategies continue to develop, or as a result of any

future acquisitions, our need for additional managerial, operational, manufacturing, sales, marketing, financial and other resources will increase. Our management, personnel and systems currently in place may not be adequate to support this future growth. Future growth would impose significant added responsibilities on members of management, including:

•managing our preclinical studies and clinical trials effectively;

•identifying, recruiting, maintaining, motivating and integrating additional employees;

•managing our internal development efforts effectively while complying with our contractual obligations to licensors, licensees, contractors and other third parties;

•improving our managerial, development, operational, information technology, and finance systems; and

•expanding our facilities.

As our operations expand, we will also need to manage additional relationships with various strategic partners, suppliers and other third parties. Our future financial performance and our ability to commercialize our product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to manage our development efforts and preclinical studies and clinical trials effectively and hire, train and integrate additional management, research and development, manufacturing, administrative and sales and marketing personnel. Our failure to accomplish any of these tasks could prevent us from successfully growing our company

Risks Relating to our Industry

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

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

•For genome editing and gene therapy products:

•recombinant proteins;

•other gene therapy/cDNAs;

•antisense;

•siRNA and microRNA approaches, exon skipping;

•small molecule drugs;

•monoclonal antibodies;

•CRISPR/Cas technology; and

•TALE proteins, meganucleases, and MegaTALs.

•Our non-therapeutic applications compete against similar technologies:

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

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

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

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

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

•substantially greater capital resources than ours;

•larger research and development staffs and facilities than ours; and

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

These organizations also compete with us to:

•attract qualified personnel;

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

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

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

Our product candidates are based on novel technologies, which makes it difficult to predict the timing and costs of development and of subsequently obtaining regulatory approval.

We have concentrated our research and development efforts on genome editing, gene therapy, gene regulation and cell therapy. The regulatory approval process for novel product candidates such as ours is unclear and may be lengthier and more expensive than the process for other, better-known or more extensively studied product candidates.

Adverse developments in clinical trials of gene therapy products conducted by others may cause the FDA or other oversight bodies to change the requirements for approval of our product candidates.

These regulatory review committees and advisory groups, and any new guidelines they promulgate, may lengthen the regulatory review process, require us to perform additional preclinical studies or clinical trials, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our current or future product candidates or lead to significant post-approval limitations or restrictions. As we advance our product candidates, we will be required to consult with these regulatory and advisory groups and comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of our product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenue, and our business, financial condition, results of operations and prospects would be harmed. Even if our product candidates are approved, we expect that the FDA will require us to submit follow-up data regarding our clinical trial subjects for a number of years after any approval. If this follow-up data shows negative long-term safety or efficacy outcomes for these patients, the FDA may revoke its approval or change the label of our products in a manner that could have an adverse impact on our business.

In addition, adverse developments in clinical trials of gene therapy or cell therapy products conducted by others may cause the FDA or other oversight bodies to change the requirements for approval of our product candidates. The FDA only recently approved the first in vivo gene therapy, LUXTURNA, and only two in vivo gene therapy products, uniQure N.V.’s Glybera and GlaxoSmithKline’s Strimvelis, have received marketing authorization from the EMA. As a result, it is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates.

Our gene therapy approach utilizes vectors derived from viruses, which may be perceived as unsafe or may result in unforeseen adverse events. Negative public opinion and increased regulatory scrutiny of gene therapy may damage public perception of the safety of our product candidates and adversely affect our ability to conduct our business or obtain regulatory approvals for our product candidates.

Gene therapy remains a novel technology, with only one in vivo gene therapy product approved for a genetic disease to date in the United States and only two in vivo gene therapy products for genetic diseases approved to date in the European Union. Public perception may be influenced by claims that gene therapy is unsafe, and gene therapy may not gain the acceptance of the public or the medical community. In particular, our success will depend upon physicians who specialize in the treatment of genetic diseases targeted by our product candidates, prescribing treatments that involve the use of our product candidates in lieu of, or in addition to, existing treatments with which they are familiar and for which greater clinical data may be available. More restrictive government regulations or negative public opinion would have an adverse effect on our business, financial condition, results of operations and prospects and may delay or impair the development and commercialization of our product candidates or demand for any products we may develop. For example, earlier gene therapy trials led to several well-publicized adverse events, including cases of leukemia and death seen in other trials using other vectors. Serious adverse events in our clinical trials, or other clinical trials involving gene therapy products or our competitors' products, even if not ultimately attributable to the relevant product candidates, and the resulting publicity,

could result in increased government regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates.

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

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

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

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

Risks Relating to our Finances

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

We have generated operating losses since we began operations in 1995. Our net losses for the years ended December 31, 2018, 2017 and 2016 were $68.9 million, $54.6 million and $71.7 million, respectively. The extent of our future losses and the timing of profitability are uncertain, and we expect to incur losses for the foreseeable future. We have been engaged in developing our ZFP technology since inception, which has and will continue to require significant research and development expenditures. To date, we have generated our funding from issuance of equity securities, revenues derived from collaboration agreements, other strategic partnerships in non-therapeutic applications of our technology, federal government research grants and grants awarded by research foundations. As of December 31, 2018, we had an accumulated deficit of $562.7 million. Since our initial public offering in 2000, we have generated an aggregate of approximately $648.7 million in gross proceeds from the sale of our equity securities. We expect to continue to incur additional operating losses for the next several years as we continue to advance our product candidates. If the time required to generate significant product revenues and achieve profitability is longer than we currently anticipate or if we are unable to generate liquidity through equity financing or other sources of funding, we may be forced to curtail or suspend our operations.

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

We have incurred significant operating losses and negative operating cash flows since inception and have not achieved profitability. We expect capital outlays and operating expenditures to increase over the next several years as we expand our infrastructure and research and product development activities. While we believe our financial resources will be adequate to fund our current operations for at least the next twelve months, we will need to raise substantial additional capital to fund the development, manufacturing and potential commercialization of our product candidates. We regularly consider fund raising opportunities and may decide, from time to time, to raise capital based on various factors, including market conditions and our plans of operation. In addition, as we focus our efforts on proprietary human therapeutics, we will need to seek FDA approvals of potential products, a process that could cost in excess of hundreds of millions of dollars per product. We may experience difficulties in accessing the capital market due to external factors beyond our control such as volatility in the equity markets for emerging biotechnology companies and general economic and market conditions both in the United States and abroad. We cannot be certain that we will be able to obtain financing on terms acceptable to us, or at all. Our failure to obtain adequate and timely funding will materially adversely affect our business and our

ability to develop our technology and products candidates and to realize the anticipated benefits of the TxCell Acquisition. Furthermore, any sales of additional equity securities may result in dilution to our stockholders and any debt financing may include business and financial covenants that restricts our operations.

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

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

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

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

•develop a market for our products; and

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

Comprehensive U.S. tax reform legislation could increase the tax burden on our orphan drug programs and adversely affect our business and financial condition.

The U.S. government enacted comprehensive tax legislation in 2017 that includes significant changes to the taxation of business entities. These changes include, among others, (i) a permanent reduction to the corporate income tax rate, (ii) a partial limitation on the deductibility of business interest expense and net operating loss carryforwards, (iii) a shift of the U.S. taxation of multinational corporations from a tax on worldwide income to a territorial system (along with certain rules designed to prevent erosion of the U.S. income tax base) and (iv) a one-time tax on accumulated offshore earnings held in cash and illiquid assets, with the latter taxed at a lower rate. Further, the comprehensive tax legislation, among other things, reduces the orphan drug tax credit from 50% to 25% of qualifying expenditures. When and if we become profitable, this reduction in tax credits may result in an increased federal income tax burden on our orphan drug programs as it may cause us to pay federal income taxes earlier under the revised tax law than under the prior law and, despite being partially off-set by a reduction in the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, may increase our total federal tax liability attributable to such programs.

Notwithstanding the reduction in the corporate income tax rate, the overall impact of this comprehensive tax legislation resulted in an overall reduction in our deferred tax assets, and our business and financial condition could still be adversely affected as additional guidance and regulations are issued with respect to the original tax law change. In addition, it is uncertain if and to what extent various states will conform to this comprehensive tax legislation. The impact of this comprehensive tax legislation on holders of our common stock is also uncertain and could be adverse. Investors should consult with their legal and tax advisors with respect to this comprehensive tax legislation and the potential tax consequences of investing in or holding our common stock.

Risks Relating to our Relationships with Collaborators and Strategic Partners

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

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

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

In addition, conflicts could arise between us and our collaborators resulting from disputes regarding our or our collaborators' or strategic partners' performance under the applicable agreement, including disputes arising from alleged breaches of our agreements with our collaborators and strategic partners. For example, we have certain confidentiality obligations to our collaborators and strategic partners under our agreements with them, and it is possible that, in connection with the data security incident we disclosed in April 2018, we could be subject to claims that we have breached our confidentiality obligations, which could result in damages payable by us and/or the affected collaborator or strategic partner seeking to terminate its agreement with us.

Any of these developments could harm our product development efforts and otherwise adversely affect our business and prospectus.

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

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

For example, under our agreements with Kite, Pfizer and Bioverativ, they have control and broad discretion over all or certain aspects of the clinical development and commercialization of any product developed under the agreement, and we will have little, if any, influence on how these programs will be conducted. Our lack of control over the clinical development in such agreements could cause delays or other difficulties in the development and commercialization of our product candidates, which may prevent us from completing the intended IND filings in a timely fashion and receiving any milestone, royalty payments and other benefits under the agreement. In addition, under their respective agreements, our third-party collaborators have certain rights to terminate the agreements by providing us with advance notices, therefore, the actual milestone payments that we may receive under these agreements may be substantially lower than the full amounts provided for under these agreements.

Our collaborators or strategic partners may decide to adopt alternative technologies or may be unable to develop commercially viable products with our technology, which would negatively impact our revenues and our strategy to develop these products.

Our collaborators or strategic partners may adopt alternative technologies, which could decrease the marketability of ZFP technology. Additionally, because many of our collaborators or strategic partners are likely to be working on more than one development project, they could choose to shift their resources to projects other than those they are working on with us. If they do so, this would delay our ability to test our technology and would delay or terminate the development of potential products based on our ZFP technology. Further, our collaborators and strategic partners may elect not to develop products arising out of our collaborative and strategic partnering arrangements or to devote sufficient resources to the development, manufacturing, marketing or sale of these products. If they terminate the collaborative relationship with us, we will be required to seek the support of other partners or collaborators. We may not have sufficient resources and expertise to develop these programs by ourselves, and we may not be able to identify a suitable partner or negotiate a favorable collaboration agreement to allow us to continue the development of these programs. If any of these events occur, we may not be able to develop our technologies or commercialize our products.

If the licensed products under our non-therapeutic license agreements are not successfully commercialized, or our third-party licensees terminate our agreements, our ability to generate revenue under these license agreements may be limited.

We have a number of collaboration agreements with third parties whereby we licensed our ZFP technologies to develop products in non- therapeutic fields, such as laboratory research reagents, protein pharmaceuticals, and, transgenic animals, as well as plant agriculture

We cannot be certain that we or our collaboration partners will succeed in the development of commercially viable products in these non-therapeutic fields of use, and there is no guarantee that we or our collaboration partners will achieve the milestones set forth in the respective license agreements. To the extent we or our collaboration partners do not succeed in developing and commercializing products or if we or our collaboration partners fail to achieve such milestones, our revenues and benefits under the license agreements will be limited. In the event our third party licensees decide to terminate the license agreements, our ability to generate revenue under such license agreements will cease.

Our collaborations with outside scientists may be subject to change, which could limit our access to their expertise.

We work with scientific advisors and collaborators at academic research institutions. These scientists are not our employees and may have other commitments that would limit their availability to us. Although our scientific advisors generally agree not to do competing work, if a conflict of interest between their work for us and their work for another entity arises, we may lose their services.

Although our scientific advisors and academic collaborators sign agreements not to disclose our confidential information, it is possible that some of our valuable proprietary knowledge may become publicly known through them, which may cause competitive harm to our business.

Risks Relating to our Intellectual Property

Because it is difficult and costly to protect our proprietary rights, and third parties may have filed patent applications that are similar to ours, we cannot guarantee the proprietary protection of our technologies and products.

Our commercial success may depend in part on obtaining and enforcing patent protection for our technology and successfully defending any of our patents that may be challenged. Obtaining and enforcing pharmaceutical and biotechnology patents is costly, time consuming and complex, and we may not be able to file and prosecute all necessary or desirable patent applications, or maintain, enforce and license any patents that may issue from such patent applications, at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and can involve complex legal and factual questions. No consistent policy regarding the breadth of claims allowed in biotechnology patents has emerged to date. Accordingly, we cannot predict the breadth of claims that may issue from any patent applications that we own or license.

We are a party to various license agreements that grant us rights under specified patents and patent applications. We are also party to various license agreements by which we grant third parties rights under specified patents and patent applications. Our current licenses contain performance obligations. If we fail to meet those obligations, the licenses could be terminated. If we are unable to continue to license these technologies on commercially reasonable terms, or at all, we may be forced to delay or terminate aspects of our product development and research activities.

With respect to our present and any future sublicenses, because our rights derive from those granted to our sublicensor, we are subject to the risk that our sublicensor may fail to perform its obligations under the master license or fail to inform us of useful improvements in, or additions to, the underlying intellectual property owned by the original licensor.

We are unable to exercise the same degree of control over intellectual property that we license from third parties as we exercise over our internally developed intellectual property. We do not control the prosecution of certain of the patent applications that we license from third parties; therefore, the patent applications may not be prosecuted as we desire or in a timely manner.

The degree of future protection for our proprietary rights is uncertain, and we cannot ensure that:

•we or our licensors were the first to make the inventions covered by each of our pending patent applications;

•we or our licensors were the first to file patent applications for these inventions;

•the patents of others will not have an adverse effect on our ability to do business;

•others will not independently develop similar or alternative technologies or reverse engineer any of our products, processes or technologies;

•any of our pending patent applications will result in issued patents;

•any patents issued or licensed to us, our collaborators or strategic partners will provide a basis for commercially viable products or will provide us with any competitive advantages;

•any patents issued or licensed to us will not be challenged and invalidated by third parties; or

•we will develop additional products, processes or technologies that are patentable.

Others have filed and in the future are likely to file patent applications that are similar to ours. We are aware that there are academic groups and other companies that are attempting to develop technology that is based on the use of zinc finger, TALE, CRISPR/Cas and other DNA-binding proteins, and that these groups and companies have filed patent applications. Several patents with claims directed to this technology have issued, although we have no current plans to use the claimed inventions. If these or other patent applications issue as patents, it is possible that the holder of any patent or patents granted on these applications may bring an infringement action against us, our collaborators, or strategic partners claiming damages and seeking to enjoin commercial activities relating to the affected products and processes. The costs of litigating the claim could be substantial regardless of outcome. Moreover, we cannot predict whether we, our collaborators, or strategic partners would prevail in any actions. In addition, if the relevant patent claims were upheld as valid and enforceable and our products or processes were found to infringe a patent or patents, we or our collaborators may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, and we may be prevented from making, using, or selling the relevant product or process unless we or our collaborators could obtain a license or were able to design around the patent claims. We can give no assurance that such a license would be available to us or our

collaborators on commercially reasonable terms, or at all, or that we would be able to successfully design around the relevant patent claims. There may be significant litigation in the genomics or cell therapy industry regarding patent and other intellectual property rights, which could subject us to litigation. If we become involved in litigation, it could consume a substantial portion of managerial and financial resources.

We rely on trade secrets to protect technology where we believe patent protection is not appropriate or obtainable. Trade secrets, however, are difficult to protect. While we require employees, academic collaborators and consultants to enter into confidentiality agreements, we may not be able to adequately protect our trade secrets or other proprietary information or enforce these confidentiality agreements.

Our collaborators, strategic partners, and scientific advisors have rights to publish data and information in which we may have rights. If we cannot maintain the confidentiality of our technology and other confidential information in connection with our collaborations and strategic partnerships, then we may not be able to receive patent protection or protect our proprietary information.

If we. are unable to obtain or protect intellectual property rights related to our product candidates, we may not be able to compete effectively in the intended markets.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our product candidates. The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our product candidates in the United States or in other foreign countries. There is no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found, which can invalidate a patent or prevent a patent from issuing from a pending patent application. Even if patents do successfully issue and even if such patents cover our product candidates, third parties may challenge their validity, enforceability or scope, which may result in such patents being narrowed or invalidated. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property, provide exclusivity for our product candidates or prevent others from designing around our claims. Our competitors may be able to circumvent our patents by developing similar or alternative product candidates in a non-infringing manner. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

If the patent applications we hold or have in-licensed with respect to our programs or product candidates fail to issue, if their breadth or strength of protection is threatened, or if they fail to provide meaningful exclusivity for our product candidates, it could dissuade companies from collaborating with us to develop product candidates, and threaten our ability to commercialize, future products. We have filed several patent applications covering our product candidates recently. We cannot offer any assurances about which, if any, patents will issue, the breadth of any such patent or whether any issued patents will be found invalid and unenforceable or will be threatened by third parties. Any successful challenge to these patents or any other patents owned by or licensed to us could deprive us of rights necessary for the successful commercialization of any product candidates that we may develop. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced. Since patent applications in the United States and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we were the first to file any patent application related to a product candidate. Furthermore, if third parties have filed such patent applications, an interference or derivation proceeding in the United States can be initiated by a third party to determine who was the first to invent any of the subject matter covered by the patent claims of our applications.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date or from the filing date of the corresponding international application. Various extensions may be available. However, the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired for a product, we may be open to competition from generic medications. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

If we are unable to protect the confidentiality of our trade secrets, the value of our technology could be materially adversely affected and our business would be harmed.

We rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our product candidate discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures have been and may in the future be breached, and we may not have adequate remedies for any breach. See also the risk factor titled, "Significant disruptions of our information technology systems or data security incidents could result in significant financial, legal, regulatory, business and reputational harm to us." In addition, our trade secrets may otherwise become known or be independently discovered by competitors.

Although we expect all of our employees and consultants to assign their inventions to us, and all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed or that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Misappropriation or unauthorized disclosure of our trade secrets could impair our competitive position and may have a material adverse effect on our business. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret. In addition, others may independently discover our trade secrets and proprietary information. For example, the FDA, as part of its Transparency Initiative, is currently considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA's disclosure policies may change in the future, if at all.

Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent material disclosure of the non-patented intellectual property related to our technologies to third parties, and there is no guarantee that we will have any such enforceable trade secret protection, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition.

Third-party claims of intellectual property infringement may prevent or delay our development and commercialization efforts.

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions, ex parte reexaminations, post-grant review, and inter partes review proceedings before the U.S. Patent and Trademark Office, or U.S. PTO, and corresponding foreign patent offices. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are pursuing development candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties.

Third parties may assert that we are employing their proprietary technology without authorization, and such parties may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. There may be third-party patents or patent applications with claims to materials,

formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. For example, we are aware of certain patents held by a third party related to certain vector manufacturing methods that are currently being used in certain of our product candidates. We have not yet finalized the commercial scale manufacturing process for any of our product candidates. If our commercial scale manufacturing process utilizes these vector manufacturing methods, and if these third-party patents are in force at the time of commercialization, we may need to use or develop a non-infringing manufacturing method or seek a license to these patents. In any event, if any third-party patents were held by a court of competent jurisdiction to cover the manufacturing methods of any of our product candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire. Similarly, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, including combination therapy, the holders of any such patents may be able to block our ability to develop and commercialize the applicable product candidate unless we obtained a license, or until such patents expires. In either case, such a license may not be available on commercially reasonable terms or at all. The inability to obtain required licenses on reasonable commercial terms, if at all, could delay or prevent the preclinical evaluation, drug development collaborations, clinical testing, and/or commercialization of the affected product candidates. Moreover, because patent applications can take many years to

issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

We may not be successful in obtaining or maintaining necessary rights to gene or cell therapy product components and processes for our development pipeline through acquisitions and in-licenses.

Presently, we believe we have rights to the intellectual property, through licenses from third parties and under patents that we own, to develop our gene and cell therapy product candidates. Because our programs may involve additional product candidates such as our recently acquired TX-200 product candidate and potential future CAR-Treg therapies that may require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in-license or use these proprietary rights. In addition, our product candidates may require specific formulations to work effectively and efficiently and these rights may be held by others. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify on commercially reasonable terms, if at all. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities.

For example, we sometimes collaborate with U.S. and foreign academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such right of first negotiation for intellectual property, we may be unable to negotiate a license within the specified time frame or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program.

In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment. If we are unable to successfully obtain rights to required third-party intellectual property rights, our business, financial condition and prospects for growth could suffer.

If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

We are a party to a number of intellectual property license agreements that are important to our business and expect to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose, various diligence, milestone, royalty and other obligations on us. If we fail to

comply with our obligations under these agreements, or we are subject to a bankruptcy, the licensor may have the right to terminate the license, in which event we would not be able to market products covered by the license.

We may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we have done so from time to time. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we may be required to expend significant time and resources to develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could harm our business significantly. We cannot provide any assurances that third-party patents do not exist that might be enforced against our current product candidates or future products, resulting in either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties.

In many cases, patent prosecution of our in-licensed technology is controlled solely by the licensor. If our licensors fail to obtain and maintain patent or other protection for the proprietary intellectual property we license from them, we could lose our rights

to the intellectual property or our exclusivity with respect to those rights, and our competitors could market competing products using the intellectual property. In certain cases, we control the prosecution of patents resulting from licensed technology. In the event we breach any of our obligations related to such prosecution, we may incur significant liability to our licensing partners. Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues and is complicated by the rapid pace of scientific discovery in our industry. Disputes may arise regarding intellectual property subject to a licensing agreement, including:

•the scope of rights granted under the license agreement and other interpretation-related issues;

•the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;

•the sublicensing of patent and other rights under our collaborative development relationships;

•our diligence obligations under the license agreement and what activities satisfy those diligence obligations;

•the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and

•the priority of invention of patented technology.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

In addition, the agreements under which we currently license intellectual property or technology from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates, which could have a material adverse effect on our business, financial conditions, results of operations, and prospects. As an example, TxCell has exclusively licensed the right to the CAR for use in TX-200 from the University of British Columbia, or UBC. Should UBC terminate this license agreement, we may have to develop or acquire the appropriate CAR which would extend our anticipated development timeline and add expense, and which could result in our failure to realize the anticipated benefits of the TxCell Acquisition.

We may be involved in lawsuits or similar proceedings to protect or enforce our patents or the patents of our licensors, which could be expensive, time-consuming and unsuccessful.

Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid, is unenforceable, in whole or in part, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly and could put our patent applications at risk of not issuing. Moreover, if we or one of our licensing partners initiated legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid and/or unenforceable. In patent litigation in the United States,

defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the U.S. PTO, or made a misleading statement, during prosecution. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post grant review, inter partes review and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover our product candidate. For example, TxCell has exclusively licensed the rights to technology related to redirected Treg cells from the Yeda Research and Development Company, or Yeda. A patent included in this exclusive license agreement with Yeda was granted in Europe in July 2016. Subsequent to this grant, the patent was opposed by several parties in May 2017 and revoked in November 2018. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection could have a material adverse impact on our business.

Interference or derivation proceedings provoked by third parties or brought by us or declared by the U.S. PTO may be necessary to determine the priority of inventions or other matters of inventorship with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all, or if a non-exclusive license is offered and our competitors gain access to the same technology. Our defense of litigation, interference, derivation, or other proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties or that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

We employ individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and independent contractors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of any of our employee's former employer or other third parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely impact our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We may also be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the U.S. PTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and/or applications. We have systems in place to remind us to pay these fees, and we employ an outside firm and rely on our outside counsel to pay these fees due to non-U.S. patent agencies. The U.S. PTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ

professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business.

Changes in patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biotechnology companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involve both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain. Changes in either the patent laws or interpretation of the patent laws in the United States or in other jurisdictions in which we seek patent protection could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. The United States enacted the Leahy-Smith America Invents Act, or the America Invents Act, which includes a number of significant changes that affect the way patent applications will be prosecuted and also may affect patent litigation. These include allowing third party submission of prior art to the U.S. PTO during patent prosecution and additional procedures to attack the validity of a patent by U.S. PTO administered post-grant

proceedings, including post-grant review, inter partes review, and derivation proceedings. Because of a lower evidentiary standard in U.S. PTO proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a U.S. PTO proceeding sufficient for the U.S. PTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. In addition, the challenged patents are not accorded the presumption of validity as they are in Federal District Court. Accordingly, a third party may attempt to use the U.S. PTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Therefore, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our owned or in-licensed patent applications and the enforcement or defense of our owned or in-licensed issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations, and prospects. Moreover, recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts, the U.S. PTO, and similar legislative, judicial and regulatory bodies in other jurisdictions, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

Risks Relating to our Business Operations

Significant disruptions of our information technology systems or data security incidents could result in significant financial, legal, regulatory, business and reputational harm to us.

We are increasingly dependent on information technology systems and infrastructure, including mobile technologies, to operate our business. In the ordinary course of our business, we collect, store, process and transmit large amounts of sensitive information, including intellectual property, proprietary business information, personal information and other confidential information. It is critical that we do so in a secure manner to maintain the confidentiality, integrity and availability of such sensitive information. We have also outsourced elements of our operations (including elements of our information technology infrastructure) to third parties, and as a result, we manage a number of third-party vendors who may or could have access to our computer networks or our confidential information. In addition, many of those third parties in turn subcontract or outsource some of their responsibilities to third parties. As a result, our information technology systems, including the functions of third parties that are involved or have access to those systems, is very large and complex. While all information technology operations are inherently vulnerable to inadvertent or intentional security breaches, incidents, attacks and exposures, the size, complexity, accessibility and distributed nature of our information technology systems, and the large amounts of sensitive information stored on those systems, make such systems potentially vulnerable to unintentional or malicious, internal and external attacks on our technology environment. Potential vulnerabilities can exploited from inadvertent or intentional actions of our employees, third-party vendors, business partners, or by malicious third parties. Attacks of this nature are increasing in their frequency, levels of persistence, sophistication and intensity, and are being conducted by sophisticated and organized groups and individuals with a wide range of motives (including, but not limited to, industrial espionage) and expertise, including organized criminal groups, “hacktivists,” nation states and others. In addition to the extraction of sensitive

information, such attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. In addition, the prevalent use of mobile devices increases the risk of data security incidents.

Significant disruptions of our, our third-party vendors' and/or business partners' information technology systems or other similar data security incidents could adversely affect our business operations and/or result in the loss, misappropriation, and/or unauthorized access, use or disclosure of, or the prevention of access to, sensitive information, which could result in financial, legal, regulatory, business and reputational harm to us. For example, in April 2018, we announced a data security incident involving the compromise of a senior executive's company email account. Upon learning of the incident on March 28, 2018, external network security experts were promptly engaged, and the incident response team worked diligently to investigate the incident. We also promptly notified federal law enforcement of the incident. The investigation concluded that the incident was limited to the compromise of the senior executive's company email account for approximately 11 weeks. The investigation did not reveal any evidence that our network or other information technology systems were otherwise compromised in connection with the incident or that the incident resulted in the disclosure of or access to personal information about patients or other individuals besides the holder of the company email account that was affected. However, proprietary, confidential and other sensitive information of ours and that of other entities was accessed and may have been compromised as a result of the incident. Unforeseen developments related to this incident could occur, which could have a further adverse impact on us. We do not maintain cyber liability insurance and will therefore have no coverage for any losses resulting from this data security incident. Any litigation or regulatory review arising from this incident could result in significant legal exposure to us. In addition, information technology system disruptions, whether from attacks on our technology environment or from computer viruses, natural disasters, terrorism, war and telecommunication and electrical failures, could result in a material disruption of our development programs and our business operations. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data.

While we aware of the company email incident described above, there is no way of knowing with certainty whether we have experienced any other data security incidents that have not been discovered. While we have no reason to believe this to be the case, attackers have become very sophisticated in the way they conceal access to systems, and many companies that have been attacked are not aware that they have been attacked. Any event, including the company email incident described above, that leads to unauthorized access, use or disclosure of personal information, including but not limited to personal information regarding our patients or employees, could disrupt our business, harm our reputation, compel us to comply with applicable federal and/or state breach notification laws and foreign law equivalents, subject us to time consuming, distracting and expensive litigation, regulatory investigation and oversight, mandatory corrective action, require us to verify the correctness of database contents, or otherwise subject us to liability under laws, regulations and contractual obligations, including those that protect the privacy and security of personal information. This could result in increased costs to us, and result in significant legal and financial exposure and/or reputational harm. In addition, any failure or perceived failure by us or our vendors or business partners to comply with our privacy, confidentiality or data security-related legal or other obligations to third parties, or any further security incidents or other inappropriate access events that result in the unauthorized access, release or transfer of sensitive information, which could include personally identifiable information, may result in governmental investigations, enforcement actions, regulatory fines, litigation, or public statements against us by advocacy groups or others, and could cause third parties, including clinical sites, regulators or current and potential partners, to lose trust in us or we could be subject to claims by third parties that we have breached our privacy- or confidentiality-related obligations, which could materially and adversely affect our business and prospects. In addition, failure to maintain effective internal accounting controls related to security breaches and cybersecurity in general could impact our ability to produce timely and accurate financial statements and subject us to regulatory scrutiny. Moreover, data security incidents and other inappropriate access can be difficult to detect, and any delay in identifying them may lead to increased harm of the type described above. While we have implemented security measures intended to protect our information technology systems and infrastructure, there can be no assurance that such measures will successfully

prevent service interruptions or further security incidents.

We may not realize the anticipated benefits of the TxCell Acquisition or be able to successfully integrate the acquired TxCell operations.

The TxCell Acquisition involves numerous uncertainties and risks, and has required, and will continue to require, significant efforts and expenditures, including with respect to integrating the acquired TxCell operations with our operations. We may not be able to accomplish this integration process smoothly or successfully. The integration of certain of the acquired TxCell operations will take time and will require the dedication of significant management resources, which may temporarily distract our management's attention from the routine business of the combined company. In any event, we may encounter unexpected difficulties, or incur unexpected costs, in connection with our transition activities and integration efforts, which include:

- the potential disruption of our historical core business;

- the risk that our relative lack of historical experience in CAR-Treg development and developing product candidates and technology for immunological diseases will not allow us to advance the development of CAR-Treg therapies, including TX-200, on the timeframes we expect, or at all;
- the strain on, and need to continue to expand, our existing operational, technical, financial and administrative infrastructure;
- the difficulties in assimilating employees and corporate cultures;
- the difficulties in effectively managing transition and integration activities given the distance between our headquarters and U.S.-based management team and TxCell's offices in France;
- the failure to retain key managers and other personnel, including the employees from the acquired TxCell business who might experience uncertainty about their future roles with us;
- the challenges in controlling additional costs and expenses in connection with and as a result of the TxCell Acquisition;
- the diversion of our management's attention to integration of operations and corporate and administrative infrastructures; and
- any unanticipated liabilities for activities of or related to TxCell or its operations, technologies or product candidates.

If any of these factors impairs our ability to integrate successfully, we may be required to spend time or money on integration activities that otherwise would be spent on the development and expansion of our business. If we fail to integrate or otherwise manage the acquired TxCell business successfully and in a timely manner, the combined company's potential to achieve the anticipated long-term strategic benefits of the TxCell Acquisition could be compromised and resulting operating inefficiencies could increase costs and expenses more than we planned, could negatively impact the market price of our common stock and could otherwise distract us from execution of our strategy. Failure to maintain effective financial controls and reporting systems and procedures could also adversely affect our ability to produce timely and accurate financial statements. In addition, while we intend to avail ourselves of the French tax credit for certain research and development related expenses, we may not receive the anticipated amount and we may also be required to make corrective actions upon any audit by the French tax authority with respect to such tax credit.

In any event, there can be no assurance that we will integrate or otherwise manage the acquired TxCell business successfully or otherwise do so without experiencing operating inefficiencies or control deficiencies. In addition, because the historical business operations of TxCell differ from our historical business operations, and the combined company has a different business mix than our historical business, we face different operational risks and challenges and the complexity of our company has increased. Significant management time and effort is required to effectively manage the increased complexity of our company following the TxCell Acquisition, and our failure to successfully do so could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

If we are unable to acquire 100% of the equity interests of TxCell, our business, financial condition and results of operations could be adversely affected.

Although we completed the TxCell Acquisition, we may not be able to acquire the remaining ordinary shares of TxCell for some period of time, if ever. As of February 15, 2019, we have acquired a total of 25,047,671 ordinary shares of TxCell, representing approximately 98.2% of the outstanding share capital and voting rights of TxCell. Until such time, if ever, that we acquire 100% of the equity interests of TxCell, we will need to consider the rights of, and duties owed to, the minority shareholders of TxCell under French law when making future decisions that might impact TxCell, its business or its operations, which could adversely affect our business and our ability to realize the anticipated benefits of the TxCell Acquisition.

We plan to continue to operate the acquired TxCell business in France, which may expose us to unanticipated costs or events.

TxCell's historical operations have been based in France and we plan to continue to operate the acquired TxCell business in France. Our operation of the acquired TxCell business in France involves significant risks, including:

- difficulty hiring and retaining appropriate personnel due to intense competition for such limited resources;
- disruptions in relations with our employees, including legacy TxCell employees; and
- compliance with regulatory requirements, including local French employment regulations and organized labor in France.

In addition, as a result of our operations in France, we have become more exposed to fluctuations in currency exchange rates between the Euro and the U.S. dollar. Given the volatility of currency exchange rates, there is no assurance that we will be able to effectively manage currency transaction and/or conversion risks. To date, we have not entered into derivative instruments to offset the impact of foreign exchange fluctuations, which fluctuations could have a material adverse effect on our financial condition and results of operations. In any event, difficulties resulting from these and other risks related to our anticipated operations in France could expose us to increased expenses, impair our development efforts, adversely affect our financial condition and results of operations, and harm our competitive position.

We are also exposed to general risks associated with our operations outside of the United States, which could adversely affect our business.

In addition to our French operations as a result of the TxCell Acquisition, we also have operations and conduct business in other countries outside the United States, and have a UK subsidiary. We may plan to expand these activities or in to additional countries in the future. Consequently, we are, and will continue to be, subject to risks inherent with operating in foreign countries, in addition to those specific risks associated with TxCell, which include:

- the increased complexity and costs inherent in managing international operations, including in geographically disparate locations;
- diverse regulatory, financial and legal requirements, and any future changes to such requirements, in one or more countries where we are located or do business;
    - differing payor reimbursement regimes, governmental payors or patient self-pay systems and price controls;
- adverse tax consequences, including changes in applicable tax laws and regulations;
- applicable trade laws, tariffs, export quotas, custom duties or other trade restrictions, and any changes to them;
- economic weakness, including inflation, or political or economic instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign currency fluctuations, which could result in increased operating expenses or reduced revenues, and other obligations incident to doing business or operating in another country;
- liabilities for activities of, or related to, our international operations;
- challenges inherent in efficiently managing employees in diverse geographies, including the need to adapt systems, policies, benefits and compliance programs to differing labor and other regulations;
- workforce uncertainty in countries where labor unrest is more common than in the United States; and
- laws and regulations relating to data security and the unauthorized use of, or access to, commercial and personal information.

Our foreign operations also expose us to risks associated with “Brexit.” In June 2016, UK voters approved a referendum to withdraw the UK's membership from the EU, which is commonly referred to as "Brexit". In March 2017, the UK government initiated the exit process under Article 50 of the Treaty of the European Union, commencing a period of up to two years for the UK and the other EU member states to negotiate the terms of the withdrawal, such period ending on March 29, 2019 unless extended. There has been limited progress so far in the negotiations and continued uncertainty in the UK government and Parliament, which increases the possibility of the UK exiting the EU on March 29, 2019 without a formal withdrawal agreement in place and of resulting significant market and economic disruption. We have operations in the UK and in France, which is in the EU, and as a result, we face risks associated with the potential uncertainty and disruptions that may lead up to and follow Brexit, including

with respect to volatility in exchange rates and interest rates and potential material changes to the regulatory regime applicable to our operations in the UK. Brexit could adversely affect European or worldwide political, regulatory, economic or market conditions and could contribute to instability in global political institutions, regulatory agencies and financial markets. For example, depending on the terms of Brexit, the UK could also lose access to the single EU market and to the global trade deals negotiated by the EU on behalf of its members. Any of these effects of Brexit, and others we cannot anticipate or that may evolve over time, could adversely affect our business, results of operations and financial condition.

If we use biological and hazardous materials in a manner that causes injury or violates laws, we may be liable for damages.

Our research and development activities involve the controlled use of potentially harmful biological materials as well as hazardous materials, chemicals, and various radioactive compounds typically employed in the study of molecular and cellular biology. We routinely use cells in culture and gene delivery vectors, and we employ small amounts of radioisotopes in trace experiments. Although we maintain up-to-date licensing and training programs, we cannot completely eliminate the risk of accidental contamination or injury from the use, storage, handling, or disposal of these materials. In the event of contamination or injury, we could be held liable for damages that result, and any liability could exceed our resources. We currently carry insurance covering certain claims arising from our use of these materials. However, if we are unable to maintain our insurance coverage at a reasonable cost and with adequate coverage, our insurance may not cover any liability that may arise. We are subject to federal, state, and local laws and regulations governing the use, storage, handling, and disposal of these materials and specified waste products.

Failure to attract, retain, and motivate skilled personnel and cultivate key academic collaborations will delay our product development programs and our research and development efforts.

Our success depends on our continued ability to attract, retain, and motivate highly qualified management and scientific personnel and our ability to develop and maintain important relationships with leading research and academic institutions and scientists. Competition for skilled and qualified personnel and academic and other research collaborations is intense. If we lose the services of personnel with the necessary skills, including the members of our senior management team, it could significantly impede the achievement of our research and development objectives. In addition, we expect to rely on the experience and expertise of TxCell's historical management team and other key personnel in the development of TX-200 and potential future CAR-Treg therapies. If we were to lose the services of a significant portion or key individuals of this team, such development and our business could be adversely affected. Moreover, if we fail to negotiate additional acceptable collaborations with academic and other research institutions and scientists, or if our existing collaborations are unsuccessful, our development programs may be delayed or may not succeed.

Third parties on which we rely and we may be adversely affected by natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Natural disasters could severely disrupt our operations and have a material adverse effect on our business, financial condition, results of operations and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and may not prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

Risks Relating to our Common Stock and Corporate Organization

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

Our stock price has been volatile and may continue to be volatile, which could cause stockholders 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 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, and our policies regarding stock transactions, a number of our employees, 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.

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 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, our stockholders 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, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

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.

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 will therefore be limited to the appreciation of their stock.

Anti-takeover provisions in our certificate of incorporation, Delaware law and our bylaws could make an acquisition of our company more difficult and could prevent attempts by our stockholders 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 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:

•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 General Corporation Law of the State of Delaware, 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.

Our amended and restated bylaws provide that a state or federal court located within the State of Delaware will be the exclusive forum for the adjudication of certain disputes, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, or employees.

Our amended and restated bylaws provide that a state or federal court located within 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 or stockholder 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, our charter or our bylaws, as to which the General Corporation Law of the State of Delaware confers jurisdiction on the Court of Chancery 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 will be deemed to have notice of and consented to the provisions of such provision.

This provision may limit a stockholder's ability 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.

ITEM 1B – UNRESOLVED STAFF COMMENTS

None.

ITEM 2 – PROPERTIES

Our corporate headquarters occupies approximately 45,600 square feet of research and office space located in Richmond, California, subject to leases that expire beginning in August 2019 through August 2026. We also have a build-to-suit lease located in Richmond, California to occupy approximately 41,400 square feet of space that expires in December 2021. We also have a build-to-suit lease located in Brisbane, California that occupies approximately 87,700 square feet of space that expires in May 2029 for which we are currently occupying the 2nd and 3rd floors. In addition, we have a property in Valbonne, France with approximately 14,036 square feet of research and office space that expires in June 2022.

ITEM 3 – LEGAL PROCEEDINGS

We are not a party to any material pending legal proceeding. From time to time, we may be involved in legal proceedings arising in the ordinary course of business.

ITEM 4 – MINE SAFETY DISCLOSURES

Not Applicable.

PART II

ITEM 5 – MARKET FOR THE REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Information

Our common stock trades on the Nasdaq Global Select Market under the symbol "SGMO".

Holders

As of February 15, 2019, there were 54 holders of record of our common stock. This number does not include "street name" or beneficial holders, whose shares are held of record by banks, brokers, financial institutions and other nominees.

Dividends

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

Stock Performance Graph

The above Stock Performance Graph and related information shall not be deemed “soliciting material” or to be “filed” with the Securities and Exchange Commission, nor shall such information be incorporated by reference into any future filing under the Securities Act of 1933 or Securities Exchange Act of 1934, each as amended, except to the extent that the Company specifically incorporates it by reference into such filing.

ITEM 6 – SELECTED FINANCIAL DATA

The following Selected Financial Data should be read in conjunction with “Item 7—Management’s Discussion and Analysis of Financial Condition and Results of Operations” and “Item 8—Financial Statements and Supplementary Data” included elsewhere in this Annual Report on Form 10-K.

Selected Financial Data

	Year Ended December 31,				
	2018(1)	2017	2016	2015	2014
	(In thousands, except per share data)				
Statement of Operations Data:					
Total revenues	$84,452	$36,567	$19,389	$39,539	$45,870
Operating expenses:					
Research and development	114,866	65,728	65,618	67,198	56,974
General and administrative	46,736	27,200	26,330	19,197	15,677
Total operating expenses	161,602	92,928	91,948	86,395	72,651
Loss from operations	(77,150)	(56,361)	(72,559)	(46,856)	(26,781)
Interest and other income, net	8,261	1,793	887	431	364
Benefit from income taxes	—	—	14	5,722	—
Net loss	(68,889)	(54,568)	(71,658)	(40,703)	(26,417)
Net loss attributable to non-controlling interest	(555)	—	—	—	—
Net loss attributable to Sangamo Therapeutics, Inc. stockholders	$(68,334)	$(54,568)	$(71,658)	$(40,703)	$(26,417)
Basic and diluted net loss per share attributable to Sangamo Therapeutics, Inc. stockholders	$(0.70)	$(0.70)	$(1.02)	$(0.58)	$(0.39)
Shares used in computing basic and diluted net loss per share attributable to Sangamo Therapeutics, Inc. stockholders	96,941	78,084	70,553	69,757	67,022

	As of December 31,				
	2018	2017	2016	2015	2014
	(In thousands)				
Balance Sheet Data:					
Cash, cash equivalents, marketable securities, and interest receivable	$400,508	$244,560	$142,759	$209,307	$226,645
Working capital	332,010	203,538	136,289	192,485	169,997
Total assets	590,395	286,741	157,891	217,235	243,212
Accumulated deficit	(562,696)	(495,479)	(440,911)	(369,253)	(328,550)

Total stockholders' equity	367,257	187,900	136,195	192,439	206,633

Note:

(1) TxCell was acquired in October 2018 and the results of operations have been included in the selected consolidated financial data since the date of acquisition (see Note 6 – Acquisition of TxCell, S.A. to our consolidated financial statements).

ITEM 7 – MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The discussion in "Management's Discussion and Analysis of Financial Condition and Results of Operations" contains trend analysis, estimates and other forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. These forward-looking statements include, without limitation, statements containing the words "believes," "anticipates," "expects," "continue," "intend," "plan," "will," and other words of similar import or the negative of those terms or expressions. Such forward-looking statements are subject to known and unknown risks, uncertainties, estimates and other factors that may cause our actual results, performance or achievements, or industry results, to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements. Actual results could differ materially from those set forth in such forward-looking statements as a result of, but not limited to, the "Risk Factors" described in Part I, Item 1A. You should read the following discussion and analysis along with the "Selected Financial Data" and the financial statements and notes attached to those statements included elsewhere in this report.

Overview

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 genome editing, gene therapy, gene regulation and cell therapy. We are focused on three therapeutic areas: inherited metabolic diseases, or IMDs, 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 acquired 98.2% of the outstanding share capital and voting rights of TxCell S.A., or TxCell, which we refer to in this report as the TxCell Acquisition, for aggregate purchase consideration of approximately $80.4 million. As of December 31, 2018, the fair value of the remaining outstanding free shares was approximately $1.3 million. The total fair value of the net assets acquired was approximately $81.7 million (see Note 6 to our consolidated financial statements – Acquisition of TxCell, S.A.).

With the TxCell Acquisition, 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 TX Cell 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 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 IMDs. We also have an ongoing Phase1/2 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. We also plan to initiate a Phase 1/2 clinical trial of for TxCell's first CAR-Treg investigational product candidate for solid organ transplant, or TX 200, in 2019.

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., for the research, development and commercialization of potential engineered cell therapies for cancer. The Kite agreement became effective in April 2018 when the waiting periods under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended and other customary closing conditions were completed. In this collaboration, we are working together with Kite on a research program under which we are designing 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, T-cell receptors, and NK-cell receptors directed to mutually agreed targets. Kite is responsible for all clinical development and commercialization of any resulting products.

In December 2017, we entered into a 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 FTLD, 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 Genzyme Corporation, to research, develop and commercialize therapeutic gene-edited cell therapy products in hemoglobinopathies, including beta-thalassemia and sickle cell disease, or SCD. Bioverativ is responsible for subsequent development, manufacturing and commercialization of licensed products.

We have incurred net losses since inception and expect to incur losses in the future as we continue our research and development activities. To date, we have funded our operations primarily through the issuance of equity securities, revenues from corporate collaborations and research grants.

Our revenues have consisted primarily of revenues from our corporate partners for ZFN and ZFP TF programs, contractual payments from strategic partners for research services and research milestones, and research grant funding. We expect revenues will continue to fluctuate from period to period and there can be no assurance that new collaborations or partner funding will continue beyond their initial terms or that we are able to meet the milestones specified in these agreements.

We expect to continue to devote substantial resources to research and development in the future and expect research and development expenses to increase in the next several years if we are successful in advancing our gene therapy and our genome editing programs in the clinic and if we are able to progress our earlier stage product candidates into clinical trials. Pursuant to the terms of the agreements with Kite and Bioverativ, certain expenses related to research and development activities will be reimbursed to us. The reimbursement funds to be received from Kite and Bioverativ will be recognized as revenue as the costs are incurred and collection is reasonably assured.

General and administrative expenses consist primarily of salaries and personnel related expenses for executive, finance and administrative personnel, stock-based compensation expenses, professional fees, allocated facilities expenses, patent prosecution expenses and other general corporate expenses. As we continue to advance our product candidates into and through the clinic, we expect the growth of our business to require increased general administrative expenses.

For the year ended December 31, 2018, we incurred a consolidated net loss of $68.9 million, or $0.70 per share, compared to a consolidated net loss of $54.6 million, or $0.70 per share, for the same period in 2017. As of December 31, 2018, we had cash, cash equivalents, marketable securities and interest receivable totaling $400.5 million compared to $244.6 million as of December 31, 2017. As of December 31, 2018, we had an accumulated deficit of $562.7 million.

Critical Accounting Policies and Estimates

The accompanying discussion and analysis of our financial condition and results of operations are based upon our consolidated financial statements and the related disclosures, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates, assumptions and judgments that affect the reported amounts in our consolidated financial statements and accompanying notes. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. We believe the following policies to be the most critical to an understanding of our financial condition and results of operations because they require us to make estimates, assumptions and judgments about matters that are inherently uncertain.

Revenue Recognition

Effective January 1, 2018, we adopted the provisions of Accounting Standards Codification, or ASC, Topic 606, Revenue from Contracts with Customers ("Topic 606") resulting in a change to our accounting policy for revenue recognition. Topic 606 establishes a unified model to determine how revenue is recognized.

Contract revenues consist of strategic partnering collaboration agreements and research activity grants and licensing. Research and licensing agreements typically include upfront signing or license fees, cost reimbursements, research services, minimum sublicense fees, milestone payments and royalties on future licensee's product sales. We have both fixed and variable consideration. Non-refundable upfront fees and funding of research and development activities are considered fixed, while milestone payments are identified as variable consideration. Our research grants are typically multi-year agreements and provide for the reimbursement of qualified expenses for research and development as defined under the terms of the grant agreement. Revenues under grant agreements are recognized when the related qualified research expenses are incurred. Deferred revenue represents the portion of research or license payments received but not earned.

In determining the appropriate amount of revenue to be recognized as we fulfill our obligations under its agreements, we perform the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations based on estimated selling prices; and (v) recognition of revenue when (or as) we satisfy each performance obligation.

A performance obligation is a promise in a contract to transfer a distinct good or service to the customer and is the unit of account in Topic 606. Our performance obligations include license rights, development services, and services associated with regulatory submission and approval processes. Significant management judgment is required to determine the level of effort required under an arrangement and the period over which we expect to complete our performance obligations under the arrangement. If we cannot reasonably estimate when our performance obligations either are completed or become inconsequential, then revenue recognition is deferred until we can reasonably make such estimates. We include the unconstrained amount of estimated variable consideration in the transaction price. The amount included in the transaction price is constrained to the amount for which it is probable that a significant reversal of cumulative revenue recognized will not occur. At the end of each subsequent reporting period, we re-evaluate the estimated variable consideration included in the transaction price and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Revenue is then recognized over the remaining estimated period of performance using the cumulative catch-up method. The estimated period of performance and project costs are reviewed quarterly and adjusted, as needed, to reflect our current assumptions regarding the timing of our deliverables.

As part of the accounting for these arrangements, we must develop assumptions that require judgment to determine the stand-alone selling price of each performance obligation identified in the contract. We used key assumptions to determine the stand-alone selling price, which may include forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success.

During 2018, revenues related to our hemophilia A collaboration agreement with Pfizer and the collaboration agreement with Kite represented 45% and 30%, respectively, of our total revenues. During 2017, revenues related to Pfizer and Bioverativ represented 47% and 34%, respectively, of our total revenues. During 2016 revenue related to Bioverativ, with Dow AgroSciences ("DAS") and Shire International GmbH, or Shire, a wholly owned subsidiary of Takeda Pharmaceutical Company Limited, or Shire, represented 46%, 26%, and 17%, respectively, of our total revenues. Receivables from collaborations are typically unsecured and are concentrated in the biopharmaceutical industry. Accordingly, we may be exposed to credit risk generally associated with biopharmaceutical companies or specific to our collaboration agreements. To date, we have not experienced any losses related to these receivables.

Funds received from third parties under contract or grant arrangements are recorded as revenue if we are deemed to be the principal participant in the arrangements because the activities under the contracts or grants are part of our development programs. Contract funds received are not refundable and are recognized when the related qualified research and development costs are incurred and there is reasonable assurance that the funds will be received. Funds received in advance are recorded as deferred revenue.

Business Combinations

In accordance with ASC Topic 805, Business Combinations, we determine and allocate the purchase price of an acquired business to the tangible and identifiable intangible assets acquired and liabilities assumed based on their estimated fair values as of the business combination date, including identifiable intangible assets that either arise from a contractual or legal right or are separable from goodwill. We base the estimated fair value of identifiable intangible assets acquired in a business combination on independent valuations that use information and assumptions provided by management, which consider management's best estimates of inputs and assumptions that a market participant would use. We allocate any excess purchase price over the estimated fair value assigned to the net tangible and identifiable intangible assets acquired and liabilities assumed to goodwill.

Transaction costs associated with acquisitions are expensed as incurred in general and administrative expenses. Results of operations and cash flows of acquired companies are included in our operating results from the date of acquisition.

Purchased Intangible Assets

Acquired intangible assets with indefinite useful lives are related to purchased in-process research and development ("IPR&D"), projects and are measured at their respective fair values as of the acquisition date. We do not amortize intangible assets with indefinite useful lives. Intangible assets related to IPR&D projects are considered to be indefinite-lived until the completion or abandonment of the associated research and development efforts. If and when development is complete, which generally occurs if and when regulatory approval to market a product is obtained, the associated assets would be deemed finite-lived and would then be amortized based on their respective estimated useful lives at that point in time.

We test IPR&D for impairment on an annual basis and in between annual tests if we become aware of any events or changes that would indicate that it is more likely than not that the fair values of the assets are below their carrying amounts. If the fair value exceeds the carrying value, then there is no impairment. Impairment losses on indefinite-lived intangible assets are recognized based solely on a comparison of the fair value of the asset to its carrying value, without consideration of any recoverability test. We have not identified any such impairment losses to date.

Goodwill

Goodwill represents the excess of the cost of an acquisition over the sum of the amounts assigned to tangible and identifiable intangible assets acquired, less liabilities assumed. Goodwill is not subject to amortization, but is tested for impairment on an annual basis and whenever events or changes in circumstances indicate the carrying amount of these assets may not be recoverable.

Comparability

We adopted Topic 606 on January 1, 2018, resulting in a change to our accounting policy for revenue recognition. We used the modified retrospective method and recognized the cumulative effect of initially applying Topic 606 as an adjustment to the opening balances of deferred revenues and accumulated deficit at January 1, 2018. Accordingly, comparative information has not been adjusted and continues to be reported under previous accounting standards (see Note 1 to our consolidated financial statements - Organization and summary of significant accounting policies, for additional information).

As noted above, we completed the TxCell Acquisition in the fourth quarter of 2018. The TxCell Acquisition was accounted for as a business combination in accordance with the guidance ASC Topic 805, Business Combinations. The operating results of TxCell after the acquisition date have been included in our consolidated financial statements. For the three months ended December 31, 2018, TxCell did not contribute any revenue. For the three months ended December 31, 2018, operating expenses related to TxCell were approximately $3.7 million.

Results of Operations

Years Ended December 31, 2018, 2017 and 2016

Revenues

	Year Ended December 31,								
	2018	2017	Change	% Change	2017	2016	Change	% Change	
	(In thousands, except percentage values)								
Revenues:									
Collaboration agreements	$84,065	$35,960	$48,105	134	%	$35,960	$18,881	$17,079	90	%
Research grants	387	607	(220)	-36	%	607	508	99	19	%
Total revenues	$84,452	$36,567	$47,885	131	%	$36,567	$19,389	$17,178	89	%

Total revenues consisted of revenues from collaboration agreements and research grants. We anticipate revenues over the next several years will be derived primarily from our collaboration agreements with Kite, Pfizer and Bioverativ as we continue to recognize in revenues upfront payments received under such agreements overtime.

The increase of $48.1 million in revenues from collaborations in 2018 compared to 2017 was primarily attributable to $25.5 million in revenue related to our agreement with Kite, $20.8 million related to the hemophilia A Pfizer Agreement, $2.2 million

related to the C9ORF72 Pfizer agreement, and $1.3 million related to our agreement with Bioverativ. During 2018, revenues related to our collaborative agreements with Pfizer, Kite and Bioverativ represented 45%, 30% and 16%, respectively, of total revenues.

The increase of $18.9 million in revenues from collaborations in 2017 compared to 2016 was primarily due to increases of $17.0 million in revenues related to the hemophilia A Pfizer agreement and $3.4 million related to our agreement with Bioverativ, partially offset by decreases of $2.1 million in royalty revenue related to our agreement with DAS, $0.8 million related to research services provided to Shire, and $0.5 million in license and royalty fees pursuant to our agreement with Sigma-Aldrich Corporation. During 2017, revenues related to our collaborative agreements with Pfizer and Bioverativ represented 47% and 34%, respectively, of total revenues.

Research grant revenues were $0.4 million, $0.6 million, and $0.5 million in 2018, 2017, and 2016, respectively. The changes in grant revenue from 2017 to 2018 and from 2016 and 2017 were not significant.

Operating Expenses

	Year Ended December 31,								
	2018	2017	Change	% Change	2017	2016	Change	% Change	
	(In thousands, except percentage values)								
Operating expenses:									
Research and development	$114,866	$65,728	$49,138	75	%	$65,728	$65,618	$ 110	0	%
General and administrative	46,736	27,200	19,536	72	%	27,200	26,330	870	3	%
Total expenses	$161,602	$92,928	$68,674	74	%	$92,928	$91,948	$ 980	1	%

Research and Development Expenses

The increase of $49.1 million in research and development expenses in 2018 was primarily due to increases of $23.9 million in clinical trial and manufacturing expenses as our programs move further into the clinic. We also had increase of $9.9 million in salaries and benefits expense, $3.8 million in lab supply expenses, $3.2 million in stock compensation expense, $2.7 million in research and pre-clinical expense, $1.3 million facilities expense and $1.0 million in other operational and professional services. These increases were primarily due to the growth of our business to support the continued advancement of our product candidates into clinical trials, main increases were in our IMD and Hemophilia clinical programs which increased approximately $26.2 million and $8.3 million, respectively.

The increase of $0.1 million in research and development expenses in 2017 was primarily due to increases of $5.5 million in salaries and benefits, $1.1 million in clinical trial and manufacturing expenses related to our hemophilia B and MPS programs, and $1.1 million in facility and operating expenses. This was primarily offset by decreases of $3.4 million in preclinical expenses, $2.5 million in lab supply expenses, $1.4 million in stock-based compensation expense, and $0.3 million in other professional services.

The table below shows research and development expenses related to our clinical and preclinical programs.

Year Ended

Programs	December 31, 2018	2017	2016
		(In thousands)	
Human Therapeutic Programs			
Hemophilia clinical programs	$23,006	$ 14,715	$7,521
IMD clinical programs	37,668	11,428	9,046
Beta-thalassemia clinical program	12,317	11,354	—
HIV (SB-728) clinical programs	1,612	2,473	4,271
Non-human Therapeutic Programs			
Preclinical and research programs	39,779	25,414	43,682
Other clinical programs and non-therapeutic programs	484	344	1,098
Total research and development expenses	$114,866	$ 65,728	$65,618

The length of time required to complete our development programs and our development costs for those programs may be impacted by the scope and timing of enrollment in clinical trials for our product candidates, our decisions to pursue development programs in other therapeutic areas, and whether we pursue development of our product candidates with a partner or collaborator or independently. For example, our product candidates are being developed in multiple therapeutic areas, and we do not yet know how many of those therapeutic areas we will continue to pursue. Furthermore, the scope and number of clinical trials required to obtain regulatory approval for each pursued therapeutic area is subject to the input of the applicable regulatory authorities, and we have not yet sought such input for all potential therapeutic areas that we may elect to pursue, and even after having given such input, applicable regulatory authorities may subsequently require additional clinical studies prior to granting regulatory approval based on new data generated by us or other companies, or for other reasons outside of our control. As a condition to any regulatory approval, we may also be subject to post-marketing development commitments, including additional clinical trial requirements. As a result of the uncertainties discussed above, we are unable to determine the duration of or complete costs associated with our development programs.

In any event, our potential therapeutic products are subject to a lengthy and uncertain regulatory process that may not result in our receipt of any necessary regulatory approvals. Failure to receive the necessary regulatory approvals would prevent us from commercializing the product candidates affected. In addition, clinical trials of our product candidates may fail to demonstrate safety and efficacy, which could prevent or significantly delay regulatory approval. A discussion of the risks and uncertainties with respect to our research and development activities, including completing the development of our product candidates, and the consequences to our business, financial position and growth prospects can be found in “Risk Factors” in Part I, Item 1A of this Annual Report on Form 10-K.

General and Administrative Expenses

The increase of $19.5 million in 2018 was primarily due to increases of $5.0 million in professional services to support compliance initiatives and expansion strategies, $4.7 million in salaries and benefits, and $2.4 million in stock-based compensation in connection with headcount growth, $1.8 million in other corporate expenses and $1.7 million in facilities and depreciation. The increases were primarily due to the growth of our business to support the continued advancement of our product candidates into clinical trials.

The increase of $0.9 million in 2017 was primarily due to increases of $1.5 million in legal expenses, $1.5 million in corporate expenses, including rebranding in connection with our name change, $1.0 million in salaries and benefits, and $1.0 million in facility expenses. This increase was primarily offset by a decrease of $4.5 million in stock-based compensation expense, as 2016 included approximately $4.1 million of stock-based compensation expense recognized in connection with the transition of our former chief executive officer.

Interest and other income, net

Interest and other income, net, was $8.3 million in 2018, $1.8 million in 2017, and $0.9 million in 2016 and primarily consisted of interest income resulting from our treasury strategy.

Benefit from income taxes

Benefit from income taxes was $0.0 million for 2018, 2017, and 2016. We recognized an immaterial amount of income tax expense/benefit during each of these years.

As of December 31, 2018, we had net operating loss carryforwards for federal and state income tax purposes of approximately $535.0 million and $161.0 million, respectively. If not utilized, the net federal and state operating loss carryforwards will expire in 2018 and 2017, respectively. We also have federal and state research tax credit carryforwards of $12.2 million and $13.0 million, respectively. The federal research credits began to expire in 2018 while the state research credits have no expiration date. Utilization of our net operating loss carryforwards and research tax credit carryforwards may be subject to substantial annual limitations due to the ownership change limitations provided by the Internal Revenue Code and similar state provisions. The annual limitation could result in the expiration of the net operating loss carryforwards and research tax credit carryforwards before use. Due to the carryforwards related to the net operating losses and research and development tax credits, we do not expect to pay any taxes related to income in the near future.

On December 22, 2017, President Trump signed the Tax Cuts and Jobs Act ("Tax Reform") into legislation. The Tax Reform made significant changes to the U.S. corporate income tax law including, but not limited to, (1) reducing the U.S. federal corporate tax

rate to 21% from 35% and (2) requiring a one-time mandatory transition tax on previously deferred foreign earnings of U.S. subsidiaries. Under ASC Topic 740, Income Taxes, the effects of changes in tax rates and laws are recognized in the period in which the new legislation is enacted. In the case of U.S. federal income taxes, the enactment date is the date the bill becomes law.

In December 2017, the Securities and Exchange Commission staff issued Staff Accounting Bulletin No.118 ("SAB 118") to provide guidance on the application of the Tax Reform when a company does not have the necessary information available, prepared, or analyzed in reasonable to detail to reflect the effects of the Tax Reform. SAB 118 provides guidance for companies under the three scenarios (1) measurement of certain income tax effects is complete, (2) measurement of certain income tax effect can be reasonably estimated, and (3) measurement of certain income tax effects cannot be reasonably estimated. Companies are to complete the accounting under ASC 740 in regards to the Tax Reform within a measurement period that does not extend one year from the date of enactment (i.e., December 22, 2018). We completed the accounting assessment with regards to the tax effects associated with the enactment of the Tax Reform. Our assessment resulted in no changes from the original estimates provided for the year ended December 31, 2017.

Liquidity and Capital Resources

Liquidity

Since inception, we have incurred significant net losses and we have funded our operations primarily through the issuance of equity securities, payments from corporate collaborators and strategic partners and research grants. Our most significant use of capital pertains to funding our preclinical and clinical research and development programs, as well as salaries and benefits for employees.

As of December 31, 2018, we had cash, cash equivalents, marketable securities and interest receivable totaling $400.5 million compared to $244.6 million as of December 31, 2017, with the increase primarily attributable to $215.8 million net proceeds from our April 2018 issuance of common stock and $150.0 million from our February 2018 collaboration and license agreement with Kite, which became effective in April 2018. Our cash and investment balances are held in a variety of interest bearing instruments, including obligations of U.S. government agencies, U.S. Treasury debt securities, corporate debt securities and money market funds. Cash in excess of immediate requirements is invested in accordance with our investment policy with a view toward capital preservation and liquidity.

In May 2017, we entered into an amended and restated sales agreement with Cowen and Company, LLC ("Cowen") pursuant to which we may offer and sell, in our sole discretion, shares of common stock having an aggregate offering price of up to $75.0 million through Cowen acting as our sales agent ("the ATM Facility"). Sales of our common stock, if any, will be made at market prices by any method that is deemed to be an "at the market offering" as defined in Rule 415 under the Securities Act of 1933, as amended. We have not sold any common stock under the ATM Facility. As of December 31, 2018, the full $75.0 million provided for under the ATM Facility remained available for sale, subject to certain conditions as specified in the agreement.

Since the beginning of 2017, we have received significant amounts of capital as upfront payments under the following collaboration arrangements: $70.0 million received in May 2017 from Pfizer under our hemophilia A agreement, $12.0 million received in January 2018 from Pfizer under our C9ORF72 agreement, and $150.0 million received in April 2018 under our collaboration agreement with Kite. Our collaboration agreements provide for the payment of development, regulatory, and commercial milestones. For more information see "Business – Collaborations" in Part I of this Annual Report on Form 10-K.

Cash Flow

Operating activities. Net cash provided by (used in) operating activities primarily reflects our net operating losses adjusted for non-cash items including stock-based compensation expense. Net cash provided by operating activities

was $37.2 million in 2018 compared to net cash provided by operating activities of $11.2 million in 2017. The increase in net cash provided by operating activities in 2018 was primarily due to the increase in deferred revenues due to the $150.0 million upfront license payment from Kite and stock-based compensation for the period offset by the net loss.

Net cash provided by operating activities was $11.2 million in 2017 compared to net cash used in operating activities of $65.9 million in 2016. The increase in net cash provided by operating activities in 2017 was primarily due to the increase in deferred revenues related to the $70.0 million upfront payment from the hemophilia A agreement with Pfizer.

Investing activities. Net cash used in investing activities was $178.1 million in 2018. Net cash used in investing activities was $77.4 million in 2017. Net cash provided by investing activities was $18.1 million in 2016. The increase in net cash used in 2018 was primarily due to the TxCell Acquisition. Additional cash flows from investing activities for all periods were primarily related to purchases, and maturities of marketable securities and also includes deposits on cash related to lease commitments.

Financing activities. Net cash provided by financing activities was $231.7 million in 2018, $97.5 million in 2017, and $0.3 million in 2016. Net cash provided by financing activities was primarily attributable to $215.8 million net proceeds from our April 2018 issuance of common stock and $16.2 million in proceeds from the exercise of stock options. Net cash provided by financing activities in 2017 was primarily attributable to the completion of an underwritten public offering of our common stock of $78.1 million, net of issuance costs, and $16.6 million in proceeds from the exercise of stock options. Net cash provided by financing activities in 2016 was primarily attributable to $1.1 million proceeds from the exercise of stock options, primarily offset by $0.8 million in taxes paid related to net share settlement of equity awards.

Operating Capital and Capital Expenditure Requirements

We anticipate continuing to incur operating losses for at least the next several years. While we expect our rate of cash usage to increase in the future, in particular to support our product development endeavors, we believe that the available cash resources as well as funds received from corporate collaborators, strategic partners and research grants will enable us to maintain our currently planned operations through at least the next twelve months from the date the financial statements are issued. Future capital requirements will be substantial and if our capital resources are insufficient to meet future capital requirements, we will need to raise additional capital to fund our operations through equity or debt financing. We regularly consider fund raising opportunities and may decide, from time to time, to raise capital based on various factors, including market conditions and our plans of operation. Additional capital may not be available on terms acceptable to us, or at all. If adequate funds are not available, or if the terms of potential funding sources are unfavorable, our business and our ability to advance our product candidate pipeline would be harmed. Furthermore, any sales of additional equity securities, including any sales under our ATM Facility, may result in dilution to our stockholders, and any debt financing may include covenants that restrict our business.

Our future capital requirements will depend on many forward looking factors, including the following:

- the initiation, progress, timing and completion of clinical trials for our product candidates and potential product candidates;
- the outcome, timing and cost of regulatory approvals;
- the success of our collaboration agreements;
- delays that may be caused by changing regulatory requirements;
- the number of product candidates that we pursue;
- the costs involved in filing and prosecuting patent applications and enforcing and defending patent claims;
    - the timing and terms of future in-licensing and out-licensing transactions;
- the cost and timing of establishing sales, marketing, manufacturing and distribution capabilities;
- the cost of procuring clinical and commercial supplies of our product candidates;
- the extent to which we acquire or invest in businesses, products or technologies; and
- the possible costs of litigation.

Off Balance Sheet Arrangements

We do not have any off balance sheet arrangements as defined in Item 303(a)(4)(ii) of Regulation S-K.

Contractual Obligations and Commercial Commitments

As of December 31, 2018, we had contractual obligations and commercial commitments as follows (in thousands):

	Payments Due by Period				
Contractual Obligations	Total	Less Than 1 Year	1-3 Years	4-5 Years	More Than 5 Years
Operating leases	$56,418	$ 3,671	$17,600	$5,649	$ 29,498
License obligations	1,318	223	625	200	270
Manufacturing obligations	8,862	8,862	—	—	—
Total contractual obligations	$66,598	$ 12,756	$18,225	$5,849	$ 29,768

Operating leases consist of base rents for facilities we occupy in Richmond, California, Brisbane, California and Valbonne, France. License obligations consist of ongoing license maintenance fees associated with cancelable in-licensed patent agreements.

ITEM 7A – QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Our exposure to market risk relates to our cash, cash equivalents and investments. The goals of our investment policy are preservation of capital, fulfillment of liquidity needs and capturing a market rate of return based on our investment policy parameters and market conditions. We select investments that maximize interest income to the extent possible within these guidelines. To achieve our goals, we maintain a portfolio of cash equivalents and investments in securities of high credit quality and with varying maturities to match projected cash needs.

The securities in our investment portfolio are not leveraged, are classified as available-for-sale and are, due to their short-term nature, subject to minimal interest rate risk. Our investments currently consist of U.S. Treasury securities, U.S. government-sponsored enterprise securities and corporate notes. Our investment policy, approved by our Board of Directors, limits the amount we may invest in any one type of investment issuer, thereby reducing credit risk concentrations. All investments have a fixed interest rate and are carried at market value, which approximates cost. We do not use derivative financial instruments in our investment portfolio. We do not believe that a change in interest rates would have a material negative impact on the value of our investment portfolio.

Foreign Currency Exchange Risk

We have operations in United States as well as in Europe. The functional currency of each foreign subsidiary is generally the local currency. We are exposed to foreign currency risk, primarily through operations of our subsidiaries in Europe which conduct business primarily in Euros. We record gains and losses within our stockholders' equity due to the translation of the European branches' financial statements into U.S. dollars.

A 10% strengthening/(weakening) in the rates used to translate the results of our foreign subsidiaries would have increased/(decreased) net loss for the year ended December 31, 2018 by approximately $0.4 million and would not have materially impacted our operating loss.

Additionally, we incur foreign currency transaction gains and losses related to the level of activity between the U.S. and Europe. In 2018, we realized foreign currency transaction losses, net of $0.6 million. A 10% unfavorable change in the Euro and U.S. dollar exchange rate on December 31, 2018 would have had an immaterial impact on foreign currency transaction losses for 2018.

ITEM 8 – FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

SANGAMO THERAPEUTICS, INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of Sangamo Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Sangamo Therapeutics, Inc. (the Company) as of December 31, 2018 and 2017, the related consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2018, and the related notes (collectively referred to as the “consolidated financial statements”). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2018 and 2017, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2018, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated March 1, 2019 expressed an unqualified opinion thereon.

Adoption of New Accounting Standard

As discussed in Note 1 to the consolidated financial statements, the Company changed its method of accounting for revenue as a result of the adoption of Accounting Standards Update (“ASU”) No. 2014-09 “Revenue from Contracts with Customers (Topic 606),” as amended, effective January 1, 2018 using the modified retrospective method.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company’s financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ ERNST & YOUNG LLP

We have served as the Company’s auditor since 1997.

Redwood City, California

March 1, 2019

SANGAMO THERAPEUTICS, INC.

CONSOLIDATED BALANCE SHEETS

(in thousands, except per share amounts)

	December 31, 2018	December 31, 2017
ASSETS		
Current assets:		
Cash and cash equivalents	$140,418	$49,826
Marketable securities	259,715	193,482
Interest receivable	375	240
Accounts receivable	4,673	3,343
Prepaid expenses and other current assets	5,340	1,506
Total current assets	410,521	248,397
Marketable securities, non-current	—	1,012
Property and equipment, net	78,723	31,066
Intangible assets	54,866	—
Goodwill	40,044	1,585
Other non-current assets	2,741	1,181
Non-current restricted cash	3,500	3,500
Total assets	$590,395	$286,741
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable and accrued liabilities	$21,457	$11,035
Accrued compensation and employee benefits	9,490	5,479
Deferred revenues	47,564	28,345
Total current liabilities	78,511	44,859
Deferred revenues, non-current	108,273	29,244
Build-to-suit lease obligation	27,689	24,738
Deferred income tax	6,705	—
Non-current liabilities	1,960	—
Total liabilities	223,138	98,841
Commitments and contingencies		
Stockholders' equity:		
Common stock, $0.01 par value; 160,000,000 shares authorized, 102,187,471 and 85,598,534 shares issued and outstanding at December 31, 2018 and December 31, 2017, respectively	1,022	856
Additional paid-in capital	929,632	682,809
Accumulated deficit	(562,696)	(495,479)
Accumulated other comprehensive loss	(1,440)	(286)
Total Sangamo Therapeutics Inc. stockholders' equity	366,518	187,900
Non-controlling interest	739	—
Total stockholders' equity	367,257	187,900
Total liabilities and stockholders' equity	$590,395	$286,741

See accompanying Notes to Consolidated Financial Statements.

SANGAMO THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS

(in thousands, except per share amounts)

	Year Ended December 31,		
	2018	2017	2016
Revenues:			
Collaboration agreements	$84,065	$35,960	$18,881
Research grants	387	607	508
Total revenues	84,452	36,567	19,389
Operating expenses:			
Research and development	114,866	65,728	65,618
General and administrative	46,736	27,200	26,330
Total operating expenses	161,602	92,928	91,948
Loss from operations	(77,150)	(56,361)	(72,559)
Interest and other income, net	8,261	1,793	887
Loss before income taxes	(68,889)	(54,568)	(71,672)
Benefit from income taxes	—	—	14
Net loss	(68,889)	(54,568)	(71,658)
Net loss attributable to non-controlling interest	(555)	—	—
Net loss attributable to Sangamo Therapeutics, Inc. stockholders	$(68,334)	$(54,568)	$(71,658)
Basic and diluted net loss per share attributable to Sangamo Therapeutics, Inc. stockholders	$(0.70)	$(0.70)	$(1.02)
Shares used in computing basic and diluted net loss per share attributable to Sangamo Therapeutics, Inc. stockholders	96,941	78,084	70,553

See accompanying Notes to Consolidated Financial Statements.

SANGAMO THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS

(in thousands)

	Year Ended December 31,		
	2018	2017	2016
Net loss	$(68,889)	$(54,568)	$(71,658)
Foreign currency translation adjustment	(1,148)	—	—
Net pension losses	(21)	—	—
Change in unrealized (loss) gain on available-for-sale securities	(4)	(306)	20
Comprehensive loss	(70,062)	(54,874)	(71,638)
Comprehensive loss attributable to non-controlling interest	(574)	—	—
Comprehensive loss attributable to Sangamo Therapeutics Inc.	$(69,488)	$(54,874)	$(71,638)

See accompanying Notes to Consolidated Financial Statements.

SANGAMO THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY

(in thousands, except share amounts)

	Common Stock		Additional Paid-in	Accumulated	Accumulated Other Comprehensive Income/	Non-controlling	Total Stockholders'
	Shares	Amount	Capital	Deficit	(Loss)	Interest	Equity
Balances at December 31, 2015	70,354,608	$ 703	$ 560,989	$ (369,253)	$ —	$ —	$ 192,439
Issuance of common stock upon exercise of stock options and in connection with restricted stock units, net of tax	314,583	3	(484)	—	—	—	(481)
Issuance of common stock under employee stock purchase plan	202,711	3	815	—	—	—	818
Stock-based compensation	—	—	15,057	—	—	—	15,057
Comprehensive loss:							
Net unrealized gain on marketable securities, net of tax	—	—	—	—	20		20
Net loss	—	—	—	(71,658)	—	—	(71,658)
Comprehensive loss	—	—	—	—	—		(71,638)
Balances at December 31, 2016	70,871,902	709	576,377	(440,911)	20		136,195
Issuance of common stock upon exercise of stock options and in connection with restricted stock units, net of tax	2,101,489	21	15,078	—	—	—	15,099
Issuance of common stock under employee stock purchase plan	253,994	2	816	—	—	—	818

Issuance of common stock under public offering, net of issuance costs	12,371,149	124	81,449				81,573
Stock-based compensation	—	—	9,089	—	—	—	9,089
Comprehensive loss:							
Net unrealized loss on marketable securities, net of tax	—	—	—	—	(306)	—	(306)
Net loss	—	—	—	(54,568)	—		(54,568)
Comprehensive loss	—	—	—	—	—	—	(54,874)
Balances at December 31, 2017	85,598,534	856	682,809	(495,479)	(286)	—	187,900
Cumulative-effect adjustment of ASC Topic 606 on January 1, 2018		—	—	1,117	—	—	1,117
Issuance of common stock upon exercise of stock options and in connection with restricted stock units, net of tax	2,103,727	20	14,447	—	—	—	14,467
Issuance of common stock under employee stock purchase plan	328,710	4	1,480	—	—	—	1,484
Issuance of common stock under public offering, net of issuance costs	14,156,500	142	215,616	—	—	—	215,758
Stock-based compensation	—	—	14,677	—	—	—	14,677
Additional paid-in capital for Acquisition of TxCell	—	—	603	—	—	—	603
Non-controlling interest upon Acquisition of TxCell	—	—	—	—	—	1,313	1,313
Comprehensive loss:							
Foreign currency translation adjustment	—	—	—	—	(1,129)	(19)	(1,148)
Net pension losses	—	—	—	—	(21)	—	(21)
Net unrealized loss on marketable securities, net of tax	—	—	—	—	(4)	—	(4)
Net loss	—	—	—	(68,334)	—	(555)	(68,889)

Comprehensive loss	—	—	—	—	—	—	(70,062)
Balances at December 31, 2018	102,187,471	$ 1,022	$ 929,632	$ (562,696)	$ (1,440)	$ 739	$ 367,257

See accompanying Notes to Consolidated Financial Statements.

SANGAMO THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

(in thousands)

	Year Ended December 31,		
	2018	2017	2016
Operating Activities:			
Net loss	$(68,889)	$(54,568)	$(71,658)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities:			
Depreciation and amortization	2,359	1,498	997
Amortization of (discount) premium on marketable securities	(5,829)	(673)	221
Foreign currency transaction losses, net	602	—	—
Net loss on disposal of property and equipment	—	12	—
Stock-based compensation	14,677	9,089	15,057
Benefit from income taxes	—	—	(14)
Build-to-suit leases	966	80	99
Net changes in operating assets and liabilities:			
Interest receivable	(135)	(16)	83
Accounts receivable	(1,330)	1,629	(2,144)
Prepaid expenses and other assets	(2,828)	(669)	(1,112)
Accounts payable and accrued liabilities	(6,372)	3,219	(2,335)
Accrued compensation and employee benefits	2,604	2,594	137
Deferred revenues	99,364	48,984	(5,214)
Non-current liabilities	1,963	—	—
Net cash provided by (used in) operating activities	37,152	11,179	(65,883)
Investing Activities:			
Acquisition of TxCell, net of cash acquired	(75,647)	—	—
Purchases of marketable securities	(451,239)	(252,328)	(218,640)
Maturities of marketable securities	391,845	178,675	237,497
Purchases of property and equipment	(43,065)	(3,751)	(732)
Net cash (used in) provided by investing activities	(178,106)	(77,404)	18,125
Financing Activities:			
Proceeds from public offering of common stock, net of issuance costs	215,758	81,573	—
Taxes paid related to net share settlement of equity awards	(254)	(654)	(776)
Proceeds from issuance of common stock	16,205	16,571	1,113
Net cash provided by financing activities	231,709	97,490	337
Effects of changes in foreign exchange rates	(163)	—	—
Net increase in cash, cash equivalents, and restricted cash	90,592	31,265	(47,421)
Cash, cash equivalents, and restricted cash, beginning of period	53,326	22,061	69,482
Cash, cash equivalents, and restricted cash, end of period	$143,918	$53,326	$22,061
Supplemental disclosure of non-cash investing activities:			
Non controlling interest for acquisition of TxCell	$1,313	$—	$—
Property and equipment included in accrued liabilities	$4,953	$1,214	$—
Build-to-suit leases included in build-to-suit liabilities	$2,950	$20,793	$3,876

See accompanying Notes to Consolidated Financial Statements.

SANGAMO THERAPEUTICS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

NOTE 1 – ORGANIZATION AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Overview

Sangamo Therapeutics, Inc. was incorporated in the State of Delaware on June 22, 1995 and changed its name from Sangamo Biosciences, Inc. in January 2017 (“the Company” or “Sangamo”). Sangamo is focused on the research, development and commercialization of novel therapeutic strategies for unmet medical needs. Sangamo’s genome editing and gene regulation technology platform is enabled by the engineering of a class of transcription factors known as zinc finger DNA-binding proteins (“ZFPs”). Potential applications of Sangamo’s technology include development of human therapeutics, plant agriculture and enhancement of pharmaceutical protein production. Sangamo will require additional financial resources to complete the development and commercialization of its products including ZFP Therapeutics.

Sangamo is currently working on a number of long-term development projects that will involve experimental technology. The projects may require several years and substantial expenditures to complete and ultimately may be unsuccessful. The Company plans to finance operations with available cash resources, collaborations and strategic partnerships funds, research grants and from the issuance of equity or debt securities. Sangamo believes that its available cash, cash equivalents and investments as of December 31, 2018, along with expected revenues from collaborations, strategic partnerships and research grants, will be adequate to fund its operations at least through the next twelve months from the date the financial statements are issued. Sangamo will need to raise substantial additional capital to fund subsequent operations and complete the development and commercialization of its products. Additional capital may not be available on terms acceptable to the Company, or at all. If adequate funds are not available, or if the terms of potential funding sources are unfavorable, the Company’s business and ability to develop its technology and ZFP Therapeutic products would be harmed. Furthermore, any sales of additional equity securities may result in dilution to the Company’s stockholders, and any debt financing may include covenants that restrict the Company’s business.

Basis of Presentation

The accompanying consolidated financial statements have been prepared in conformity with generally accepted accounting principles in the United States of America (“U.S. GAAP”) and include the accounts of the Company and its subsidiaries. All intercompany balances and transactions have been eliminated in the consolidated financial statements.

Business Combinations

The Company accounts for acquisitions in accordance with Accounting Standards Codification (“ASC”) Topic 805, Business Combinations (“ASC Topic 805”). ASC Topic 805 establishes principles and requirements for recognizing and measuring the total consideration transferred to and the assets acquired, liabilities assumed and any non-controlling interests in the acquired target in a business combination. ASC Topic 805 also provides guidance for recognizing and measuring goodwill acquired in a business combination; requires purchased in-process research and development to

be capitalized at fair value as an intangible asset at the time of acquisition; requires acquisition-related expenses and restructuring costs to be recognized separately from the business combination; expands the definition of what constitutes a business; and requires the acquirer to disclose information that users may need to evaluate and understand the financial effect of the business combination.

Cash and Cash Equivalents

Sangamo considers all highly-liquid investments purchased with original maturities of three months or less at the purchase date to be cash equivalents. Cash and cash equivalents consist of deposits in money market investment accounts.

Marketable Securities

Sangamo classifies its marketable securities as available-for-sale and records its investments at estimated fair value based on quoted market prices or observable market inputs of almost identical assets, with the unrealized holding gains and losses included in accumulated other comprehensive loss.

The Company’s investments are subject to a periodic impairment review. The Company recognizes an impairment charge when a decline in the fair value of its investments below the cost basis is judged to be other-than-temporary. The Company considers various factors in determining whether to recognize an impairment charge, including the length of time and extent to which the fair value has been less than the Company’s cost basis, the financial condition and near-term prospects of the investee, and the Company’s

intent and ability to hold the investment for a period of time sufficient to allow for any anticipated recovery in the market value. Realized gains and losses on available-for-sale securities are included in other income, which is determined using the specific identification method.

Fair Value Measurements

The carrying amounts for financial instruments consisting of cash and cash equivalents, accounts receivable, accounts payable and accrued liabilities approximate fair value due to their short maturities. Marketable securities are stated at their estimated fair values. The counterparties to the agreements relating to the Company's investment securities consist of the U.S. Treasury, governmental agencies, various major corporations and financial institutions with high credit standing.

Property and Equipment

Property and equipment are stated at cost, less accumulated depreciation and amortization. Depreciation is calculated using the straight-line method based on the estimated useful lives of the related assets (generally three to five years). For leasehold improvements, amortization is calculated using the straight-line method based on the shorter of the useful life or the lease term. The Company reviews its property and equipment for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable.

Use of Estimates

The preparation of consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the amounts reported in the financial statements and the accompanying notes. On an ongoing basis, management evaluates its estimates, including critical accounting policies or estimates related to revenue recognition, clinical trial accruals, fair value of assets and liabilities, including from acquisitions, and stock-based compensation. Estimates are based on historical experience and on various other market specific and other relevant assumptions that the Company believes to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results could differ from those estimates.

Revenue Recognition

Revenues from research activities made under strategic partnering agreements and collaborations are recognized as the services are provided when there is persuasive evidence that an arrangement exists, delivery has occurred, the price is fixed or determinable, and collectability is reasonably assured. Revenue generated from research and licensing agreements typically includes upfront signing or license fees, cost reimbursements, research services, minimum sublicense fees, milestone payments and royalties on future licensee's product sales.

Effective January 1, 2018, the Company adopted the provisions of ASC Topic 606, Revenue from Contracts with Customers ("Topic 606") using the modified retrospective method, resulting in a change to its accounting policy for revenue recognition. Topic 606 establishes a unified model to determine how revenue is recognized. The adoption of this pronouncement did not have material impact to the Company's consolidated financial statements. Topic 606 supersedes the revenue recognition requirements in Topic 605, Revenue Recognition ("Topic 605") as detailed below.

The Company's contract revenues consist of strategic partnering collaboration agreements and research activity grants and licensing. Research and licensing agreements typically include upfront signing or license fees, cost reimbursements, research services, minimum sublicense fees, milestone payments and royalties on future licensee's product sales. The Company has both fixed and variable consideration. Non-refundable upfront fees and funding of research and development activities are considered fixed, while milestone payments are identified as variable consideration. Sangamo's research grants are typically multi-year agreements and provide for the reimbursement of

qualified expenses for research and development as defined under the terms of the grant agreement. Revenues under grant agreements are recognized when the related qualified research expenses are incurred. Deferred revenue represents the portion of research or license payments received but not earned.

In determining the appropriate amount of revenue to be recognized as it fulfills its obligations under its agreements, the Company performs the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations based on estimated selling prices; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation.

A performance obligation is a promise in a contract to transfer a distinct good or service to the customer and is the unit of account in Topic 606. The Company’s performance obligations include license rights, development services, and services associated

with regulatory submission and approval processes. Significant management judgment is required to determine the level of effort required under an arrangement and the period over which the Company expects to complete its performance obligations under the arrangement. If the Company cannot reasonably estimate when its performance obligations either are completed or become inconsequential, then revenue recognition is deferred until the Company can reasonably make such estimates. The Company includes the unconstrained amount of estimated variable consideration in the transaction price. The amount included in the transaction price is constrained to the amount for which it is probable that a significant reversal of cumulative revenue recognized will not occur. At the end of each subsequent reporting period, the Company re-evaluates the estimated variable consideration included in the transaction price and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Revenue is then recognized over the remaining estimated period of performance using the cumulative catch-up method. The estimated period of performance and project costs are reviewed quarterly and adjusted, as needed, to reflect the Company's current assumptions regarding the timing of its deliverables.

As part of the accounting for these arrangements, the Company must develop assumptions that require judgment to determine the stand-alone selling price of each performance obligation identified in the contract. The Company uses key assumptions to determine the stand-alone selling price, which may include forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success.

Funds received from third parties under contract or grant arrangements are recorded as revenue if the Company is deemed to be the principal participant in the arrangements because the activities under the contracts or grants are part of the Company's development programs. Contract funds received are not refundable and are recognized when the related qualified research and development costs are incurred and there is reasonable assurance that the funds will be received. Funds received in advance are recorded as deferred revenue.

During 2018, revenues related to the hemophilia A collaboration agreement with Pfizer Inc. ("Pfizer") and Kite Pharma, Inc. ("Kite"), a wholly-owned subsidiary of Gilead Sciences, Inc., represented 45% and 30%, respectively, of the Company's total revenue. During 2017, revenues related to Pfizer and Bioverativ represented 47% and 34%, respectively, of the Company's total revenue. During 2016 revenue related to Bioverativ, Dow AgroScience, LLC ("DAS") and Shire International GmbH, a wholly owned subsidiary of Takeda Pharmaceuticals Company Limited ("Shire") represented 46%, 26%, and 17%, respectively, of total revenue. Receivables from collaborations are typically unsecured and are concentrated in the biopharmaceutical industry. Accordingly, the Company may be exposed to credit risk generally associated with biopharmaceutical companies or specific to its collaboration agreements. To date, the Company has not experienced any losses related to these receivables.

Research and Development Expenses

Research and development costs are expensed as incurred. Research and development expenses consist of direct and research-related allocated overhead costs such as facilities costs, salaries and related personnel costs, and material and supply costs. In addition, research and development expenses include costs related to clinical trials, validation of the Company's testing processes and procedures as well as related overhead expenses. Research and development costs incurred in connection with collaborator-funded activities are expensed as incurred. Costs to acquire technologies that are utilized in research and development that have no alternative future use are expensed as incurred.

Stock-based Compensation

The Company measures and recognizes compensation expense for all stock-based payment awards made to Sangamo employees and directors, including employee share options, restricted stock units ("RSUs") and employee stock purchases related to the Employee 2010 Stock Purchase Plan, as amended ("ESPP"), based on estimated fair values at the award grant date. The fair value of stock-based awards is amortized over the vesting period of the award using a straight-line method.

To estimate the fair value of an award, the Company uses the Black-Scholes option pricing model. This model requires inputs such as expected life, expected volatility and risk-free interest rate. These inputs are subjective and generally require significant analysis and judgment to develop. While estimates of expected life and volatility are derived primarily from the Company's historical data, the risk-free rate is based on the U.S. Treasury yield curve in effect at the time of grant commensurate with the expected life assumption. Further, in the first quarter of 2017 the Company adopted Accounting Standards Update ("ASU") 2016-09 and accounts for forfeitures in the period they occur. The adopted ASU did not have a material impact on the Company's consolidated financial statements.

Indefinite-lived Intangible Assets

As part of the acquisition of TxCell S.A ("TxCell") (see Note 6 – Acquisition of TxCell, S.A) the Company recognized indefinite-lived intangible assets for in-process research and development and goodwill as further discussed below. ASC Topic 350, Intangibles-Goodwill and Other, and related updates require companies to test indefinite-lived intangible assets for impairment

annually, and more frequently if indicators of impairment exist. ASC Topic 350 includes an optional qualitative assessment for testing indefinite-lived intangible assets for impairment that permits companies to assess whether it is more likely than not (i.e., a likelihood of greater than 50%) that an indefinite-lived intangible asset is impaired. If a company concludes based on the qualitative assessment that it is not more likely than not that the fair value of an indefinite-lived intangible asset or, in the case of goodwill, that the fair value of the related reporting unit, is less than carrying value, it would not have to determine the asset's or reporting unit's fair value, as applicable

In-Process Research and Development

Intangible assets related to in-process research and development costs ("IPR&D"), are considered to be indefinite-lived until the completion or abandonment of the associated research and development efforts. If and when development is complete, which generally occurs if and when regulatory approval to market a product is obtained, the associated assets would be deemed finite-lived and would then be amortized based on their respective estimated useful lives at that point in time. Prior to completion of the research and development efforts, the assets are considered indefinite-lived. During this period, the assets will not be amortized but will be tested for impairment on an annual basis and between annual tests if the Company becomes aware of any events occurring or changes in circumstances that would indicate a reduction in the fair value of the IPR&D projects below their respective carrying amounts.

During the fourth quarter of 2018, the Company performed an assessment of the qualitative factors affecting the fair value of its IPR&D projects. If the fair value exceeds the carrying value, then there is no impairment. Impairment losses on indefinite-lived intangible assets are recognized based solely on a comparison of the fair value of an asset to its carrying value, without consideration of any recoverability test. The Company has not identified any such impairment losses to date.

Goodwill

Goodwill represents the excess of the consideration transferred over the estimated fair values of assets acquired and liabilities assumed in a business combination and is considered to be indefinite-lived. Goodwill is not amortized but is tested for impairment on an annual basis and between annual tests if the Company becomes aware of any events occurring or changes in circumstances that would indicate an impairment of goodwill has occurred. During the fourth quarter of 2018, the Company performed an assessment of the qualitative factors affecting the fair value of its reporting unit and concluded that it was not more likely than not that the fair value of its reporting unit was less than carrying value and that, as a result, it is not more likely than not that goodwill is impaired.

Balance as of December 31, 2017	$1,585
Goodwill acquired	38,995
Foreign currency translations adjustment	(536)
Balance as of December 31, 2018	$40,044

Foreign Currency Translation

The functional currency of the Company's foreign subsidiaries is primarily the Euro. Monetary assets and liabilities denominated in foreign currencies are translated to U.S. dollars using the exchange rates at the balance sheet date. Foreign currency translation adjustments are recorded as a component of Other Comprehensive Income within stockholders' equity. Revenues and expenses from our foreign subsidiaries are translated using the monthly average exchange rates in effect during the period in which the transactions occur. Foreign currency transaction gains and

losses are recorded in Interest and Other Income, net, on our Consolidated Statements of Operations.

Income Taxes

Income tax expense has been provided using the liability method. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax bases of assets and liabilities as measured by the enacted tax rates that will be in effect when these differences reverse. The Company provides a valuation allowance against net deferred tax assets if, based upon the available evidence, it is not more likely than not that the deferred tax assets will be realized.

The Company recognizes a tax benefit from an uncertain tax position only if it is more likely than not that the tax position will be sustained on examination by the taxing authorities, based on the technical merits of the position. The tax benefits recognized in The Company’s consolidated financial statements from such positions are measured based on the largest benefit that has a greater than 50% likelihood of being realized. The Company recognizes interest and penalties associated with tax matters as part of the income tax provision and include accrued interest and penalties with the related income tax liability on its consolidated balance sheets

Net Loss Per Share

Basic net loss per share has been computed by dividing net loss by the weighted-average number of shares of common stock outstanding during the period. Diluted net loss per share is calculated by dividing net loss by the weighted-average number of shares of common stock and potential dilutive securities outstanding during the period.

Because Sangamo is in a net loss position, diluted net loss per share excludes the effects of common stock equivalents consisting of options and RSUs, which are all anti-dilutive. All stock options and RSUs outstanding were excluded from the calculation of diluted net loss per share for all periods presented. Stock options and RSUs outstanding at the end of 2018, 2017 and 2016 were 9,048,793, 8,367,628, and 9,578,322, respectively.

Segments

The Company operates in one segment. Management uses one measure of profitability and does not segregate its business for internal reporting. As of December 31, 2018, substantially all of the Company's assets were maintained in the United States. As of December 31 2017, all of the Company's assets were maintained in the United States. For the years ended December 31, 2018, 2017 and 2016, substantially all of the Company's revenues and operating expenses were generated and incurred in the United States.

Recent Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board ("FASB") issued ASU 2014-09, Revenue from Contracts with Customers ("Topic 606"). This standard outlines a single comprehensive model for entities to use in accounting for revenue arising from contracts with customers and supersedes most current revenue recognition guidance, including industry-specific guidance. The main principle of Topic 606 is to recognize revenues when promised goods or services are transferred to customers in an amount that reflects the consideration that is expected to be received for those goods or services. Topic 606 provides companies with two implementation methods: (i) apply the standard retrospectively to each prior reporting period presented (full retrospective application); or (ii) apply the standard retrospectively with the cumulative effect of initially applying the standard as an adjustment to the opening balance of retained earnings of the annual reporting period that includes the date of initial application (modified retrospective application). The Company adopted Topic 606 effective January 1, 2018, using the modified retrospective method with a cumulative effect adjustment of $1.1 million reflected as a decrease to the opening balance of accumulated deficit and a decrease to deferred revenues, respectively. Prior period amounts are not adjusted and continue to be reported in accordance with our historical accounting under Topic 605.

Refer below for a summary of the amount by which each financial statement line item that was affected by the impact of the cumulative adjustment and as compared with the guidance that was in effect prior to the adoption:

	Impact of Topic 606 Adoption on Consolidated Balance Sheet as of January 1, 2018		
(in thousands)	As reported under Topic 606	Adjustments	Balances without adoption of Topic 606
Deferred revenue, current portion	$29,626	$ 1,281	$28,345
Deferred revenue, noncurrent portion	26,846	(2,398)	29,244

Accumulated deficit	(494,362)	1,117	(495,479)

	Impact of Topic 606 Adoption on Consolidated Balance Sheet as of December 31, 2018		
(in thousands)	As reported under Topic 606	Adjustments	Balances without adoption of Topic 606
Deferred revenue, current portion	$47,564	$ 15,553	$63,117
Deferred revenue, noncurrent portion	108,273	(879)	107,394
Accumulated deficit	(562,696)	(14,674)	(577,370)

	Impact of Topic 606 Adoption on Consolidated Statement of Operations and Comprehensive Loss for the Year Ended December 31, 2018		
(in thousands, except per share amounts)	As reported under Topic 606	Adjustments	Balances without adoption of Topic 606
Collaboration revenue	$84,065	$ (13,558)	$70,507
Net loss	(68,334)	(13,558)	(81,892)
Net loss per share - basic and diluted:	(0.70)	(0.14)	(0.84)

	Impact of Topic 606 Adoption on Consolidated Statement of Cash Flows for the Year Ended December 31, 2018		
(in thousands)	As reported under Topic 606	Adjustments	Balances without adoption of Topic 606
Net loss	$(68,334)	$ (13,558)	$(81,892)
Changes in deferred revenue	99,364	13,558	112,922

In November 2016, the FASB issued ASU 2016-18, Statement of Cash Flows (“Topic 230”). The Company adopted Topic 230 in the beginning of 2018, which requires the statement of cash flows to explain the change during the period relating to total cash, cash equivalents, and restricted cash. The Company adopted this standard using the retrospective transition method by restating its consolidated statements of cash flows to include restricted cash of $3.5 million as of January 1, 2018 and in the ending cash, cash equivalents, and restricted cash balances for the year ended December 31, 2018. The restricted cash balance consists of a letter of credit for $3.5 million established as a deposit for the Brisbane build-to-suit lease. Net cash flows for the year ended December 31, 2017, changed as a result of including restricted cash with cash and cash equivalents when reconciling the beginning-of-period and end-of-period amounts presented on the consolidated statements of cash flows.

The following table provides a reconciliation of cash, cash equivalents, and restricted cash within the consolidated statements of cash flows that sum to the total of the same amounts in the statement of cash flows for the years ended December 31, 2018 and 2017, respectively (in thousands):

	Year Ended December 31,	
	2018	2017
Cash and cash equivalents	$140,418	$49,826
Restricted cash	3,500	3,500

Total cash, cash equivalents, and restricted cash	$143,918	$53,326

Not yet adopted

In November 2018, the FASB issued ASU 2018-18, Collaborative Arrangements (Topic 808): Clarifying the Interaction between Topic 808 and Topic 606, which clarifies that certain transactions between participants in a collaborative arrangement should be accounted for under ASC Topic 606 when the counterparty is a customer. In addition, Topic 808 precludes an entity from presenting consideration from a transaction in a collaborative arrangement as revenue from contracts with customers if the counterparty is not a customer for that transaction. This guidance will be effective for the Company beginning January 1, 2020. The Company is currently evaluating the impact of the adoption of this standard on its consolidated financial statements.

In February 2016 the FASB issued ASU 2016-02, Leases ("ASU 2016-02"). ASU 2016-02 amends a number of aspects of lease accounting, including requiring lessees to recognize almost all leases with a term greater than one year as a right-of-use asset and corresponding liability, measured at the present value of the lease payments. The guidance will become effective for the Company beginning in the first quarter of 2019 with early adoption permitted and will be adopted using a modified retrospective approach. The Company is adopting the new standard on January 1, 2019 and using the effective date as the date of initial application. Consequently, financial information will not be updated and the disclosures required under the new standard will not be provided for dates and periods before January 1, 2019.

The new standard provides a number of optional practical expedients in transition. The Company expects to elect the practical expedients to not reassess its prior conclusions about lease identification under the new standard, to not reassess lease classification, and to not reassess initial direct costs. The Company will not elect the practical expedient allowing the use-of-hindsight which would require the Company to reassess the lease term of its leases based on all facts and circumstances through the effective date and will not elect the practical expedient pertaining to land easements as this is not applicable to the current contract portfolio.

The new guidance also provides practical expedients for ongoing lease accounting. The Company expects to elect the recognition exemption for short-term lease for all leases that qualify. Under this exemption, the Company will not recognize right of

use (“ROU”) assets or lease liabilities for those leases that qualify as a short-term lease, which includes not recognizing ROU assets or lease liabilities for existing short-term leases of those assets in transition. The Company also will elect the practical expedient to not separate lease and non-lease components for all equipment and real-estate leases.

The Company expects that this standard will have a material effect on the financial statements. While the Company continues to assess the various impacts of adoption, the most significant effects will primarily relate to (1) the recognition of a right-of-use assets and lease liabilities on the balance sheet for the Company’s existing operating leases; (2) the derecognition of existing assets and liabilities for sale-leaseback transactions arising from build-to-suit lease arrangements for which construction is complete and the Company is leasing the constructed asset that currently do not qualify for sale accounting; (3) the derecognition of existing assets and liabilities for certain assets under construction in build-to-suit lease arrangements that the Company will lease when construction is complete; and (4) providing significant new disclosures about leasing activities

NOTE 2 –FAIR VALUE MEASUREMENT

The Company measures certain assets and liabilities at fair value on a recurring basis, including cash equivalents, available-for-sale securities and the free share liability. Fair value is determined based on a three-tier hierarchy under the authoritative guidance for fair value measurements and disclosures that prioritizes the inputs used in measuring fair value as follows:

Level 1: Unadjusted quoted prices in active markets that are accessible at the measurement date for identical, unrestricted assets or liabilities;

Level 2: Quoted prices in markets that are not active, or inputs which are observable, either directly or indirectly, for substantially the full term of the asset or liability; and

Level 3: Prices or valuation techniques that require inputs that are both significant to the fair value measurement and unobservable (i.e., supported by little or no market activity).

The fair value measurements of cash equivalents, available-for-sale securities and the free share liability are identified at the following levels within the fair value hierarchy (in thousands):

	December 31, 2018 Fair Value Measurements			
	Total	Level 1	Level 2	Level 3
Assets:				
Cash equivalents:				
Money market funds	$103,291	$103,291	$—	$—
Total	103,291	103,291	—	—
Marketable securities:				
Commercial paper securities	177,224	—	177,224	—
Corporate debt securities	63,870	—	63,870	—
U.S. government-sponsored entity debt securities	18,621	—	18,621	—
Total	259,715	—	259,715	—
Total cash equivalents and marketable securities	$363,006	$103,291	$259,715	—
Liabilities:				

Free share liability	$154	—	—	$154
Total	$154	—	—	$154

	December 31, 2017 Fair Value Measurements			
	Total	Level 1	Level 2	Level 3
Assets:				
Cash equivalents:				
Money market funds	$24,290	$24,290	$—	$ —
Commercial paper securities	4,595	—	4,595	—
Total	28,885	24,290	4,595	—
Marketable securities:				
Commercial paper securities	110,247	—	110,247	—
Corporate debt securities	75,755	—	75,755	—
U.S. government-sponsored entity debt securities	8,492	—	8,492	—
Total	194,494	—	194,494	—
Total cash equivalents and marketable securities	$223,379	$24,290	$199,089	$ -

Investments

The Company generally classifies its marketable securities as Level 2. Instruments are classified as Level 2 when observable market prices for identical securities that are traded in less active markets are used. When observable market prices for identical securities are not available, such instruments are priced using benchmark curves, benchmarking of like securities, sector groupings, matrix pricing and valuation models. These valuation models are proprietary to the pricing providers or brokers and incorporate a number of inputs, including, listed in approximate order of priority: benchmark yields, reported trades, broker/dealer quotes, issuer spreads, two-sided markets, benchmark securities, bids, offers and reference data including market research publications. For certain security types, additional inputs may be used, or some of the standard inputs may not be applicable. Evaluators may prioritize inputs differently on any given day for any security based on market conditions, and not all inputs listed are available for use in the evaluation process for each security evaluation on any given day.

Free Share Liability

As a result of the July 20, 2018 Share Purchase Agreement (“SPA”)(see Note 6 – Acquisition of TXCELL S.A.), the Company entered into arrangements with the holders of approximately 477,000 “free shares” of TxCell pursuant to which the Company has the right to purchase (call option) such shares from the holders thereof and such holders have the right to sell (put option) to the Company such shares from time to time through mid-2021 (the “Free Shares Options”). The purchase price for each such free share acquired by the Company upon exercise of a Free Shares Option will be based on the performance of the Company’s stock price from the announcement of the transactions contemplated by the SPA and Tender Offer Agreement (“TOA”) through the time of purchase the Free Shares Options purchase price was valued at €2.58 per share or approximately $2.99 per share using an exchange rate of $1.16, as of the date of the Acquisition. For example, if the Company’s stock price increases during that time period, the Free Shares Options purchase price per share will proportionately increase. However, if the Company’s stock price decreases the Free Shares Options purchase price is limited to a minimum purchase price of €2.58 per share, subject to certain exceptions. The options were classified as liabilities within Level 3 of the Fair Value hierarchy as the Company utilized a binomial-lattice pricing model (the “Monte Carlo simulation model”) that involved certain market conditions to estimate the fair value of the options. The application of the Monte Carlo simulation model required the use of a complex assumptions including the Company’s stock price, TxCell’s stock price, EUR to USD exchange rate,

estimated volatility of each stock price and exchange rate, and risk-free rates based on the implied yield currently available through the European Central Bank with a remaining term equal to the expected life of the options. The assumptions used in this simulation model are reviewed each reporting period and adjusted, as needed, with any change in estimated fair value recorded on the Company's consolidated statements of operations. There were no changes in the fair value of the free share liability in 2018.

Free Shares Liability assumptions:	December 31, 2018
Sangamo Stock Price (USD)	11.48
TxCell Stock Price (EUR)	2.58
EUR/ USD Exchange Rate	0.873
Sangamo Stock Price (USD) Volatility Estimate	79.90%
TxCell Stock Price (EUR) Volatility Estimate	8.59%
EUR/ USD Exchange Rate Volatility Estimate	7.66%
Risk Free Rate	Varies by expected exercise date

NOTE 3 – MARKETABLE SECURITIES

The table below summarizes the Company's cash equivalents and available-for-sale securities (in thousands):

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized (Losses)	Estimated Fair Value
December 31, 2018				
Cash equivalents:				
Money market funds	$ 103,291	$ —	$ —	$ 103,291
Total	103,291	—	—	103,291
Available-for-sale securities:				
Commercial paper securities	177,353	—	(129)	177,224
Corporate debt securities	63,981	—	(111)	63,870
U.S. government-sponsored entity debt securities	18,640	—	(19)	18,621
Total	259,974	—	(259)	259,715
Total cash equivalents and available-for-sale securities	$ 363,265	$ —	$ (259)	$ 363,006
December 31, 2017				
Cash equivalents:				
Money market funds	$ 24,290	$ —	$ —	$ 24,290
Commercial paper securities	4,595	—	—	4,595
Total	28,885	—	—	28,885
Available-for-sale securities:				
Commercial paper securities	110,365	—	(118)	110,247
Corporate debt securities	75,886	—	(131)	75,755
U.S. government-sponsored entity debt securities	8,498	—	(6)	8,492
Total	194,749	—	(255)	194,494
Total cash equivalents and available-for-sale securities	$ 223,634	—	$ (255)	$ 223,379

As of December 31, 2018, all of the Company's investments had maturity dates within one year as of the balance sheet date. The Company had no material realized losses from the sale of available-for-sale securities for the years ended December 31, 2018, 2017 or 2016. Sangamo has the intent and ability to hold its investments for a period of time sufficient to allow for any anticipated recovery in market value. No investments were other-than-temporarily impaired at either December 31, 2018 or 2017.

NOTE 4 – STOCK-BASED COMPENSATION

The following table shows total stock-based compensation expense recognized in the accompanying consolidated statements of operations (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Research and development	$ 8,249	$ 5,031	$ 6,463
General and administrative	6,428	4,058	8,594

Total stock-based compensation expense	$14,677	$9,089	$15,057

As of December 31, 2018, total stock-based compensation expense related to unvested stock options to be recognized in future periods was $35.4 million, which is expected to be expensed over a weighted-average period of 2.68 years. As of December 31, 2018, total stock-based compensation expense related to unvested RSUs to be recognized in future periods was $4.1 million, which is expected to be expensed over a weighted-average period of 2.18 years. There was no capitalized stock-based employee compensation expense as of either December 31, 2018, 2017 or 2016.

Valuation Assumptions

Employee stock-based compensation expense was determined using the Black-Scholes option valuation model. Option valuation models require the input of subjective assumptions and these assumptions can vary over time.

The Company bases its determination of expected volatility through its assessment of the historical volatility of its common stock. The Company relied on its historical exercise and post-vested termination activity for estimating its expected term for use in determining the fair value of these options.

The weighted-average estimated fair value per share of options granted during 2018, 2017 and 2016 was $11.39, $4.10, and $3.14, respectively, based upon the assumptions used in the Black-Scholes valuation model. The assumptions used for estimating the fair value of the employee stock options are as follows:

	Year Ended December 31,		
	2018	2017	2016
Risk-free interest rate	2.53-2.86%	1.86-2.28%	1.13-1.61%
Expected life of option (in years)	5.59-5.73	5.73-5.83	5.28-5.29
Expected dividend yield of stock	0%	0%	0%
Expected volatility	0.72-0.75	0.71-0.72	0.68-0.70

Employees purchased approximately 328,710, 253,994 and 202,711 shares of common stock through the ESPP at an average exercise price of $4.51, $3.22, and $4.04 per share during 2018, 2017 and 2016, respectively. The weighted-average estimated fair value of shares purchased under the Company's ESPP during 2018, 2017 and 2016 were $7.07, $2.37 and $2.27, respectively, based upon the assumptions used in the Black-Scholes valuation model.

The weighted–average assumptions used for estimating the fair value of the ESPP purchase rights are as follows:

	Year Ended December 31,		
	2018	2017	2016
Risk-free interest rate	2.16-2.44%	0.84-0.76%	0.41-0.80%
Expected life of option (in years)	0.5-2	0.5-2.0	0.5-2.0
Expected dividend yield of stock	0%	0%	0%
Expected volatility	0.73-0.86	0.81-0.82	0.71-0.76

NOTE 5 – MAJOR CUSTOMERS, PARTNERSHIPS AND STRATEGIC ALLIANCES

Collaboration Agreements

Kite Pharma, Inc.

In February 2018, the Company entered into a collaboration and license agreement with Kite, for the research, development and commercialization of potential engineered cell therapies for cancer. Kite will be responsible for all

clinical development and commercialization of any resulting products. The Kite agreement became effective on April 5, 2018 when the waiting periods under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, and other customary closing conditions were completed.

Subject to the terms of this agreement, the Company granted Kite an exclusive, royalty-bearing, worldwide, sublicensable license, under the Company's relevant patents and know-how, to develop, manufacture and commercialize, for the purpose of treating cancer, specific cell therapy products that may result from the research program and that are engineered ex vivo using selected zinc finger nucleases ("ZFNs") and adeno-associated viral vectors ("AAVs") developed under the research program, to express chimeric antigen receptors ("CARs"), T-cell receptors ("TCRs") or NK-cell receptors ("NKRs") directed to candidate targets.

During the research program term and subject to certain exceptions, except pursuant to this agreement, the Company is prohibited from researching, developing, manufacturing and commercializing, for the purpose of treating cancer, any cell therapy product that, as a result of ex vivo genome editing, expresses a CAR, TCR or NKR that is directed to a target expressed on or in a human cancer cell. After the research program term concludes and subject to certain exceptions, except pursuant to this agreement, the Company will be prohibited from developing, manufacturing and commercializing, for the purpose of treating cancer, any cell therapy product that, as a result of ex vivo genome editing, expresses a CAR, TCR or NKR that is directed to a candidate target.

Following the effective date, in April 2018, the Company received a $150.0 million upfront payment from Kite. In addition, Kite will reimburse the Company's direct costs to conduct service under the joint research program provisions of the agreement, and Kite will be responsible for all subsequent development, manufacturing and commercialization of any licensed products. Sangamo is

also eligible to receive contingent development- and sales-based milestone payments that could total up to $3.01 billion if all of the specified milestones set forth in this agreement are achieved. Of this amount, approximately $1.26 billion relates to the achievement of specified research, clinical development, regulatory and first commercial sale milestones, and approximately $1.75 billion relates to the achievement of specified sales-based milestones if annual worldwide net sales of licensed products reach specified levels. Each development- and sales-based milestone payment is payable (i) only once for each licensed product, regardless of the number of times that the associated milestone event is achieved by such licensed product, and (ii) only for the first ten times that the associated milestone event is achieved, regardless of the number of licensed products that may achieve such milestone event. In addition, the Company will be entitled to receive escalating, tiered royalty payments with a percentage in the single digits based on potential future annual worldwide net sales of licensed products. These royalty payments will be subject to reduction due to patent expiration, entry of biosimilar products to the market and payments made under certain licenses for third-party intellectual property.

The initial research term of the agreement is six years. Kite has an option to extend the research term for up to two additional one-year periods for a separate fee of $10.0 million per year. All contingent payments under the agreement, when earned, will be non-refundable and non-creditable. The Company concluded the transaction price under this agreement is $185.9 million and includes the upfront license fee of $150.0 million and $35.9 million estimated reimbursable service costs for identified research projects over the estimated performance period. Further the Company concluded estimated fees for the presumed exercise of the research term extension options and all milestone amounts are fully constrained. As part of its evaluation of the constraint, the Company considered numerous factors, including the fact that achievement of the milestones at this time is uncertain and contingent upon future periods when the uncertainty related to the variable consideration is resolved. The Company will re-evaluate the transaction price, including the estimated variable consideration included in the transaction price and all constrained amounts, in each reporting period and as uncertain events are resolved or other changes in circumstances occur. None of the development and sales-based milestone payments have been included in transaction price.

Kite has the right to terminate this agreement, in its entirety or on a per licensed product or per candidate target basis, for any reason after a specified notice period. Each party has the right to terminate this agreement on account of the other party’s bankruptcy or material, uncured breach.

The Company has identified the primary performance obligations within the Kite agreement as a license to the technology and on-going services. The Company concluded that the license is not discrete as it does not have stand-alone value to Kite apart from the services to be performed by the Company pursuant to the agreement. As a result, the Company recognizes revenue from the upfront payment on a straight-line basis through June 2024, the estimated period the Company will perform research services. The estimated period of performance and project cost is reviewed quarterly and adjusted, as needed, to reflect the Company’s current assumptions regarding the timing of its deliverables. As of December 31, 2018, the Company had deferred revenue of $131.5 million related to this agreement. During the year ended December 31, 2018 the Company recognized revenue of approximately $18.5 million related to the upfront fee that was received upon effectiveness of the agreement and approximately $7.0 million from research services.

Pfizer Inc.

SB-525 Global Collaboration and License Agreement

In May 2017, the Company entered into an exclusive, global collaboration and license agreement with Pfizer, pursuant to which it established a collaboration for the research, development and commercialization of SB-525, its gene

therapy product candidate for hemophilia A, and closely related products.

Under this agreement, the Company is 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. Sangamo may also collaborate in the research and development of additional AAV-based gene therapy products for hemophilia A.

The Company received an upfront fee of $70.0 million and is eligible to receive development milestone payments contingent on the achievement of specified clinical development, intellectual property, regulatory and first commercial sale milestones for SB-525 and potentially other products. In addition, Sangamo is eligible to receive up to $208.5 million in payments upon the achievement of specified clinical development, intellectual property and regulatory milestones and up to $266.5 million in payments upon first commercial sale milestones for SB-525 and potentially other products. The total amount of potential clinical development, intellectual property, regulatory, and first commercial sale milestone payments, assuming the achievement of all specified milestones in the hemophilia A Pfizer agreement, is up to $475.0 million, which includes up to $300.0 million for SB-525 and up to $175.0 million for other products that may be developed under the agreement, subject to reduction on account of payments made under certain licenses for third party intellectual property. In addition, Pfizer agreed to pay the Company royalties for each potential licensed product developed under the agreement that are an escalating tiered, double-digit percentage of the annual net sales of such product and are subject to reduction due to patent expiration, entry of biosimilar products to the market and payment made under certain licenses for third party intellectual property. To date, no milestone payments have been received and no products have been approved and therefore no royalty fees have been earned under the hemophilia A Pfizer agreement. Sangamo is responsible for internal and external research costs as part of the upfront fee and has the ability to request additional reimbursement from Pfizer if certain conditions are met.

None of the clinical or regulatory milestones have been included in the $70.0 million transaction price, as all milestone amounts are fully constrained. As part of its evaluation of the constraint, the Company considered numerous factors, including the fact that achievement of the milestones at this time is uncertain and contingent upon future periods when the uncertainty related to the variable consideration is resolved. The Company will re-evaluate the transaction price, including its estimated variable consideration included in the transaction price and all constrained amounts, in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

Subject to the terms of the agreement, the Company granted Pfizer an exclusive, worldwide, royalty-bearing license, with the right to grant sublicenses, to use certain technology controlled by the Company for the purpose of developing, manufacturing and commercializing SB-525 and related products. Pfizer granted the Company a non-exclusive, worldwide, royalty free, fully paid license, with the right to grant sublicenses, to use certain manufacturing technology developed under the agreement and controlled by Pfizer to manufacture the Company’s products that utilize the AAV delivery system. During a specified period, neither the Company nor Pfizer will be permitted to clinically develop or commercialize, outside of the collaboration, certain AAV-based gene therapy products for hemophilia A.

Unless earlier terminated, the agreement has a term that continues, on a per product and per country basis, until the later of (i) the expiration of patent claims that cover the product in a country, (ii) the expiration of regulatory exclusivity for a product in a country, and (iii) fifteen years after the first commercial sale of a product in a country. Pfizer has the right to terminate the agreement without cause in its entirety or on a per product or per country basis. The agreement may also be terminated by either party based on an uncured material breach by the other party or the bankruptcy of the other party. Upon termination for any reason, the license granted by the Company to Pfizer to develop, manufacture and commercialize SB-525 and related products will automatically terminate. Upon termination by the Company for cause or by Pfizer in any country or countries, Pfizer will automatically grant the Company an exclusive, royalty-bearing license under certain technology controlled by Pfizer to develop, manufacture and commercialize SB-525 in the terminated country or countries.

The Company has identified the performance obligations within the hemophilia A Pfizer agreement as a license to the technology and on-going services. The Company concluded that the license is not discrete as it does not have stand-alone value to Pfizer apart from the services to be performed by the Company pursuant to the agreement. As a result, the Company recognizes revenue from the upfront payment based on proportional performance through 2020, the estimated period the Company will perform research services. The estimated period of performance and project

cost is reviewed quarterly and adjusted, as needed, to reflect the Company's current assumptions regarding the timing of its deliverables. As of December 31, 2018, the Company had deferred revenue of $10.0 million related to this agreement. During the year ended December 31, 2018 and 2017, the Company recognized revenue of $37.8 million and $17.0 million, respectively, related to the upfront fee that was received.

C9ORF72 Research Collaboration and License Agreement

In December 2017, the Company entered into a separate exclusive, global collaboration and license agreement with Pfizer for the development and commercialization of potential gene therapy products that use ZFP TFs to treat ALS and frontotemporal lobar degeneration ("FTLD") linked to mutations of the C9ORF72 gene. Pursuant to this agreement, the Company agreed to work with Pfizer on a research program to identify, characterize and preclinically develop ZFP-TFs that bind to and specifically reduce expression of the mutant form of the C9ORF72 gene.

The Company received a $12.0 million upfront payment from Pfizer and is eligible to receive up to $60.0 million in development milestone payments from Pfizer contingent on the achievement of specified preclinical development, clinical development and first commercial sale milestones, and up to $90.0 million commercial milestone payments if annual worldwide net sales of the licensed products reach specified levels. In addition, Pfizer will pay the Company royalties based on an escalating tiered, mid- to high-single digit percentage of the annual worldwide net sales of the licensed products. These royalty payments are subject to reduction due to patent expiration, entry of biosimilar products to the market and payments made under certain licenses for third party intellectual property. Each party will be responsible for the cost of its performance of the research program. Pfizer will be operationally and financially responsible for subsequent development, manufacturing and commercialization of the licensed products.

None of the clinical or regulatory milestones have been included in the $12.0 million transaction price, as all milestone amounts are fully constrained. As part of its evaluation of the constraint, the Company considered numerous factors, including the fact that achievement of the milestones at this time is uncertain and contingent upon future periods when the uncertainty related to the variable consideration is resolved. The Company will re-evaluate the transaction price, including is estimated variable consideration included in the transaction price and all constrained amounts, in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

Subject to the terms of this agreement, the Company granted Pfizer an exclusive, royalty-bearing, worldwide, license under the Company’s relevant patents and know-how to develop, manufacture and commercialize gene therapy products that use resulting ZFP-TFs that satisfy pre-agreed criteria. During a specified period, neither the Company nor Pfizer will be permitted to research, develop, manufacture or commercialize outside of the collaboration any ZFPs that specifically bind to the C9ORF72 gene.

Unless earlier terminated, the agreement has a term that continues, on a per licensed product and per country basis, until the later of (i) the expiration of patent claims that cover the licensed product in a country, (ii) the expiration of regulatory exclusivity for a licensed product in a country, and (iii) fifteen years after the first commercial sale of a licensed product in a major market country. Pfizer also has the right to terminate the agreement without cause in its entirety or on a per product or per country basis. The agreement may also be terminated by either party based on an uncured material breach by the other party or the bankruptcy of the other party. The agreement will also terminate if the Company is unable to identify any lead candidates for development within a specified period of time or if Pfizer elects not to advance a lead candidate beyond a certain development milestone within a specified period of time. Upon termination for any reason, the license granted by the Company to Pfizer to develop, manufacture and commercialize licensed products under the agreement will automatically terminate. Upon termination by the Company for cause or by Pfizer without cause for any licensed product or licensed products in any country or countries, the Company will have the right to negotiate with Pfizer to obtain a non-exclusive, royalty-bearing license under certain technology controlled by Pfizer to develop, manufacture and commercialize the licensed product or licensed products in the terminated country or countries.

Following termination by the Company for Pfizer’s material breach, Pfizer will not be permitted to research, develop, manufacture or commercialize ZFPs that specifically bind to the C9ORF72 gene for a period of time. Following termination by Pfizer for the Company’s material breach, the Company will not be permitted to research, develop, manufacture or commercialize ZFPs that specifically bind to the C9ORF72 gene for a period of time.

The Company has identified the performance obligations within this agreement as a license to the technology and on-going services. The Company concluded that the license is not discrete as it does not have stand-alone value to Pfizer apart from the services to be performed by the Company pursuant to the agreement. As a result, the Company recognizes revenue from the upfront payment based on proportional performance through March 31, 2019 the estimated period the Company will perform research services. The estimated period of performance and project cost is reviewed quarterly and adjusted, as needed, to reflect the Company’s current assumptions regarding the timing of its deliverables. As of December 31, 2018, the Company had deferred revenue of $9.8 million related to this agreement. During the year ended December 31, 2018 the Company recognized revenue of $2.2 million related to the upfront fee

that was received upon entering into the agreement.

Bioverativ, a Sanofi Genzyme company.

In January 2014, the Company entered into an exclusive worldwide collaboration and license agreement with Bioverativ to develop therapeutics for hemoglobinopathies, focused on beta-thalassemia and sickle cell disease ("SCD"). Under the agreement, the Company is jointly conducting two research programs: the beta-thalassemia program and the SCD program. In the beta-thalassemia program, the Company is responsible for all discovery, research and development activities through the first human clinical trial. In the SCD program, both parties are responsible for research and development activities through the submission of an investigational new drug ("IND") application for ZFP therapeutics intended to treat SCD.

Under both programs, Bioverativ is responsible for subsequent worldwide clinical development, manufacturing and commercialization of licensed products developed under the agreement. At the end of the specified research terms for each program or under certain specified circumstances, Bioverativ has the right to step in and take over any of the Company's remaining activities. Furthermore, the Company has an option to co-promote in the United States any licensed products to treat beta-thalassemia and SCD developed under the agreement, and Bioverativ will compensate the Company for such co-promotion activities. Subject to the terms of the agreement, the Company has granted Bioverativ an exclusive, royalty-bearing license, with the right to grant sublicenses, to use certain ZFP and other technology controlled by the Company for the purpose of researching, developing, manufacturing and commercializing licensed products developed under the agreement. The Company also granted Bioverativ a non-exclusive, worldwide, royalty-free, fully paid license, with the right to grant sublicenses, under the Company's interest in certain other intellectual property developed pursuant to the agreement. During the term of the agreement, the Company is not permitted to research, develop, manufacture or commercialize, outside of the agreement, certain gene therapy products that target genes relevant to the licensed products.

Under the agreement, the Company received an upfront license fee of $20.0 million and is eligible to receive development and sales milestone payments upon the achievement of specified regulatory, clinical development and sales milestones. In addition, the Company will also be eligible to receive up to $115.8 million in payments upon the achievement of specified clinical development and regulatory milestones, as well as up to $160.5 million in payments upon the achievement of specified sales milestones. The total amount of potential regulatory, clinical development, and sales milestone payments, assuming the achievement of all specified milestones in the agreement, is up to $276.3 million. In addition, the Company will receive royalty payments for each licensed product that are a tiered double-digit percentage of annual net sales of each product. Bioverativ reimburses Sangamo for agreed upon costs incurred in connection with research and development activities conducted by Sangamo. To date, no milestone payments have been received and no products have been approved and therefore no royalty fees have been earned under the Bioverativ agreement.

The agreement may be terminated by (i) the Company or Bioverativ for the uncured material breach of the other party, (ii) the Company or Bioverativ for the bankruptcy or other insolvency proceeding of the other party; (iii) Bioverativ, upon 180 days' advance written notice to the Company and (iv) Bioverativ, for certain safety reasons upon written notice to, and after consultation with, the Company. As a result, actual future milestone payments could be lower than the amounts stated above.

All contingent payments under the agreement, when earned, will be non-refundable and non-creditable. The transaction price of $75.7 million includes the upfront license fee of $20.0 million and $55.7 million estimated reimbursable service costs for identified research projects over the estimated performance period, as all milestone amounts are fully constrained. As part of its evaluation of the constraint, the Company considered numerous factors, including the fact that achievement of the milestones at this time is uncertain and contingent upon future periods when the uncertainty related to the variable consideration is resolved. The Company will re-evaluate the transaction price, including the estimated variable consideration included in the transaction price and all constrained amounts, in each reporting period and as uncertain events are resolved or other changes in circumstances occur. None of the clinical or regulatory milestones have been included in transaction price.

The Company has identified the performance obligations within this arrangement as a license to the technology and on-going research services activities. The Company concluded that the license is not discrete as it does not have stand-alone value to Bioverativ apart from the research services to be performed pursuant to the agreement. As a result, the Company recognizes revenue from the upfront payment based on proportional performance through 2022, the estimated period the Company will perform research services. The estimated period of performance and project cost is reviewed quarterly and adjusted, as needed, to reflect the Company's current assumptions regarding the timing of its deliverables. As of December 31, 2018, the Company had deferred revenue of $4.6 million related to this agreement.

Revenues recognized under the Bioverativ Agreement for the years ended December 31, 2018, 2017 and 2016 are as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Revenue related to Bioverativ agreement:			
Recognition of upfront fee	$4,013	$1,769	$2,321
Research services	9,503	10,489	6,565
Total	$13,516	$12,258	$8,886

California Institute for Regenerative Medicine

In May 2018, the California Institute for Regenerative Medicine ("CIRM") granted a Strategic Partnership Award for $8.0 million to fund the clinical studies of a potentially curative ZFP Therapeutic for the treatment of beta-thalassemia based on the application of Sangamo's ZFN genome editing technology. The grant exists through December 31, 2022 and provides matching funds to support the evaluate ST-400, a gene-edited cell therapy candidate for people with transfusion-dependent beta-thalassemia. As of December 31, 2018, the Company had received $1.7 million under the award.

Under the terms of the CIRM grants, the Company is obligated to pay royalties and licensing fees based on a low single digit royalty percentage on net sales of CIRM-funded product candidates or CIRM-funded technology. The Company has the option to decline any and all amounts awarded by CIRM and as an alternative to revenue sharing, the Company has the option to convert the award to a loan. No such election has been made as of the date of the issuance of these financial statements. In the event that the Company terminates a CIRM-funded clinical trial, it will be obligated to repay the remaining CIRM funds on hand, therefore as of December 31, 2018, the $1.8 million, including $0.1 million of interest, related to this award is recorded as a loan in other long-term liabilities on the accompanying consolidated balance sheet

Amended Collaboration and License Agreement with Shire International GmbH in Human Therapeutics

In January 2012, the Company entered into a collaboration and license agreement with Shire to research, develop and commercialize a ZFP therapeutic for treating Huntington's disease. The Company received an upfront license fee of $13.0 million. In 2014, Sangamo recognized a $1.0 million milestone payment related to the hemophilia program. Shire does not have any milestone payment obligations, but is required to pay single digit percentage royalties to the Company, up to a specified maximum cap, on the commercial sales of therapeutic products for Huntington's disease. The Company is required to pay single digit percentage royalties to Shire, up to a specified maximum cap, on commercial sales of therapeutic products from programs returned under the original agreement (which include blood clotting Factors VIII and IX) that use two zinc fingers.

Pursuant to the agreement, the Company granted Shire an exclusive, world-wide, royalty-bearing license, with the right to grant sublicenses, to use the Company's ZFP technology for the purpose of developing and commercializing human therapeutic and diagnostic products for the HTT gene. During the term of the agreement, the Company is not permitted to research, develop or commercialize, outside of the agreement, certain products that target the HTT gene. The Company satisfied the deliverables and research services responsibilities within the amended arrangement which were completed in 2017. The agreement may be terminated by (i) the Company or Shire, in whole or in part, for the uncured material breach of the other party, (ii) the Company or Shire for the bankruptcy or other insolvency proceeding of the other party and (iii) Shire, in its entirety, effective upon at least 90 days' advance written notice.

The Company has concluded that the license is not a separate unit of accounting as it does not have stand-alone value to Shire apart from the research services to be performed pursuant to the Shire agreement. The Company satisfied the deliverables and research services responsibilities within the amended arrangement which were completed in 2017. As a result, the Company recognized the remaining $2.3 million of deferred revenue from the upfront payment during the year ended December 31, 2017.

Revenues recognized under the Shire agreement for the years ended December 31, 2018, 2017 and 2016, were $0.0 million, $2.4 million and $3.3 million, respectively.

Agreement with Sigma-Aldrich Corporation (Sigma) in Laboratory Research Reagents, Transgenic Animal and Commercial Protein Production Cell-line Engineering

In 2007, Sangamo entered into a license agreement with Sigma to provide Sigma with access to Sangamo's proprietary ZFP technology and the exclusive right to use the technology to develop and commercialize research reagent products and services in the research field, excluding certain agricultural research uses that Sangamo previously licensed to DAS. Sangamo developed laboratory research reagents using its ZFP technology over a three-year research services period. Sangamo has since transferred the ZFP manufacturing technology to Sigma.

In October 2009, Sangamo expanded its license agreement with Sigma. In addition to the original terms of the license agreement, Sigma received exclusive rights to develop and distribute ZFP-modified cell lines for commercial production of protein pharmaceuticals and certain ZFP-engineered transgenic animals for commercial applications. Under the terms of the agreement, Sigma made an upfront cash payment of $20.0 million consisting of a $4.9 million purchase of 636,133 shares of Sangamo common stock, valued at $4.9 million, and a $15.1 million upfront license fee. Sangamo is also eligible to receive commercial license fees of $5.0 million based upon a percentage of net sales and sublicensing revenue and thereafter a reduced royalty rate of 10.5% of net sales and sublicensing revenue. In addition, upon the achievement of certain cumulative commercial milestones, Sigma will make milestone

payments to Sangamo up to an aggregate of $25.0 million. Sangamo does not have additional ongoing performance obligations under the agreement.

Revenues recognized under the agreement with Sigma for the years ended December 31, 2018, 2017 and 2016, were $0.5 million, $0.7 million and $1.3 million, respectively.

Agreement with Dow AgroSciences in Plant Agriculture

In 2005, Sangamo entered into an exclusive commercial license with DAS, with an initial three-year research term. Under this agreement, Sangamo is providing DAS with access to its proprietary ZFP technology and the exclusive right to use the technology to modify the genomes or alter the nucleic acid or protein expression of plant cells, plants, or plant cell cultures. Sangamo has retained rights to use plants or plant-derived products to deliver ZFP TFs or ZFNs into humans or animals for diagnostic, therapeutic or prophylactic purposes. In 2008 DAS exercised its option and obtained a commercial license to sell products incorporating or derived from plant cells generated using the Company's ZFP technology. The exercise of the option triggered a one-time commercial license fee of $6.0 million, payment of the remaining $2.3 million of the previously agreed upon $4.0 million in research milestones, development and commercialization milestone payments for each product, and royalties on sales of products. Furthermore, DAS has the right to sublicense Sangamo's ZFP technology to third parties for use in plant cells, plants, or plant cell cultures, and Sangamo will be entitled to 25% of any cash consideration received by DAS under such sublicenses. In December 2010 the Company amended its agreement with DAS to extend the period of reagent manufacturing services and research services through December 31, 2012.

The agreement with DAS also provides for minimum sublicense fees each year due to Sangamo every October, provided the agreement is not terminated by DAS. Annual fees range from $250,000 to $3.0 million and total $25.3 million over 11 years unless terminated at any time by DAS. The Company does not have any performance obligations. In the event of any termination of the agreement, all rights to use the Company's ZFP technology will revert to Sangamo, and DAS will no longer be permitted to practice Sangamo's ZFP technology or to develop or, except in limited circumstances, commercialize any products derived from the Company's ZFP technology.

Revenues under the agreement with DAS were $3.0 million, $3.0 million, and $5.1 million during 2018, 2017 and 2016, respectively.

NOTE 6 – ACQUISITION OF TXCELL S.A.

On July 20, 2018, Sangamo entered into a SPA with certain shareholders of TxCell S.A., a French société anonyme ("TxCell"), and the Company and TxCell entered into a TOA, pursuant to which the Company agreed to acquire 100% of the equity interests of TxCell. On October 1, 2018 (the "Acquisition Date"), the Company completed the acquisition of 13,519,036 ordinary shares of TxCell ("TxCell Ordinary Shares"), representing approximately 53% of the outstanding share capital and voting rights of TxCell, pursuant to the SPA (the "Block Transaction"). TxCell specializes in developing cellular immunotherapy platforms that use regulator T cells ("Tregs") to treat severe autoimmune and inflammatory diseases and the Company expects that the acquisition of TxCell will accelerate its entry into the clinic with a CAR-Treg therapy.

The Company also entered into arrangements with the holders of approximately 477,000 "free shares" of TxCell pursuant to which the Company has the right to purchase (call option) such shares from the holders thereof and such holders have the right to sell (put option) to the Company such shares from time to time through mid-2021 (the "Free Shares Options"). Of the 477,000 approximately 453,000 are related to vested free shares, with the remaining related to

unvested free shares. The purchase price for each such free share acquired by the Company upon exercise of a Free Shares Option will be based on the performance of the Company's stock price from the announcement of the transactions contemplated by the SPA and TOA through the time of purchase (as of October 1, 2018 ("the Acquisition Date") the Free Shares Options purchase price was valued at €2.58 per share or approximately $2.99 per share using an exchange rate of $1.16). For example, if the Company's stock price increases during that time period, the Free Shares Options purchase price per share will proportionately increase. However, if the Company's stock price decreases the Free Shares Options purchase price is limited to a minimum purchase price of €2.58 per share, subject to certain exceptions. The fair value of the Free Shares Options was estimated to be $0.2 million, based on an option pricing method, and such value is included in the purchase consideration. The fair value of the Free Shares Options will vary based on future changes in the Company's stock price during the option period with such changes in fair value being recognized in operations. The fair value of the outstanding shares of TxCell, to which the Free Share Options relate, is recorded as a noncontrolling interest (see further details related to noncontrolling interest below).

In September 2018, the Company also provided TxCell with a $5.2 million loan (the “TxCell Loan”) that was deemed to be part of the purchase consideration for accounting purposes. The TxCell Loan, together with the cash paid to acquire the TxCell Ordinary Shares, $40.5 million, and the estimated fair value of the Free Shares Options, $0.2 million, comprise the aggregate purchase consideration of $45.9 million, as of the Acquisition Date.

Management estimated the fair value of tangible and intangible assets and liabilities in accordance with the applicable accounting guidance for business combinations and utilized the services of third-party valuation consultants. Balances subject to adjustment primarily include the valuations of acquired assets (tangible and intangible), liabilities assumed, as well as tax-related matters. During the measurement period, the Company may record adjustments to the provisional amounts recognized. The Company expects the allocation of the consideration transferred to be final within the measurement period (up to one year from the Acquisition Date).

The TxCell Acquisition was accounted for as a business combination in accordance with ASC Topic 805, Business Combinations. The operating results of TxCell after the Acquisition Date have been included in the Company’s Consolidated Statements of Operations. For the three months ended December 31, 2018, TxCell did not contribute any revenue. For the three months ended December 31, 2018, operating expenses related to TxCell were approximately $3.7 million.

Fair Value Estimate of Assets Acquired and Liabilities Assumed

Under ASC Topic 805, an acquirer recognizes and consolidates assets acquired, liabilities assumed, and any non-controlling interest at 100% of their fair values as of the acquisition date (regardless of the acquirer’s percentage ownership in the acquiree). As goodwill is calculated as a residual, all goodwill of the acquired business, not just the acquirer’s share, is recognized under this “full-goodwill” approach. Recognized goodwill is allocated between the controlling and non-controlling interests. Although this allocation is not presented separately on the acquirer’s balance sheet, it is necessary so that a goodwill impairment charge recognized in a period following the business combination by an acquirer is appropriately allocated between controlling and non-controlling interests. There were no goodwill impairments during 2018 and, as noted below, substantially all of the non-controlling interest on the Acquisition Date was subsequently acquired by the Company and, accordingly, substantially all of the goodwill is allocated to the Company as of December 31, 2018.

The following table summarizes the estimated fair value of the net assets acquired as of the Acquisition Date (in thousands):

	October 1, 2018
Consideration transferred	$ 45,911
Fair value of non-controlling interest	35,829
Fair value of TxCell	$ 81,740
Cash	4,779
Current assets	2,427
	1,857

Property and equipment		
IPR&D	55,019	
Other assets	155	
Current liabilities	(9,761	)
Assumed debt liabilities	(4,933	)
Deferred tax liability, net	(6,798	)
Fair value of net identifiable assets acquired	42,745	
Goodwill	38,995	
Total fair value of net assets acquired	$ 81,740	

Consideration Transferred

Consideration transferred as of October 1, 2018 consists of the 13,519,036 TxCell Ordinary Shares acquired by the Company on the Acquisition Date of approximately $2.99 per share, the $5.2 million TxCell Loan and approximately $0.2 million for the fair value of the free shares.

Noncontrolling Interest

The fair value of the non-controlling interest at the Acquisition Date was based on the $2.99 acquisition price per share for the 11,981,867 Ordinary Shares that were not purchased by the Company on the Acquisition Date.

On November 1, 2018, pursuant to the TOA, the Company commenced a cash tender offer (the "Offer") to acquire all of the TxCell Ordinary Shares not held by the Company for the same per share price paid in the Block Transaction. Following the completion of the Offer on November 23, 2018, the Company initiated compulsory squeeze-out procedures applicable to French public companies to acquire the remaining TxCell Ordinary Shares, other than the free shares that were subject to the Free Share Options. Subsequent to the Acquisition Date and through December 31, 2018, the Company acquired 11,528,635 TxCell Ordinary Shares which, when aggregated with the 13,519,036 Ordinary Shares acquired at the Acquisition Date, resulted in the Company owning 98.2% of all TxCell Ordinary Shares as of December 31, 2018. The 11,528,635 shares acquired subsequent to the Acquisition Date were acquired for total consideration of approximately $33.9 million, or $2.94 per share. As of December 31, 2018 the aggregate purchase consideration was approximately $80.4 million through the completion of this purchase, with approximately 453,000 Ordinary Shares (vested free shares), which remain outstanding and are subject to purchase by the Company as noted above, with an estimated fair value of approximately $1.3 million.

Non-controlling interest as of December 31, 2018 was as follows (in thousands):

	Total
Non-controlling interest at January 1, 2018	$—
Non-controlling interest at acquisition	35,829
Shares acquired post acquisition	(34,516)
Non-controlling interest of acquired entity	1,313
Foreign currency effect	(19)
Loss attributable to non-controlling interest	(555)
Non-controlling interest at December 31, 2018	$739

Intangible Assets

Identified intangible assets of $55.0 million primarily relates to IPR&D. The fair value of this asset was determined utilizing a weighted market, cost, and income valuation approach. IPR&D is an intangible asset classified as indefinite-lived until the completion or abandonment of the associated research and development effort, and will be amortized over an estimated useful life to be determined at the date the project is completed. The IPR&D is tested for impairment annually and if the Company concludes the technology is no longer realizable, the asset will be immediately expensed. There was no impairment for the year ended December 31, 2018.

Goodwill

Goodwill of $39.0 million represents the excess of the fair value of the consideration transferred plus the fair value of the noncontrolling interest in TxCell over the fair value of the assets acquired and liabilities assumed. Goodwill represents the anticipated benefits of using TxCell's expertise within the emerging fields of Treg and CAR-Treg (which are Tregs genetically modified with a chimeric antigen receptor).

The Company tests goodwill for impairment on an annual basis or sooner, if deemed necessary. As of December 31, 2018, there were no changes in the goodwill recorded from the TxCell Acquisition. This goodwill is not deductible for income tax purposes. There was no impairment or the year ended December 31, 2018.

Pro Forma Information

The following unaudited supplemental pro forma information presents the Company's financial results as if the TxCell Acquisition had occurred on January 1, 2017. This supplemental pro forma information has been prepared for comparative purposes and does not purport to be indicative of what would have occurred had the TxCell Acquisition been made on January 1, 2017, nor are they indicative of any future results.

	Year Ended December 31,	
	2018	2017
	(in thousands, except per share amounts)	
Revenue	$86,182	$39,091
Loss from operations	(86,253)	(68,221)
Net loss	(79,735)	(66,350)
Net loss per share, basic	(0.82)	(0.85)

To complete the purchase transaction, the Company incurred approximately $2.1 million of acquisition costs, which were recognized as general and administrative expense for the year ended December 31, 2018.

NOTE 7 – PROPERTY AND EQUIPMENT, NET

Property and equipment, net consist of the following (in thousands):

	December 31 ,	
	2018	2017
Laboratory equipment	$11,466	$7,572
Furniture and fixtures	3,840	1,494
Leasehold improvements	3,640	3,425
Buildings	3,876	3,876
Total	22,822	16,367
Less: accumulated depreciation and amortization	(9,310)	(6,951)
Construction in progress	65,211	21,650
	$78,723	$31,066

Depreciation and amortization expense was $2.4 million in 2018, $1.5 million in 2017 and $1.0 million in 2016. In 2018 the Company capitalized $2.0 million in interest related to the fair value of the Brisbane building and $41.8 million of construction costs in construction in progress under the build-to-suit lease guidance (see Note 14). In 2017 the Company capitalized $20.9 million related to the fair value of the Brisbane building and $0.3 million of construction costs in construction in progress under the build-to-suit lease guidance. Build-to-suit properties are classified within property and equipment, net, along with a corresponding build-to-suit lease obligation for the same amount. The Brisbane and Point Pinole buildings will depreciate over the period of their lease, respectively.

NOTE 8 – COMMITMENTS AND CONTINGENCIES

Sangamo occupies office and laboratory space under operating leases in Richmond, CA. In May 2018, Sangamo amended its lease agreement for its corporate headquarters wherein the lease was extended through August 2026. The Company has three additional properties located in Richmond, CA. This includes two leases, one to occupy approximately 7,700 square feet of research and office space that expires in August 2019, and another to occupy approximately 6,200 square feet of office space that expires in July 2021. Sangamo also has two build-to-suit leases to occupy approximately 41,400 square feet of space in Richmond, CA that expires in December 2021 and approximately 87,700 square feet of space in Brisbane, CA that expires in May 2029. In addition, the Company leases a property in Valbonne, France with approximately 14,036 square feet of research and office space that expires in June 2022. Rent expense related to these lease agreements was $2.3 million, $1.1 million, and $1.0 million for 2018, 2017 and 2016, respectively. Future minimum payments under lease obligations at December 31, 2018 consist of the following (in thousands):

Fiscal Year:	
2019	$3,671
2020	5,950
2021	6,042

2022	5,608
2023	5,649
Thereafter	29,498
Total minimum payments	$56,418

The Company also has $1.3 million of license obligations related to its intellectual property.

Contingencies

Sangamo is not party to any material pending legal proceeding. From time to time, Sangamo may be involved in legal proceedings arising in the ordinary course of business.

NOTE 9 – STOCKHOLDERS' EQUITY

Preferred Stock

The Company has 5,000,000 preferred shares authorized, which may be issued at the discretion of the Company's Board of Director's discretion.

Common Stock

In April 2018, Sangamo completed an underwritten public offering of its common stock, in which the Company sold an aggregate of 14.2 million shares of its common stock at a public offering price of $16.25 per share. The net proceeds to Sangamo from the sale of shares in this offering, after deducting underwriting discounts and commissions and other offering expenses, were approximately $215.8 million.

In June 2017, Sangamo completed an underwritten public offering of its common stock, in which the Company sold an aggregate of 11.5 million shares of its common stock at a public offering price of $7.25 per share. The net proceeds to Sangamo from the sale of shares in this offering, after deducting underwriting discounts and commissions and other offering expenses, were approximately $78.1 million.

At-the-Market Offering Agreements

On December 7, 2016, the Company entered into an “at the market” offering agreement with Cowen and Company, LLC (“Cowen”), pursuant to which the Company may issue and sell from time to time up to $75.0 million of the Company’s common stock through the bank as the sales agent (“ATM Agreement”).

In May 2017, the Company entered into an amended and restated sales agreement with Cowen and Company, LLC (“Cowen”) pursuant to which the Company may offer and sell, in its sole discretion, shares of common stock having an aggregate offering price of up to $75.0 million through Cowen acting as the sales agent (the “ATM Facility”). Sales of the Company’s common stock, if any, will be made at market prices by any method that is deemed to be an “at the market offering” as defined in Rule 415 under the Securities Act of 1933, as amended. The Company has not sold any common stock under the ATM Facility. As of December 31, 2018, the full $75.0 million provided for under the ATM Facility remained available for sale, subject to certain conditions as specified in the agreement

Stock Incentive Plan

In April 2013, the Company’s Board of Directors adopted, subject to stockholder approval, the Company’s 2013 Stock Incentive Plan (“the 2013 Plan”) as the successor to the Company’s 2004 Stock Incentive Plan (the “2004 Plan”). At the Annual Meeting of Stockholders held on June 12, 2013, the 2013 Plan was approved by the Company’s stockholders and became effective. In connection with the approval by stockholders of the 2013 Plan, outstanding awards under the 2004 Plan were transferred to the 2013 Plan. The 2004 Plan was terminated and no further awards will be made pursuant to the 2004 Plan.

Under the 2013 Plan, the exercise price per share of options granted will generally not be less than 100% of the fair value per share of common stock on the grant date, and the option term will not exceed ten years. If the person to whom the option is granted is a 10 percent stockholder, and the option granted qualifies as an Incentive Stock Option Grant, then the exercise price per share will not be less than 110 percent of the fair value per share of common stock on the grant date, and the option term will not exceed five years. Options granted under the 2013 Plan generally vest over four years at a rate of 25% one year from the grant date and one thirty-sixth per month thereafter and expire ten years after the grant, or earlier upon employment termination. Certain options previously granted under the 2004 Plan to the Company’s non-employee directors are structured so that they may be exercised prior to vesting, with the related shares subject to Sangamo’s right to repurchase any shares that have not vested pursuant to the vesting schedule in effect for such award at the exercise price paid if the option holder’s board service terminates. Approximately 14.1 million shares were initially reserved for issuance under the 2013 Plan, including 9.7 million shares of common stock subject to outstanding awards previously granted under the 2004 Plan that were transferred to the 2013 Plan, and an additional 4.4 million shares of common stock.

The number of shares of common stock reserved for issuance under the 2013 Plan will be reduced: (i) on a 1-for-1 basis for each share of common stock subject to a stock option or stock appreciation right granted under the plan,

(ii) on a 1-for-1 basis for each share of common stock issued pursuant to a full value award granted under the plan prior to the plan effective date, and (iii) by a fixed ratio of 1.33 shares of common stock for each share of common stock issued pursuant to a full-value award granted under the plan on or after the plan effective date.

Shares subject to any outstanding options or other awards under the 2013 Plan that expire or otherwise terminate prior to the issuance of the shares subject to those options or awards will be available for subsequent issuance under the 2013 Plan. Any unvested shares issued under the 2013 Plan that the Company subsequently purchases, pursuant to repurchase rights under the 2013 Plan, will be added back to the number of shares reserved for issuance under the 2013 Plan on a 1-for-1 basis or a 1.33-for-1 basis (depending on the ratio at which the share reserve was debited for the original award) and will accordingly be available for subsequent issuance in accordance with the terms of the plan.

In June 2015, the Company's stockholders were asked to vote to approve the amendment and restatement of the Company's 2013 Plan in order to increase the number of shares in our common stock reserved for issuance over the term of the 2013 Plan by 5,300,000 shares. At the Annual Meeting of Stockholders held on June 22, 2015, the amendment and restatement of the Company's 2013 Stock Incentive Plan was approved by the Company's stockholders and became effective.

On November 10, 2017, the Compensation committee of the Company's Board of Directors approved the amendment and restatement of the 2013 Plan, to reserve an additional one million shares of the Company's common stock to be used exclusively for grants of awards to individuals who were not previously employees or non-employee directors of the Company (or following a bona fide period of non-employment with the Company), as an inducement material to each such individual's entry into employment with the Company within the meaning of Rule 5635(c)(4) of the NASDAQ Listing Rules, or Rule 5635(c)(4). The 2013 Plan was amended and restated by the Compensation Committee without stockholder approval pursuant to Rule 5635(c)(4).

In April 2018, the Compensation Committee of the Company's Board of Directors approved the Sangamo Therapeutics, Inc. 2018 Equity Incentive Plan (the "2018 Plan"), subject to approval by the Company's stockholders. The 2018 Plan is the 2013 Plan. The 2018 Plan became effective on June 11, 2018 upon approval at the Company's Annual Meeting of Stockholders. In connection with the approval of the 2018 Plan, no additional equity awards will be granted under the 2013 Plan, however all outstanding equity awards under the 2013 Plan will continue to be subject to the terms and conditions as set forth in the agreements evidencing such awards and the terms of the 2013 Plan.

The exercise price of a stock option granted under the 2018 Plan may not be less than 100% of the fair market value of our common stock subject to the stock option on the date of grant, and the option term will not exceed ten years. If the person to whom the stock option is granted is a 10 percent stockholder of the Company, and the stock option granted qualifies as an Incentive Stock Option Grant, then the exercise price per share will not be less than 110% of the fair market value of the Company's common stock on the date of grant, and the option term will not exceed five years. Generally, stock options granted under the 2018 Plan vest over four years at a rate of twenty-five percent (25%) on the one-year anniversary of the date of grant and one forty-eighth (1/48) per month thereafter and expire ten years after the date of grant, or earlier upon termination of employment or services to the Company.

The number of shares of common stock reserved for issuance under the 2018 Plan will be reduced: (i) on a 1-for-1 basis for each share of common stock subject to a stock option or stock appreciation right granted under the plan, (ii) by a fixed ratio of 1.33 shares of common stock for each share of common stock issued pursuant to a full-value award granted under the plan.

Shares subject to any outstanding stock options or other awards under the 2018 Plan that expire or otherwise terminate prior to the issuance of the shares subject to those stock options or awards will be available for subsequent issuance under the 2018 Plan. Any unvested shares issued under the 2018 Plan that the Company subsequently purchases, pursuant to repurchase rights under the 2018 Plan, will be added back to the number of shares reserved for issuance under the 2018 Plan on a 1-for-1 basis or a 1.33-for-1 basis (depending on the ratio at which the share reserve was debited for the original award) and will accordingly be available for subsequent issuance in accordance with the terms of the 2018 Plan.

Employee Stock Purchase Plan

In June 2018, the Company's stockholders approved the amendment and restatement of the ESPP. As amended, the ESPP provides a total reserve of 4,600,000 shares of common stock for issuance under the ESPP. Eligible employees may purchase common stock at 85 percent of the lesser of the fair market value of the Company's common stock on the first day of the applicable two-year offering period or the last day of the applicable six-month purchase period.

Stock Option Activity

A summary of Sangamo's stock option activity is as follows:

	Number of Shares	Weighted-Average Exercise per Share Price	Weighted-Average Remaining Contractual Term (In years)	Aggregate Intrinsic Value (In thousands)
Options outstanding at December 31, 2017	8,287,456	$ 7.77		
Options granted	3,115,078	$ 17.78		
Options exercised	(2,028,328)	$ 7.12		
Options canceled	(648,114)	$ 11.15		
Options outstanding at December 31, 2018	8,726,092	$ 11.23	7.35	$ 24,468
Options vested and expected to vest at December 31, 2018	8,726,092	$ 11.23	7.35	$ 24,468
Options exercisable at December 31, 2018	3,699,150	$ 8.91	5.39	$ 12,702

Newly created shares are issued upon exercises of options. There were no shares subject to Sangamo's right of repurchase as of December 31, 2018. The intrinsic value of options exercised was $27.0 million, $12.3 million and $0.1 million during 2018, 2017 and 2016, respectively.

At December 31, 2018, the aggregate intrinsic values of outstanding and exercisable options were $24.5 million and $12.7 million, respectively. The aggregate intrinsic value of options vested and expected to vest as of December 31, 2018, 2017 and 2016 was $24.5 million, $71.7 million and $0.0 million, respectively.

The following table summarizes information with respect to stock options outstanding at December 31, 2018:

	Options Outstanding and Exercisable		Options Exercisable	
Range of Exercise Price	Number of Shares of Common Stock subject to options	Weighted-Average Remaining Contractual Life (In years)	Number of Shares of Common Stock subject to options	Weighted-Average Exercise Price
$2.55 - $3.20	352,920	7.56	91,772	$ 3

$3.50 - $3.50	1,171,546	8.00	520,209	$	4
$3.55 - $5.70	894,224	5.06	589,511	$	5
$5.72 - $7.20	915,176	7.42	610,840	$	7
$7.70 - $9.99	897,995	6.18	566,601	$	9
$10.16 - $12.72	936,327	6.91	403,714	$	12
$12.80 - $15.00	1,213,226	6.37	694,173	$	14
$15.11 -$19.80	758,250	8.74	216,830	$	16
$20.05 - $20.05	1,003,728	9.06	—	$	-
$20.85 - $24.95	582,700	9.08	5,500	$	21
	8,726,092	7.35	3,699,150	$	9

Restricted Stock Units

During 2018, 2017 and 2016, the Company awarded 346,055, 12,600, and 60,000 RSUs, respectively. The RSUs awarded in 2018, 2017 and 2016 had an average grant date fair value per award of $17.87, $15.85 and $5.16, respectively. These awards generally vest as follows: one-third of the award will vest in a series of three successive equal annual installments. The aggregate fair value of RSUs vested during 2018, 2017 and 2016 was $0.6 million, $1.2 million and $4.8 million, respectively.

A summary of Sangamo's RSU activity is as follows:

	Number of Shares	Weighted-Average Remaining Contractual Term (In years)	Aggregate Intrinsic Value (In thousands)
RSUs outstanding at December 31, 2017	80,172		
RSUs awarded	346,055		
RSUs released	(55,592)		
RSUs forfeited	(47,934)		
RSUs outstanding at December 31, 2018	322,701	1.25	3,705
RSUs vested and expected to vest at December 31, 2018	322,701	1.25	$ 3,705

RSUs that vested in 2018, 2017 and 2016 were net-share settled such that the Company withheld shares with value equivalent to the employees' minimum statutory obligation for the applicable income and other employment taxes, and remitted the cash to the appropriate taxing authorities. The total shares withheld were approximately 20,193, 42,243, and 165,181 for 2018, 2017 and 2016, respectively, and were based on the value of the RSUs on their respective issuance dates as determined by the Company's closing stock price. Total payments for the employees' tax obligations to taxing authorities were $0.3 million, $0.7 million and $0.8 million in 2018, 2017 and 2016, respectively and are reflected as a financing activity within the accompanying consolidated statements of cash flows. These net-share settlements had the effect of share repurchases by the Company as they reduced and retired the number of shares that would have otherwise been issued as a result of the vesting and did not represent an expense to the Company.

As of December 31, 2018, there were 9,491,418 shares reserved for future awards under the Company's 2013 Plan and 3,006,964 shares of common stock reserved for future issuance under the Purchase Plan.

NOTE 10 – INCOME TAXES

The domestic and foreign components of loss before income taxes were as follows (in thousands):

	December 31,		
	2018	2017	2016
Domestic	$(65,695)	$(54,568)	$(71,672)
Foreign	(3,194)	—	—
Loss before income taxes	$(68,889)	$(54,568)	$(71,672)

The benefit for income taxes consisted of the following (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Benefit for income taxes:			
Current:			
Federal	$—	$—	$—
State	—	—	—
Foreign	—	—	—
Subtotal	—	—	—
Deferred:			
Federal	—	—	(12)
State	—	—	(2)
Foreign	—	—	—
Subtotal	—	—	(14)
Income tax benefit	$—	$—	$(14)

The difference between the benefit for income taxes and the amount computed by applying the federal statutory income tax rate (21%) to loss before taxes is explained as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Tax at federal statutory rate	$(14,467)	$(18,553)	$(24,369)
State taxes, net	(2,849)	795	(747)
Federal rate change	—	53,045	—
Foreign rate differential	(177)	—	—
Non-deductible stock-based compensation	(2,729)	2,120	2,781
Research credits	(1,005)	(869)	(1,424)
Change in valuation allowance	20,271	(36,575)	23,773
Other	956	37	(28)
Income tax benefit	$—	$—	$(14)

Note:

(1) For the years ended December 31, 2016 and 2017 the statutory tax rate was 34%. For the year ended December 31, 2018, as a result of Tax Reform, the statutory tax rate was decreased to 21%.

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of the Company's deferred tax assets are as follows (in thousands):

	December 31,	
	2018	2017
Assets:		
Deferred tax assets:		
Net operating loss carryforwards	$138,896	$91,308
Research and development tax credit carryforwards	16,829	15,147
Stock-based compensation	3,801	3,168
Deferred revenue	3,191	934
Build to suit lease liability	6,400	5,232
Other	604	366
Total deferred tax asset	169,721	116,155
Valuation allowance	158,150	112,833
Net deferred tax assets	$11,571	$3,322
Liabilities:		
Intangible assets	(14,100)	—

Fixed Assets	(4,176)	(3,322)
Net deferred tax liability	(18,276)	(3,322)
Total deferred tax liability	$(6,705)	$—

In October 2018, the Company acquired TxCell incorporated in France. The Company recorded goodwill and intangible assets as part of accounting for the acquisition of TxCell. There is no corresponding tax basis for the goodwill or intangible assets. A portion of the intangible assets acquired were for the use in a particular research and development project IPR&D and are considered indefinite-lived assets with no tax basis.

The changes in the fair value of the unrealized gain/loss on securities investment are recorded as a component of accumulated other comprehensive income, net of a provision for income taxes.

A valuation allowance is recorded when it is more likely than not that all or some portion of the deferred income tax assets will not be realized. The Company regularly assesses the need for a valuation allowance against its deferred income tax assets by considering both positive and negative evidence related to whether it is more likely than not that the Company’s deferred income tax assets will be realized. In evaluating the Company’s ability to recover its deferred income tax assets within the jurisdiction from which they arise, the Company considers all available positive and negative evidence, including scheduled reversals of deferred income tax

liabilities, projected future taxable income, tax-planning strategies, and results of recent operations. Accordingly, based upon the Company's analysis of these factors the net deferred tax assets have been substantially offset by a valuation allowance. The valuation allowance increase (decreased) by $45.3 million, $(28.9) million and $23.8 million for the years ended December 31, 2018, 2017 and 2016, respectively. As of December 31, 2018, Sangamo had net operating loss carryforwards for federal and state income tax purposes of approximately $535.0 million and $161.0 million, respectively. If not utilized, the net federal and state operating loss carryforwards will expire in 2018 and 2017, respectively. The Company's French NOL is $130.0 million which carries over indefinitely. The Company also has federal and state research tax credit carryforwards of $12.2 million and $13.0 million, respectively. The federal research credits began to expire in 2018 while the state research credits have no expiration date. Utilization of the Company's net operating loss carryforwards and research tax credit carryforwards may be subject to substantial annual limitations due to the ownership change limitations provided by the Internal Revenue Code and similar state provisions. The annual limitation could result in the expiration of the net operating loss carryforwards and research tax credit carryforwards before utilization.

On December 22, 2017, President Trump signed the Tax Cuts and Jobs Act ("Tax Reform") into legislation. The Tax Reform makes significant changes to the U.S. corporate income tax law including, but not limited to, (1) reducing the U.S. federal corporate tax rate to 21% from 35% and (2) requiring a one-time mandatory transition tax on previously deferred foreign earnings of U.S. subsidiaries. Under ASC Topic 740, the effects of changes in tax rates and laws are recognized in the period in which the new legislation is enacted. In the case of U.S. federal income taxes, the enactment date is the date the bill becomes law. In the current year the Company has accounted for additional provisions that impact the Company including but not limited to "global intangible low-taxed income ("GILTI"). The Company has completed an analysis for FDII and GILTI and due to the results of the Company, there is currently no impact for these provisions. In addition, the Company's GILTI policy election is to treat GILTI as a period cost if and when incurred and does not plan on calculating the deferred impact on GILTI.

On December 22, 2017, the SEC staff issued Staff Accounting Bulletin No. 118 ("SAB 118") which provides guidance on accounting for the tax effects of the Tax Reform. SAB 118 provides a measurement period that should not extend beyond one year from the Tax Reform enactment date for companies to complete the accounting under ASC Topic 740 for the year ended December 31, 2017. In accordance with SAB 118, a company must reflect the income tax effects of those aspects of the Tax Reform for which the accounting under ASC Topic 740 is complete. The Company has finished their analysis as of the measurement period closing of December 22, 2018 after application of law changes were reviewed by the Company. There were no subsequent adjustments as the conclusions have remained the same.

The Company intends to reinvest the earnings of its non-U.S. subsidiaries in those operations. The Company does not provide for U.S. income taxes on the earnings of foreign subsidiaries because the Company intends to reinvest such earnings offshore indefinitely. However, if these funds were repatriated, the Company would be required to accrue and pay applicable United States taxes (if any) and withholding taxes payable. It is not practicable to estimate the amount of the deferred tax liability associated with the repatriation of cash due to the complexity of its hypothetical calculation.

The Company files federal and state income tax returns with varying statutes of limitations. The tax years from 2002 forward remain open to examination due to the carryover of net operating losses or tax credits. The Company also files UK and French income tax returns, and the tax years from 2008 and thereafter remain open in the UK and 2015 and thereafter in France are still subject to examination.

The Company's practice is to recognize interest and/or penalties related to income tax matters in income tax expense. As of December 31, 2018, the Company had no accrued interest and/or penalties. The unrecognized tax benefits may change during the next year for items that arise in the ordinary course of business. In the event that any unrecognized tax benefits are recognized, the effective tax rate will not be affected.

The following table summarizes the activity related to the Company's unrecognized tax benefits (in thousands):

	December 31,		
	2018	2017	2016
Beginning balance	$5,659	$5,045	$8,330
Additions based on tax positions related to the current year	636	622	1,023
Additions for tax positions of prior years	(7)	(8)	27
Reductions for tax positions of prior years	—	—	(4,335)
Ending balance	$6,288	$5,659	$5,045

NOTE 11 – ACCOUNTS PAYABLE AND ACCRUED LIABILITIES

Accounts payable and accrued liabilities consist of the following (in thousands):

	December 31 ,	
	2018	2017
Accounts payable	$3,355	$16
Accrued research and development expenses	10,999	7,898
Accrued professional fees	1,930	1,318
Deferred rent	204	417
Other	4,969	1,386
Total accounts payable and accrued liabilities	$21,457	$11,035

NOTE 12 – EMPLOYEE BENEFIT PLAN

The Company sponsors a defined-contribution savings plan under Section 401(k) of the Internal Revenue Code covering all full-time employees (“Sangamo 401(k) Plan”). The Sangamo 401(k) Plan is intended to qualify under Section 401 of the Internal Revenue Code.

The Company matched employee contributions equal to 50% for the first 8% in 2018 and 2017 and 6% in 2016, up to a limit of $4,000 in 2018 and 2017, and $3,000 in 2016. Matching funds are fully vested when contributed. Contributions to the Sangamo 401(k) Plan by the Company were $0.8 million, $0.5 million, and $0.3 million for the years ended December 31, 2018, 2017 and 2016, respectively.

NOTE 13 – QUARTERLY FINANCIAL DATA (UNAUDITED)

The following table sets forth certain unaudited quarterly financial data for the eight quarters ended December 31, 2018. The unaudited information set forth below has been prepared on the same basis as the audited information contained herein and includes all adjustments necessary to present fairly the information set forth. The operating results for any quarter are not indicative of results for any future period. All data is in thousands except per share data.

	2018				2017			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Revenues	$12,637	$21,416	$23,562	$26,837	$3,425	$8,253	$11,812	$13,077
Expenses	33,634	40,556	39,803	47,609	20,217	21,021	24,847	26,843
Net loss	(20,187)	(16,640)	(12,843)	(19,219)	(16,632)	(12,491)	(12,354)	(13,091)
Net loss attributable to non-controlling interest	—	—	—	(555)	—	—	—	—

Net loss attributable to Sangamo Therapeutics, Inc.	(20,187)	(16,640)	(12,843)	(18,664)	(16,632)	(12,491)	(12,354)	(13,091)
Basic and Diluted Net loss per share attributable to Sangamo Therapeutics, Inc.	(0.23)	(0.17)	(0.13)	(0.18)	(0.23)	(0.17)	(0.15)	(0.15)

NOTE 14 – BUILD-TO-SUIT LEASES

Brisbane Build-to-Suit Lease

In November 2017, the Company entered into a long-term property lease which includes construction by the lessor of a building with approximately 87,700 square feet of space, in Brisbane, California. Substantial completion of the building is estimated to occur in the first half of 2019. The lease agreement expires in May 2029, approximately ten years after substantial completion of the building. A letter of credit for $3.5 million was established as the deposit and is classified within other non-current assets in the consolidated financial statements. The Company has two options to extend the lease term for up to a combined additional ten years.

The Company is deemed, for accounting purposes only, to be the owner of the entire project including the building shell, even though it is not the legal owner as a result of the cold shell condition of the building and involvement in the construction process. In connection with the Company’s accounting for this transaction, the Company capitalized the costs of construction as a build-to-suit property within property and equipment, net, and recognize a corresponding build-to-suit lease obligation, including interest. Fair

value of the building was estimated at $20.9 million using comparable market prices per square foot for similar space for public real estate transactions in the surrounding area and is considered a Level 2 fair value measurement. As of December 31, 2018, $2.0 million was capitalized related to interest with a corresponding build-to-suit lease obligation recognized related to this lease for the building and $41.8 million was capitalized related to the construction.

Point Pinole Build-to-Suit Lease

In December 2015, the Company entered into a long-term property lease which includes construction by the lessor of a building with approximately 41,400 square feet of space, in Richmond, California. Substantial completion of the building was accomplished in December 2016 at which time the lease commenced.

Construction was completed on the facility and a portion of the monthly lease payment gets allocated to land rent and recorded as an operating lease expense and the non-interest portion of the amortized lease payments to the landlord related to the rent of the building is applied to reduce the build-to-suit lease obligation.

The Company is deemed, for accounting purposes only, to be the owner of the entire project including the building shell, even though it is not the legal owner. In connection with the Company's accounting for this transaction, the Company capitalized the costs of construction as a build-to-suit property within property and equipment, net, and recognized a corresponding build-to-suit lease obligation for the same amount. As of December 31, 2016, $3.9 million of costs were capitalized in buildings with a corresponding build-to-suit lease obligation recognized related to this lease.

In February 2019, the Company terminated the long term property lease, and will account for the termination in accordance with the new lease standard in the first quarter of 2019.

ITEM 9 – CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A – CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to provide reasonable assurance that information required to be disclosed in our Exchange Act reports is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission's rules and forms and that such information is

accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate, to allow timely decisions regarding required disclosure.

Under the supervision of our principal executive officer and principal financial officer, we evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) of the Exchange Act) as of December 31, 2018. Based on that evaluation, as of December 31, 2018, our principal executive officer and principal financial officer have concluded that our disclosure controls and procedures were effective at the reasonable assurance level.

Inherent Limitations on Controls and Procedures

Our management, including the principal executive officer and principal financial officer, does not expect that our disclosure controls and procedures and our internal control over financial reporting will prevent all error and all fraud. A control system, no matter how well designed and operated, can only provide reasonable assurances that the objectives of the control system are met. The design of a control system reflects resource constraints; the benefits of controls must be considered relative to their costs. Because there are inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, for our company have been or will be detected. As these inherent limitations are known features of the disclosure and financial reporting processes, it is possible to design into the processes safeguards to reduce, though not eliminate, these risks. These inherent limitations include the realities that judgments in decision-making can be faulty and that breakdowns occur because of simple error or mistake. Controls can also be circumvented by the individual acts of some persons, by collusion of two or more people, or by management override of the control. The design of any system of controls is based in part upon certain

assumptions about the likelihood of future events. While our disclosure controls and procedures and our internal control over financial reporting are designed to provide reasonable assurance of achieving their objectives, there can be no assurance that any design will succeed in achieving its stated goals under all future conditions. Over time, controls may become inadequate because of changes in conditions or deterioration in the degree of compliance with the policies or procedures. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining an adequate internal control over financial reporting (as such term is defined in Rules 13a-15(f) and 15d-15(f) of the Exchange Act) for our company. Our management, including our principal executive officer and principal financial officer, conducted an evaluation of the effectiveness of our internal control over financial reporting based on the framework set forth in the "Internal Control—Integrated Framework" issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework). Based on an evaluation under that framework, our management concluded that our internal control over financial reporting was effective at the reasonable assurance level as of December 31, 2018.

The effectiveness of our internal control over financial reporting as of December 31, 2018 has been audited by Ernst & Young LLP, an independent registered public accounting firm, as stated in their report, which is included herein.

In accordance with guidance issued by the Securities and Exchange Commission, companies are permitted to exclude acquisitions from their final assessment of internal control over financial reporting for the first fiscal year in which the acquisition occurred. Our management's evaluation of internal control over financial reporting excluded the internal control activities of TxCell S.A., or TxCell, which we acquired on October 1, 2018, as discussed in Note 6 to our Consolidated Financial Statements, "Acquisition of TxCell, S.A.". We have included the financial results of TxCell in the consolidated financial statements from the date of acquisition. Total operating expenses and net loss subject to TxCell's internal control over financial reporting represented 2% and 5% of our consolidated results for the fiscal year ended December 31, 2018. Total assets subject to TxCell's internal control over financial reporting constituted 3% of our consolidated total assets as of December 31, 2018.

Changes in Internal Control over Financial Reporting

There have been no changes in our internal control over financial reporting identified in connection with the evaluation required by Rules 13a-15(d) and 15d-15(d) of the Exchange Act that occurred during the three months ended December 31, 2018 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Sangamo Therapeutics, Inc.

Opinion on Internal Control over Financial Reporting

We have audited Sangamo Therapeutics, Inc.'s internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control – Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, Sangamo Therapeutics, Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2018, based on the COSO criteria.

As indicated in the accompanying Management's Report on Internal Control over Financial Reporting, management's assessment of and conclusion on the effectiveness of internal control over financial reporting did not include the internal controls of TxCell S.A., which is included in the 2018 consolidated financial statements of the Company and constituted 3% of total assets as of December 31, 2018 and 2% and 5% of operating expenses and net loss, respectively, for the year then ended. Our audit of internal control over financial reporting of the Company also did not include an evaluation of the internal control over financial reporting of TxCell S.A.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the 2018 consolidated financial statements of the Company and our report dated March 1, 2019 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that

our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ ERNST & YOUNG LLP

Redwood City, California

March 1, 2019

ITEM 9B – OTHER INFORMATION

None

PART III

Certain information required by Part III is omitted from this Report on Form 10-K because we intend to file our definitive Proxy Statement for our next Annual Meeting of Stockholders, pursuant to Regulation 14A of the Securities Exchange Act of 1934, as amended, or the 2019 Proxy Statement, no later than April 30, 2019, and certain information to be included in the 2019 Proxy Statement is incorporated herein by reference.

ITEM 10 – DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this item is to be included in our 2019 Proxy Statement as follows:

- The information relating to our directors and nominees for director is to be included in the section entitled "Proposal No. 1: Election of Directors;"
    - The information relating to our executive officers is to be included in the section entitled "Executive Officers;"
- The information relating to our audit committee, audit committee financial expert and procedures by which stockholders may recommend nominees to our Board of Directors is to be included in the section entitled "Corporate Governance and Board Matters;" and
- The information regarding compliance with Section 16(a) of the Exchange Act is to be included in the section entitled "Section 16(a) Beneficial Ownership Reporting Compliance."

Such information is incorporated herein by reference to our 2019 Proxy Statement, provided that if the 2019 Proxy Statement is not filed within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, the omitted information will be included in an amendment to this Annual Report on Form 10-K filed not later than the end of such 120-day period.

ITEM 11 – EXECUTIVE COMPENSATION

The information required by this item is to be included in our 2019 Proxy Statement under the sections entitled "Executive Compensation," "Director Compensation," "Corporate Governance and Board Matters—Compensation Committee Interlocks and Insider Participation" and "Corporate Governance and Board Matters—Compensation Committee Report" and is incorporated herein by reference, provided that if the 2019 Proxy Statement is not filed within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, the omitted information will be included in an amendment to this Annual Report on Form 10-K filed not later than the end of such 120-day period.

ITEM 12 – SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by this item with respect to equity compensation plans is to be included in our 2019 Proxy Statement under the section entitled "Equity Compensation Plan Information" and the information required by this item with respect to security ownership of certain beneficial owners and management is to be included in our 2019 Proxy

Statement under the section entitled “Security Ownership of Certain Beneficial Owners and Management” and in each case is incorporated herein by reference, provided that if the 2019 Proxy Statement is not filed within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, the omitted information will be included in an amendment to this Annual Report on Form 10-K filed not later than the end of such 120-day period.

ITEM 13 – CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this item is to be included in our 2019 Proxy Statement under the sections entitled “Certain Relationships and Related Transactions” and “Corporate Governance and Board Matters—Board Independence” and is incorporated herein by reference, provided that if the 2019 Proxy Statement is not filed within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, the omitted information will be included in an amendment to this Annual Report on Form 10-K filed not later than the end of such 120-day period.

ITEM 14 – PRINCIPAL ACCOUNTING FEES AND SERVICES

The information required by this item is to be included in our 2019 Proxy Statement under the section entitled “Proposal No. 2: Ratification of Independent Registered Public Accounting Firm” and is incorporated herein by reference, provided that if the 2019 Proxy Statement is not filed within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, the omitted information will be included in an amendment to this Annual Report on Form 10-K filed not later than the end of such 120-day period.

PART IV

ITEM 15 – EXHIBITS, FINANCIAL STATEMENT SCHEDULES

(a) The following documents are included as part of this Annual Report on Form 10-K:

1. Financial Statements—See Index to Consolidated Financial Statements in Item 8.

2. Financial Statement Schedules—Not Applicable.

3. Exhibits

Exhibit Number	Description of Document
2.1	Share Purchase Agreement dated July 20, 2018 among the Company and the Selling TxCell Shareholders named on the signature page thereto (incorporated by reference to Exhibit 2.1 to the Company's Current Report on Form 8-K filed July 23, 2018).
2.2	Amendment Agreement to the Share Purchase Agreement dated October 1, 2018 between the Company and TxCell S.A. (incorporated by reference to Exhibit 2.2 to the Company's Current Report on Form 8-K filed November 6, 2018).
2.3	Tender Offer Agreement dated July 20, 2018 between the Company and TxCell S.A. (incorporated by reference to Exhibit 2.2 to the Company's Current Report on Form 8-K filed July 23, 2018).
2.4	Amendment No. 1 to the Tender Offer Agreement dated October 1, 2018 between the Company and TxCell S.A. (incorporated by reference to Exhibit 2.4 to the Company's Current Report on Form 8-K filed November 6, 2018).
3.1	Seventh Amended and Restated Certificate of Incorporation, as amended (incorporated by reference to Exhibit 3.1 to the Company's Quarterly Report on Form 10-Q filed August 9, 2017).
3.2	Third Amended and Restated Bylaws (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed June 15, 2018).
4.1	Form of Specimen Common Stock Certificate (incorporated by reference to Exhibit 4.1 to the Company's Current Report on Form 8-K filed January 6, 2017).
10.1(+)	Amended and Restated 2013 Stock Incentive Plan (the "2013 Plan") (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed May 10, 2018).
10.2(+)	2018 Equity Incentive Plan (the "2018 Plan") (incorporated by reference to Exhibit 99.1 to the Company's Registration Statement on Form S-8 (File No. 333-225552) filed June 11, 2018).
10.3(+)	2018 Equity Incentive Plan French Stock-Options Sub-Plan (the "French Options Sub-Plan").
10.4(+)	2018 Equity Incentive Plan French Restricted Stock Unit Award Sub-Plan (the "French RSU Sub-Plan").
10.5(+)	Form of Restricted Stock Unit Award Agreement under the 2013 Plan (incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K filed June 14, 2013).
10.6(+)	Form of Notice of Grant of Stock Option under the 2013 Plan (incorporated by reference to Exhibit 10.3 to the Company's Current Report on Form 8-K filed June 14, 2013).
10.7(+)	Form of Stock Option Agreement under the 2013 Plan (incorporated by reference to Exhibit 10.4 to the Company's Current Report on Form 8-K filed June 14, 2013).

10.8(+) Form of Notice of Grant of Stock Option – Director Initial Grant under the 2013 Plan (incorporated by reference to Exhibit 10.5 to the Company's Current Report on Form 8-K filed June 14, 2013).

10.9(+) Form of Notice of Grant of Stock Option – Director Annual Grant under the 2013 Plan (incorporated by reference to Exhibit 10.6 to the Company's Current Report on Form 8-K filed June 14, 2013).

10.10(+) Form of Automatic Stock Option Agreement under the 2013 Plan (incorporated by reference to Exhibit 10.7 to the Company's Current Report on Form 8-K filed June 14, 2013).

10.11(+) Form of Stock Option Grant Notice and Form of Option Agreement (U.S. employees) under the 2018 Plan (incorporated by reference to Exhibit 99.2 to the Company's Current Report on Form 8-K filed June 15, 2018).

Exhibit Number	Description of Document
10.12(+)	Form of Stock Option Grant Notice and Form of Option Agreement (non-employee directors) under the 2018 Plan (incorporated by reference to Exhibit 99.3 to the Company's Current Report on Form 8-K filed June 15, 2018).
10.13(+)	Form of Stock Option Grant Notice and Form of Option Agreement (U.K. employees) under the 2018 Plan (incorporated by reference to Exhibit 99.4 to the Company's Current Report on Form 8-K filed June 15, 2018).
10.14(+)	Form of Stock Option Grant Notice (French employees) under the 2018 Plan and the French Options Sub-Plan.
10.15(+)	Form of Stock Option Agreement (French Employees) under the 2018 Plan and the French Options Sub-Plan.
10.16(+)	Form of Restricted Stock Unit Grant Notice and Form of Restricted Stock Unit Award Agreement (U.S. employees) under the 2018 Plan (incorporated by reference to Exhibit 99.5 to the Company's Current Report on Form 8-K filed June 15, 2018).
10.17(+)	Form of Restricted Stock Unit Grant Notice and Form of Restricted Stock Unit Award Agreement (non-employee directors) under the 2018 Plan (incorporated by reference to Exhibit 99.6 to the Company's Current Report on Form 8-K filed June 15, 2018).
10.18(+)	Form of Restricted Stock Unit Grant Notice and Form of Restricted Stock Unit Award Agreement (U.K. employees) under the 2018 Plan (incorporated by reference to Exhibit 99.7 to the Company's Current Report on Form 8-K filed June 15, 2018).
10.19(+)	Form of Restricted Stock Unit Grant Notice and Form of Restricted Stock Unit Award Agreement (French employees) under the 2018 Plan and the French RSU Sub-Plan.
10.20(+)	Amended and Restated Severance Plan.
10.21(+)	Amended and Restated Incentive Compensation Plan (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed May 10, 2018).
10.22(+)	Form of Indemnification Agreement (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed August 6, 2015).
10.23(+)	Employment Agreement between the Company and Alexander (Sandy) Macrae, dated May 17, 2016 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed August 4, 2016).
10.24(+)	Employment Agreement between the Company and Kathy Yi, dated February 28, 2017 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed May 10, 2017).
10.25(+)	Employment Agreement between the Company and Edward Conner, dated November 1, 2016 (incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q filed May 10, 2017).
10.26(+)	Employment Agreement between the Company and Heather D. Turner, effective February 12, 2018.
10.27(+)	Employment Agreement between the Company and Stéphane Boissel, effective October 1, 2018.
10.28(+)	Employment Agreement between the Company and Adrian Woolfson, effective January 21 2019.
10.29	Triple Net Laboratory Lease between the Company and Point Richmond R&D Associates II, LLC, dated May 23, 1997 (incorporated by reference to Exhibit 10.5 to the Company's Registration Statement on Form S-1 (Reg. No. 333-30314), as amended, filed February 24, 2000).
10.30	First Amendment to Triple Net Laboratory Lease between the Company and Point Richmond R&D Associates II, LLC, dated March 12, 2004 (incorporated by reference to Exhibit 10.20 to the Company's Annual Report on Form 10-K filed February 23, 2005).
10.31	Second Amendment to Triple Net Laboratory Lease between the Company and Point Richmond R&D Associates II, LLC, dated March 15, 2007 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed November 4, 2013).
10.32	Third Amendment to Triple Net Laboratory Lease between the Company and Point Richmond R&D Associates II, LLC, dated August 1, 2013 (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed November 4, 2013).
10.33	

	Fourth Amendment to Triple Net Laboratory Lease between the Company and Point Richmond R&D Associates II, LLC, dated June 10, 2016.
115	

Exhibit Number	Description of Document
10.34	Fifth Amendment to Triple Net Laboratory Lease between the Company and Point Richmond R&D Associates II, LLC, dated July 10, 2017.
10.35	Sixth Amendment to Triple Net Laboratory Lease between the Company and Point Richmond R&D Associates II, LLC, dated May 11, 2018 (incorporated by reference to Exhibit 10.9 to the Company's Quarterly Report on Form 10-Q filed August 8, 2018).
10.36	Lease Agreement between the Company and Marina Boulevard Property, LLC dated November 3, 2017 (incorporated by reference to Exhibit 10.21 to the Company's Annual Report on Form 10-K filed March 1, 2018).
10.37	First Amendment to Lease Agreement between the Company and Marina Boulevard Property, LLC dated January 1, 2019.
10.38	Amended and Restated Sales Agreement between the Company and Cowen LLC, dated May 26, 2017 (incorporated by reference to Exhibit 1.1 to the Company's Current Report on Form 8-K filed May 26, 2017).
10.39†	Amended and Restated Collaboration and License Agreement between the Company and Shire International GmbH, dated September 1, 2015 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed October 30, 2015).
10.40†	Global Research, Development and Commercialization Collaboration and License Agreement between the Company and Biogen MA Inc. (Bioverativ Inc.), dated January 8, 2014 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed May 7, 2014).
10.41†	Letter Amendment to Global Research, Development and Commercialization Collaboration and License Agreement between the Company and Biogen MA Inc. (Bioverativ Inc.), dated December 14, 2015 (incorporated by reference to Exhibit 10.63 to the Company's Annual Report on Form 10-K filed February 18, 2016).
10.42†	Letter Agreement and Waiver between the Company and Biogen MA Inc. (Bioverativ Inc.), dated March 24, 2016 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed May 5, 2016).
10.43†	Collaboration and License Agreement between the Company and Pfizer Inc., dated May 10, 2017 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed August 9, 2017).
10.44†	Research Collaboration and License Agreement between the Company and Pfizer Inc., dated December 28, 2017 (incorporated by reference to Exhibit 10.40 to the Company's Annual Report on Form 10-K filed March 1, 2018).
10.45†	Collaboration and License Agreement between the Company and Kite Pharma, Inc., dated February 20, 2018 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed May 5, 2018).
21.1	Subsidiaries of the Company
23.1	Consent of Independent Registered Public Accounting Firm.
24.1	Power of Attorney (included on signature page).
31.1	Rule 13a-14(a) Certification of Principal Executive Officer.
31.2	Rule 13a-14(a) Certification of Principal Financial Officer.
32.1*	Certification Pursuant to 18 U.S.C. Section 1350.
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

† Confidential treatment has been granted for certain information contained in this document pursuant to an order of the Securities and Exchange Commission. Such information has been omitted and filed separately with the Securities and Exchange Commission.

(+) Indicates management contract or compensatory plan or arrangement.

* The certifications attached as Exhibit 32.1 accompany this Annual Report on Form 10-K pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, and shall not be deemed "filed" by the Company for purposes of Section 18 of the Securities Exchange Act of 1934, as amended.

ITEM 16 – FORM 10-K SUMMARY

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, on March 1, 2019.

Date: March 1, 2019

SANGAMO THERAPEUTICS, INC.

By: / S / ALEXANDER MACRAE
Alexander Macrae
President, and Chief Executive Officer

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Alexander Macrae, Kathy Y. Yi, and Heather Turner, and each of them, as his or her true and lawful attorneys-in-fact and agents, each with the full power of substitution, for him or her and in his or her name, place or stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this Annual Report on Form 10-K, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or their, his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated:

Signature	Title	Date
/ S / ALEXANDER MACRAE Alexander Macrae	President, Chief Executive Officer (Principal Executive Officer) and Director	March 1, 2019
/ S / Kathy Y. Yi Kathy Y. Yi	Executive Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)	March 1, 2019
/ S / H. STEWART PARKER H. Stewart Parker	Director and Chairman of the Board	March 1, 2019
/ S / Robert F. Carey Robert F Carey	Director	March 1, 2019
	Director	

/ S / STEPHEN G. DILLY, M.B.B.S, PH.D Stephen G. Dilly, M.B.B.S, Ph.D		March 1, 2019
/s/ Roger Jeffs, PH.D Roger Jeffs, Ph.D	Director	March 1, 2019
/s/ STEVEN J. MENTO, PH.D Steven J. Mento, Ph.D	Director	March 1, 2019
/ S / SAIRA RAMASASTRY Saira Ramasastry	Director	March 1, 2019
/ S / Joseph S. Zakrzewski Joseph S. Zakrzewski	Director	March 1, 2019
/ S / Karen Smith, M.D, PH.D, M.B.A., L.L.M. Karen Smith, M.D., Ph.D, M.B.A., L.L.M.	Director	March 1, 2019