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, 2022

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.)**
7000 Marina Blvd.	
Brisbane, California	**94005**
(Address of principal executive offices)	**(Zip Code)**

(510) 970-6000
(Registrant's telephone number, including area code)

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.01 per share	**SGMO**	**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 whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an 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 has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

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

The aggregate market value of the common stock held by non-affiliates of the registrant based upon the closing sale price of the common stock on June 30, 2022 (the last business day of the registrant's most recently completed second fiscal quarter), as reported on the Nasdaq Global Select Market was $632,920,753. 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 17, 2023, a total of 168,483,317 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 2023 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.

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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 Securities Exchange Act of 1934, as amended, or the Exchange Act. These statements relate to our future events, including our anticipated operations, research, development, manufacturing and commercialization activities, clinical trials, operating results and financial condition. These forward-looking statements 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 research and development of product candidates and potential commercialization of any resulting approved products;
- the initiation, scope, rate of progress, enrollment, dosing, 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 our product candidates, including the durability of therapeutic effects;
- the therapeutic and commercial potential of technologies used by us in our product candidates, including our gene therapy and cell therapy technologies, zinc finger, or ZF, technology platform, zinc finger nucleases, or ZF nucleases, and zinc finger transcriptional regulators, or ZF-TRs, which include zinc finger repressors, or ZF-Rs, and zinc finger activators, or ZF-As;
- our ability to establish and maintain collaborations and strategic partnerships and realize the expected benefits of such arrangements, including our ability to find a potential new collaboration partner for the BIVV003 program;
- anticipated revenues from existing and new collaborations and the timing thereof;
- our estimates regarding the impact of the COVID-19 pandemic on our business and operations and the business and operations of our collaborators, including clinical trials and manufacturing, and our ability to manage such impacts;
- 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 or from our own in-house manufacturing facilities;
- the ability of Sangamo and our collaborators and strategic partners to obtain and maintain regulatory approvals for product candidates and the timing and costs associated with obtaining regulatory approvals;
- our ability to comply with, and the impact of, regulatory requirements, obligations and restrictions on our business and operations;
- 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 and maintain rights to the technologies required to develop and commercialize our product candidates;
- competitive developments, including the impact on our competitive position of rival products and product candidates and our ability to meet such competition;
- 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;
- conditions and events that raise doubt about our ability to continue as a going concern;
- 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 use of future dates or by terms such as: "anticipates," "believes," "continues," "could," "estimates," "expects," "intends," "may," "plans," "seeks," "should," "will" and similar expressions intended to identify forward-looking statements. These statements reflect our current views with respect to future events, are based on assumptions and are subject to risks and uncertainties. Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. We discuss many of these risks in greater detail under the headings "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" in this Annual Report on Form 10-K. Except as required by law, we undertake no obligation to update or revise any forward-looking statements to reflect new information or future events or developments. Readers are cautioned not to place undue reliance on the forward-looking statements, which speak only as of the date of this Annual Report on Form 10-K.

SUMMARY OF RISK FACTORS

Our business involves significant risks. Below is a summary of the material risks that our business faces, which makes an investment in our common stock speculative and risky. This summary does not address all these risks. These risks are more fully described below under the heading "Risk Factors" in Part I, Item 1A of this Annual Report on Form 10-K. Before making investment decisions regarding our common stock, you should carefully consider these risks. The occurrence of any of the events or developments described below could have a material adverse effect on our business, results of operations, financial condition, prospects and stock price. In such event, the market price of our common stock could decline, and you could lose all or part of your investment. There are also additional risks not described below that are either not presently known to us or that we currently deem immaterial, and these additional risks could also materially impair our business, operations or market price of our common stock.

- We are a clinical-stage biotechnology company with no approved products or product revenues. Our success depends substantially on clinical trial results demonstrating safety and efficacy of our product candidates to the satisfaction of regulatory authorities. Obtaining positive clinical trial results and regulatory approvals is expensive, lengthy, challenging and unpredictable and may never occur for any product candidates.
- Success in research and preclinical studies or early clinical trial results may not be indicative of results obtained in later trials. Likewise, preliminary, initial or interim data from clinical trials may be materially different from final data.
- Many of our product candidates are based on novel ZF technologies that have yet to yield any approved commercially viable therapeutic products.
- We have incurred significant operating losses since inception and anticipate continued losses for the foreseeable future. We may never become profitable.
- We will need substantial additional funding to execute our operating plan and continue to operate as a going concern. We may be unable to raise additional capital on favorable terms, if at all, which would harm or preclude our ability to develop our technology and product candidates and could delay or terminate some or all of our programs. Future sales and issuances of equity securities could also result in substantial dilution to our stockholders.
- We rely heavily on collaborations with larger biopharmaceutical companies to generate revenues and develop, obtain regulatory approvals for and commercialize many of our product candidates. If conflicts arise with our collaborators or if the collaborations terminate for any reason, our revenues and product development efforts would be negatively impacted.
- Biotechnology and genomic medicine are highly competitive businesses. Our competitors may develop rival technologies and products that are superior to or are commercialized more quickly than our technologies and product candidates.
- Manufacturing genomic medicines is complex, expensive, highly regulated and risky. We currently rely heavily on third-party manufacturers and have limited experience manufacturing products ourselves. Manufacturing challenges may result in unexpected costs, supply interruptions and harm and delay to our product development efforts.
- Even if we obtain regulatory approvals for our product candidates, our approved products may not gain market acceptance among physicians and patients and adequate coverage and reimbursement from third-party payors and may not demonstrate commercial viability.
- We may not be able to obtain, maintain and enforce necessary and desirable intellectual property protections for our technologies and product candidates in all desired jurisdictions, which could adversely affect the value of our technologies and our product development efforts and could increase the risks of costly, lengthy and distracting litigation with unpredictable results.
- Third parties, who may or may not be competitors, may allege that we are infringing, misappropriating, or otherwise practicing in an unauthorized manner their patents or other proprietary rights. Such allegations may result in infringement actions, other misappropriation actions or threats of such actions, all of which could increase the risks of costly, lengthy and distracting litigation with unpredictable results.
- Our success depends on hiring, integrating and retaining additional highly qualified skilled employees and retaining current key executives and employees, which may be challenging given that the competition for these individuals is intense.

- The COVID-19 pandemic could continue to adversely impact our business and operations and the business and operations of our collaborators, manufacturers and other business partners. If such impacts become material, our revenues and product development efforts could be negatively impacted.
- The market price of our common stock has been and will likely continue to be volatile, and you could lose all or part of any investment in our common stock.

PART I

ITEM 1 – BUSINESS

OVERVIEW

We are a clinical-stage genomic medicine company committed to translating ground-breaking science into medicines that transform the lives of patients and families afflicted with serious diseases. We plan to deliver on this mission through development of our clinical and preclinical product candidates, leveraging our novel science and our in-house manufacturing capabilities.

Our Product Candidates

Today, we are in the clinic with our first wave gene therapy and autologous cell therapy candidates. Our second wave long-term development strategy is to focus on leveraging our optimized zinc finger, or ZF, technology, a differentiated tool that we are using to develop genomic medicines, including autologous and allogeneic cell therapies and *in vivo* genome engineering therapies.

Our current clinical-stage product candidates are:

- Isaralgagene civaparvovec, also known as ST-920, our wholly-owned gene therapy product candidate for the treatment of Fabry disease, is currently being evaluated in our Phase 1/2 STAAR clinical study, and we are progressing plans for a potential Phase 3 clinical trial;
- TX200, our wholly-owned Chimeric Antigen Receptor, or CAR, engineered regulatory T cell, or CAR-Treg, cell therapy product candidate for the prevention of immune-mediated rejection in HLA-A2 mismatched kidney transplantation, is currently being evaluated in our Phase 1/2 STEADFAST clinical study;
- Giroctocogene fitelparvovec, also known as SB-525, a gene therapy product candidate for the treatment of moderately severe to severe hemophilia A, is currently being evaluated in the registrational Phase 3 AFFINE clinical trial. We are developing giroctocogene fitelparvovec with our collaborator Pfizer Inc., or Pfizer; and
- BIVV003, our zinc finger nuclease, or ZF nuclease, gene-edited cell therapy product candidate for the treatment of sickle cell disease, or SCD, is currently being evaluated in our Phase 1/2 PRECIZN-1 clinical study. BIVV003 is a wholly-owned Sangamo program following the transition from Sanofi S.A., or Sanofi, to Sangamo in June 2022. As discussed below, we recently made the strategic decision to halt further material investments in the BIVV003 program beyond completion of the Phase 1/2 PRECIZN-1 study in order to prioritize deployment of resources to our Fabry and TX200 programs.

Our preclinical development is focused in two innovative priority areas: (i) CAR-Treg cell therapies for autoimmune disorders and (ii) genome engineering for neurological diseases. Indications for our preclinical programs include neurodevelopmental disorders, cancer, inflammatory bowel disease, or IBD, tauopathies and neurodegenerative diseases such as amyotrophic lateral sclerosis, or ALS, multiple sclerosis, or MS, and Huntington's disease, some of which we are developing with our collaborators Biogen MA, Inc. and Biogen International GmbH, which we refer to together as Biogen, Novartis Institutes for BioMedical Research, Inc., or Novartis, Pfizer, Takeda Pharmaceutical Company Limited, or Takeda, and Kite Pharma, Inc.

Our multiple collaborations with biopharmaceutical companies bring us important financial and strategic benefits and reinforce the potential of our research and development efforts and our ZF technology platform. They leverage our collaborators' therapeutic and clinical expertise and commercial resources with the goal to bring our medicines more rapidly to patients. We believe these collaborations reflect the value of our ZF technology platform and will potentially expand the addressable markets of our product candidates. To date, we have received approximately $815.0 million in upfront licensing fees, milestone payments and proceeds from sale of our common stock to collaborators and have the opportunity to earn up to $6.7 billion in potential future milestone payments from our collaborations, in addition to potential product royalties.

Our Novel Science

We are a leader in the research and development of zinc finger proteins, or ZFPs, which are abundantly occurring human proteins that have evolved to regulate the genome through interactions with DNA and regulatory proteins. We have developed and optimized a proprietary synthetic ZF technology platform with potential clinical utility in (i) genome editing and epigenetic regulation, which we refer to together as genome engineering, and (ii) gene-edited cell therapy, which we refer to as cell therapy.

Our strategy is to translate our differentiated and versatile ZF technology platform to product candidates with best- or first-in-class clinical potential. For example, ZFPs can be engineered to make ZF nucleases, which are proteins that can be used

to edit genomes by specifically modifying DNA sequences by knocking in or knocking out select genes. ZFPs can also be engineered to make zinc finger transcriptional regulators, or ZF-TRs, which are proteins that can be used to regulate genomes by selectively increasing or decreasing gene expression.

In the process of developing these genome engineering technologies, we have additionally accrued significant scientific, manufacturing and development capabilities, as well as related know-how, that are broadly applicable to the field of gene therapy, which we have used to develop our gene therapy product candidates.

Finally, we have also leveraged our ZF technology platform and technologies obtained through acquisitions to become a leader in researching and developing CAR-Treg product candidates for the treatment of autoimmune and inflammatory diseases in broad patient populations, including kidney transplant rejection, MS and IBD. CAR-Tregs are considered to have enhanced suppressive function over polyclonal Tregs due to the antigen-specificity introduced by the CAR.

Our In-house Manufacturing

We believe that our in-house manufacturing capacity provides us a competitive advantage. We currently operate an adeno-associated virus, or AAV, manufacturing facility in our Brisbane, California headquarters and cell therapy manufacturing facilities in Brisbane, California and Valbonne, France. Our manufacturing strategy is to provide greater flexibility, quality and control by building a balanced and necessary capacity achieved through our in-house manufacturing and contract manufacturing organization, or CMO, partnerships, investing in manufacturing processes and analytics and developing a strong supply chain. Our CMOs enable this flexibility by providing us with access to AAV manufacturing capacity up to a 2000 liter bioreactor scale.

Business Updates

Isaralgagene civaparvovec - Fabry Disease

On February 22, 2023, we announced updated preliminary clinical data from our Phase 1/2 STAAR study evaluating isaralgagene civaparvovec, or ST-920, a wholly owned gene therapy product candidate for the treatment of Fabry disease, in advance of our presentation at the 19th Annual WORLD*Symposium* on February 24, 2023. A summary of the data is below. This announcement included data on the 13 patients treated with isaralgagene civaparvovec as of the cutoff date of October 20, 2022, including kidney biopsy data on two patients. Since the cutoff date, an additional four patients have been dosed in the Phase 1/2 STAAR study, resulting in a total of 17 patients dosed to date. A total of 20 sites are now active and recruiting. Progress in the study continues with additional male and female patients currently in screening.

The Phase 1/2 STAAR study expansion phase is ongoing and preparations for a potential Phase 3 clinical trial actively progress. A Phase 3 trial start is anticipated by the end of 2023, depending on regulatory interactions, and dosing of the first patient may occur as early as the first part of 2024. The completion of dosing in the Phase 1/2 expansion phase is expected by the end of 2023 and is not expected to be a gating factor for the commencement of the Phase 3 trial.

In December 2022, one patient in the study expansion phase experienced a Grade 3 serious adverse event, or SAE, of shoulder enthesopathy requiring hospitalization that occurred 14 days following infusion. The event has since fully resolved, and the patient remains enrolled in the study. The Principal Investigator and the Safety Monitoring Committee for the study assessed the SAE as possibly related to treatment, and the SAE was reported to regulatory authorities. The Safety Monitoring Committee has since determined that the study may proceed without modification, and this event was reported to other investigators for awareness.

Summary of Updated Preliminary Clinical Data from Phase 1/2 STAAR Study of Isaralgagene Civaparvovec Announced on February 22, 2023 in Advance of Presentation at 19th Annual World*Symposium* on February 24, 2023

- The STAAR study is an ongoing Phase 1/2 multicenter, open-label, dose-ranging clinical study designed to assess the safety and tolerability of a single infusion of isaralgagene civaparvovec in Fabry disease patients ≥ 18 years of age. Patients are infused intravenously with a single dose and followed for 52 weeks. A separate long-term follow-up study is underway to monitor the patients treated in this study for up to five years following treatment. The study design provides for at least two patients to be dosed in each dose cohort, with a potential expansion in each cohort. Patients who are on stable enzyme replacement therapy, or ERT, may withdraw ERT after treatment in a controlled and monitored fashion at the discretion of the patient and the investigator.
- The dose escalation phase includes males with classic Fabry disease. The subsequent study expansion phase, which commenced in the second half of 2022, will also treat females, as well as patients with more severe Fabry-associated cardiac or renal disease. The study's primary endpoint is the incidence of treatment-emergent adverse events, or AEs. Additional safety evaluations include routine hematology, chemistry, and liver tests; vital sign monitoring; electrocardiogram; echocardiogram; serial alpha-fetoprotein testing and magnetic resonance imaging, or MRI, of the liver

to monitor for potential formation of any liver mass. Secondary endpoints include change from baseline at specific time points over the one-year study period in alpha-galactosidase A, or α-Gal A, activity, globotriaosylceramide, or Gb3, and lyso-Gb3 levels in plasma; frequency of ERT infusion; and changes in renal function and cardiac function (left ventricular mass) measured by cardiac MRI and rAAV2/6 vector clearance. Key exploratory endpoints include quality of life, Fabry symptoms and neuropathic pain scores; and immune response to AAV6 capsid and α-Gal A.

- As of the October 20, 2022 cutoff date, 13 patients, ranging in age from 22 to 67 years, were treated with isaralgagene civaparvovec, nine in the dose escalation phase and four in the expansion phase of the study. Baseline characteristics of these 13 patients are shown in Table 1 below. In the dose escalation phase, two patients were dosed in Cohort 1 at the dose of $0.5x10^{13}$ vg/kg, two patients were dosed in Cohort 2 at the dose of $1x10^{13}$ vg/kg, three patients were dosed in Cohort 3 at the dose of $3x10^{13}$ vg/kg, and two patients were dosed in Cohort 4 at the dose of $5x10^{13}$ vg/kg. In the expansion phase, four patients were dosed at the dose of $5x10^{13}$ vg/kg, including one female patient in the cardiac cohort and three male patients in the α-Gal A Ab positive cohort. As of the October 20, 2022 cutoff date, the first treated patient had been followed for at least 26 months post dosing, and the most recently treated patient had been followed for two weeks post dosing.
- As of the October 20, 2022 cutoff date, isaralgagene civaparvovec continued to be generally well tolerated across all the dose cohorts in the 13 treated patients, and no prophylactic corticosteroids or other immune modulating agents had been administered. A summary of the treatment-related AEs reported as of the October 20, 2022 cutoff date is shown in Table 2 below. One patient in Cohort 1, two patients in Cohort 2, one patient in Cohort 3, two patients in Cohort 4 and four patients in the expansion phase exhibited treatment-related AEs for a total of 30 events, which were all graded as mild (Grade 1) or moderate (Grade 2). No treatment-related SAEs were reported. No gene therapy-related AEs were observed, including: no administration of corticosteroids for transaminase elevations, no clinically significant decreases in platelets and no cardiac events. One expansion phase patient experienced a Grade 1 allergic reaction that was treated with diphenhydramine.
- Results of plasma α-Gal A activity, as of the supplemental cutoff date of November 15, 2022 for α-Gal A activity, for the nine treated patients in the dose escalation phases and the four treated patients in the expansion phase are shown in Tables 3 and 4, and described in further detail, below. Sustained, elevated expression of α-Gal A activity was observed in thirteen patients for over two years for the longest treated patient as of the November 15, 2022 supplemental cutoff date.
- As of the November 15, 2022 supplemental cutoff date, the nine patients treated in the dose escalation phase sustained elevated α-Gal A activity ranging from 3.7-fold to 67.6-fold of mean normal as at the last date of measurement. For these patients, a rapid increase in α-Gal A activity was observed four to eight weeks after ST-920 dosing. ERT withdrawal was completed for all five patients who began the study on ERT, with continued supraphysiological levels of α-Gal A activity demonstrated following ERT withdrawal. None of these patients have required the resumption of ERT as of February 22, 2023. For naïve and pseudo-naïve patients in the dose escalation phase, Cohort 4 patients exhibited significantly higher levels of α-Gal A activity compared to those patients in lower dose cohorts. Elevated levels of α-Gal A activity were sustained in all of these patients as of the supplemental cutoff date.
- As of the November 15, 2022 supplemental cutoff date, the first three patients dosed in the expansion phase at the $5x10^{13}$ vg/kg dose exhibited a rapid increase in α-Gal A activity following dosing, sustained for up to 14 weeks as at the last date of measurement. The fourth patient had increased to within normal range at four weeks of dosing. The first female patient dosed in the study demonstrated a similar response profile to males as of the supplemental cutoff date.
- Results of globotriaosylsphingosine (lyso-Gb3) levels as of the October 20, 2022 cutoff date for the 13 treated patients are shown in Tables 5 and 6 below. Naïve and pseudo-naïve patients treated in the dose expansion and escalation phases with baseline lyso-Gb3 levels above 80 ng/mL experienced 40-65% reduction in levels. Naïve and pseudo-naïve patients with lower baseline lyso-Gb3 levels under 25 ng/mL who were treated with the $5x10^{13}$ vg/kg dose experienced reductions in lyso-Gb3 levels of 54%. Lyso-Gb3 continued to decrease in two patients as of the October 20, 2022 cutoff date. For those naïve and pseudo-naive patients in the lower dose levels ($0.5x10^{13}$ vg/kg and $1x10^{13}$ vg/kg), lyso-Gb3 levels were stable for up to 25 months. For patients in the dose escalation phase who started the study on ERT, lyso-Gb3 levels following ERT withdrawal remained within the range of levels and variability normally observed in patients treated with ERT. In these participants, α-Gal A activity remained elevated, and no patient had experienced symptoms requiring the resumption of ERT as of the cutoff date. For the patient in the expansion phase who started the study on ERT, withdrawal of ERT had not yet been completed as of the October 20, 2022 cutoff date.
- Results of kidney biopsy and podocytes in urine as of the October 20, 2022 for patients 8 and 9 are shown in Tables 7 and 8 below. Globotriaosylceramide (Gb3) is a fatty substrate that accumulates in the cells of Fabry disease patients and can result in damage to multiple organs, including the kidneys, heart and central nervous system. As of the October 20, 2022 cutoff date, the kidney biopsy for patient 9 – who exhibited a high number of Gb3 inclusions and high plasma lyso-Gb3 levels at baseline – demonstrated a 78% clearance in Gb3 inclusions per peritubular capillary, or PTC, from an average of 8.7 inclusions per PTC at baseline to 1.9 inclusions per PTC at week 24. This assessment was made by two blinded pathologists who independently scored digital images of the sectioned kidney from baseline and six-month biopsies,

adjudicated by a third independent pathologist. In addition, this patient exhibited a 77% reduction in urinary podocyte loss after six months. The kidney biopsy for patient 8 – who exhibited a lower number of Gb3 inclusions and lower levels of plasma lyso-Gb3 upon baseline – demonstrated stable PTC inclusions six-months post dosing, with an average of 3.5 inclusions per PTC at baseline and 3.7 inclusions per PTC at week 24. This patient also exhibited a 97% reduction in urinary podocyte loss after six months.

- A clinically meaningful and statistically significant increase was reported in mean general health scores measured across all patients treated in the dose escalation phase, as measured by the SF-36 general health survey, or the SF-36. The SF-36 is a well-validated and widely used generic questionnaire to comprehensively evaluate health related quality of life. The 36 items assess eight health-related domains (comprising physical function, physical role, bodily pain, general health, vitality, social function, emotional role, and mental health) that are summarized by the physical component score and the mental component score. Studies of cross-sectional differences between clinically defined patient groups have suggested a 3-to-5-point change on any SF-36 scale as a minimally clinically important difference, or MCID. As of the October 20, 2022 cutoff date, patients in the dose escalation phase demonstrated stable or improved general health scores, as measured by the SF-36. The average improvement from baseline for this domain score demonstrated a statistically significant [mean=19.6, 95% CL: [7.8, 31.4], p=0.0100 (paired t-test)] MCID change at week 52.

Table 1: Baseline Patient Characteristics

					FOS-MSSI							
			Age (years)	ERT	Total Max 65.5		General Max 14.5	Neuro Max 15	Cardiac Max 18	Renal Max 18	*GLA* Mutation	Length of Follow-up
Dose Escalation	Cohort 1 0.5×10^{13} vg/kg	1	48	Agalsidase beta	Moderate	30.5	6.5	7	13	4	G261D	26 M
		2	25	Pseudo-naïve	Mild	12	4	8	0	0	T141I	25 M
	Cohort 2 1×10^{13} vg/kg	3	42	Pseudo-naïve	Moderate	20.5	8.5	9	3	0	W340R	21 M
		4	22	Agalsidase beta	Mild	10	4	6	0	0	S297Y	17 M
	Cohort 3 3×10^{13} vg/kg	5	39	Agalsidase beta	Moderate	23	5	8	6	4	Q283X	12 M
		6	42	Agalsidase beta	Mild	18.5	8.5	2	8	0	N215S	9 M
		7	51	Agalsidase beta	Severe	40.5	11.5	12	13	4	c.801+ 3A>G	6 M
	Cohort 4 5×10^{13} vg/kg	8	49	Naïve	Moderate	20	2	1	9	8	P362L	6 M
		9	40	Naïve	Mild	18.5	3.5	6	9	0	T141I	6 M
Expansion	Cardiac	12	67 Female	Agalsidase beta	Mild	17.5	5.5	3	9	0	D266N	4 W
	α-Gal A Ab+ Males	10	34	Pseudo-naïve	Moderate	32.5	7.5	7	14	4	N34S	10 W
		11	49	Agalsidase beta	Moderate	28	1.2	9	3	4	Y134S	9W
		13	38	Agalsidase beta	Mild	17.5	6.5	5	6	0	A348GfsX27 insertion	2 W

Data cut: October 20, 2022

FOS-MSSI Total Score Classification: Mild ≤18; Moderate (Mod) = 19-38; Severe >38

FOS-MSSI, Fabry Outcome Survey Mainz Severity Score Index, kg, kilogram; M, months; Max, Maximum; vg, viral genomes, W, weeks

Table 2: Treatment-Related Adverse Events

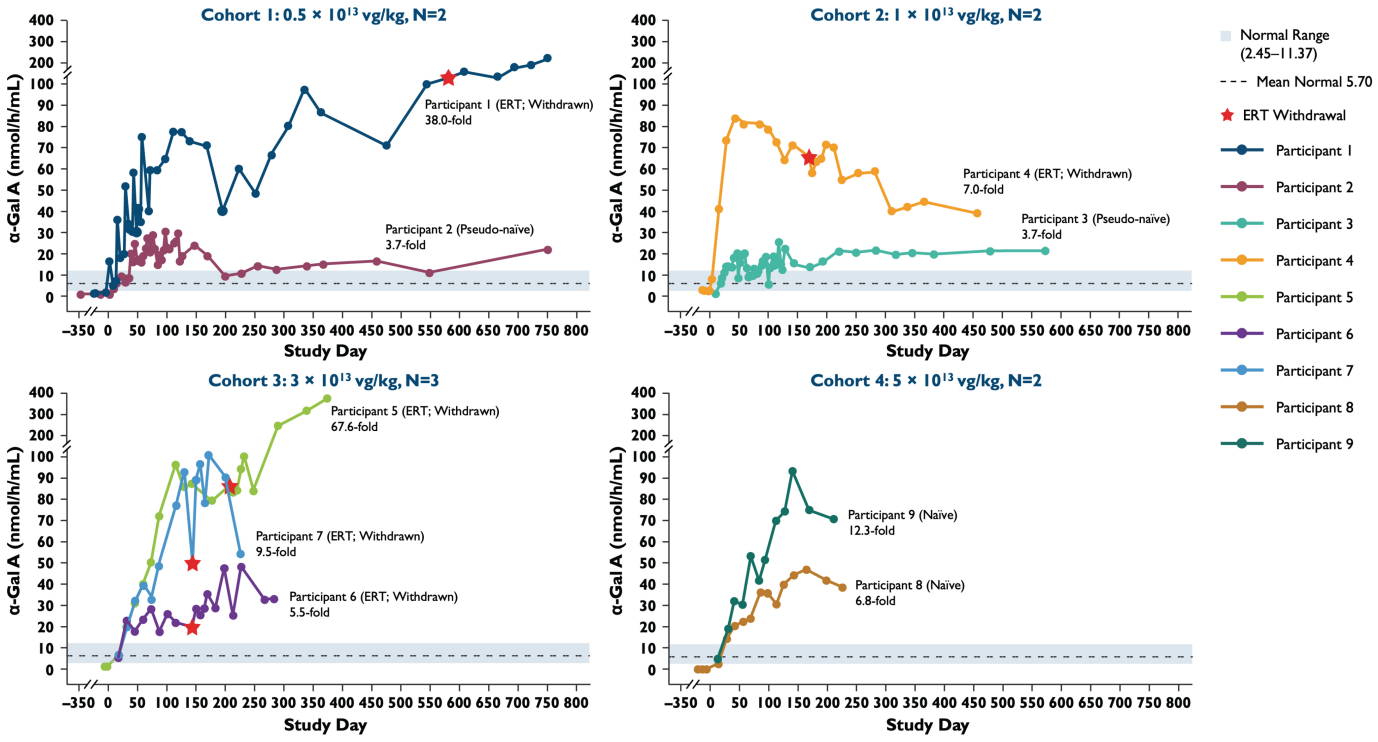
	Dose Escalation Cohorts								Expansion Groups 5×10^{13} vg/kg N = 4		Total N = 13	
	Cohort 1 0.5×10^{13} vg/kg N = 2		Cohort 2 1×10^{13} vg/kg N = 2		Cohort 3 3×10^{13} vg/kg N = 3		Cohort 4 5×10^{13} vg/kg N = 2					
	N	Events	N	Events	N	Events	N	Events	N	Events	N (%)	Events
Adverse Events	2	30	2	20	3	29	2	10	4	18	13 (100%)	107
Treatment Related Adverse Events	1	3	2	3	1	6	2	6	4	12	10 (77%)	30
Serious Adverse Events (Unrelated)	0	0	0	0	1	1	0	0	0	0	1 (7.7%)	1

Data cut: October 20, 2022

Length of follow-up ranged from 2 weeks to 26 months

vg/kg, vector genomes per kilogram of total body weight

Table 3: Expression of α-Gal A Activity in Dose Escalation Cohorts

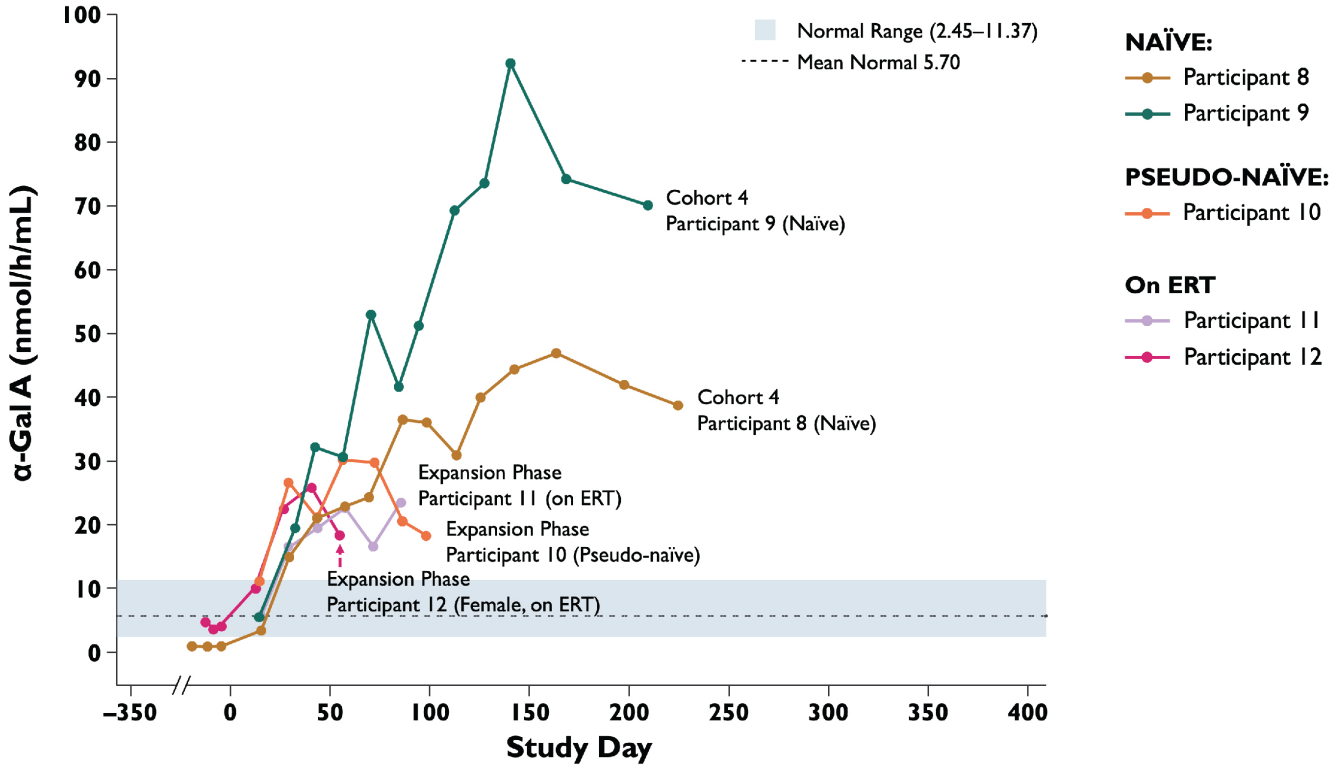


Data cut: November 15, 2022

Plasma α-Gal A activity measured using 3-hour reaction time. Normal range determined in healthy males. Fold change from normal mean was calculated at last measured time point.

Long Term Follow-up Data: Data points > Study Day 365. α-Gal A, alpha galactosidase A; ERT, enzyme replacement therapy

Table 4: Cohort 4 and Expansion Phase α -Gal A Activity

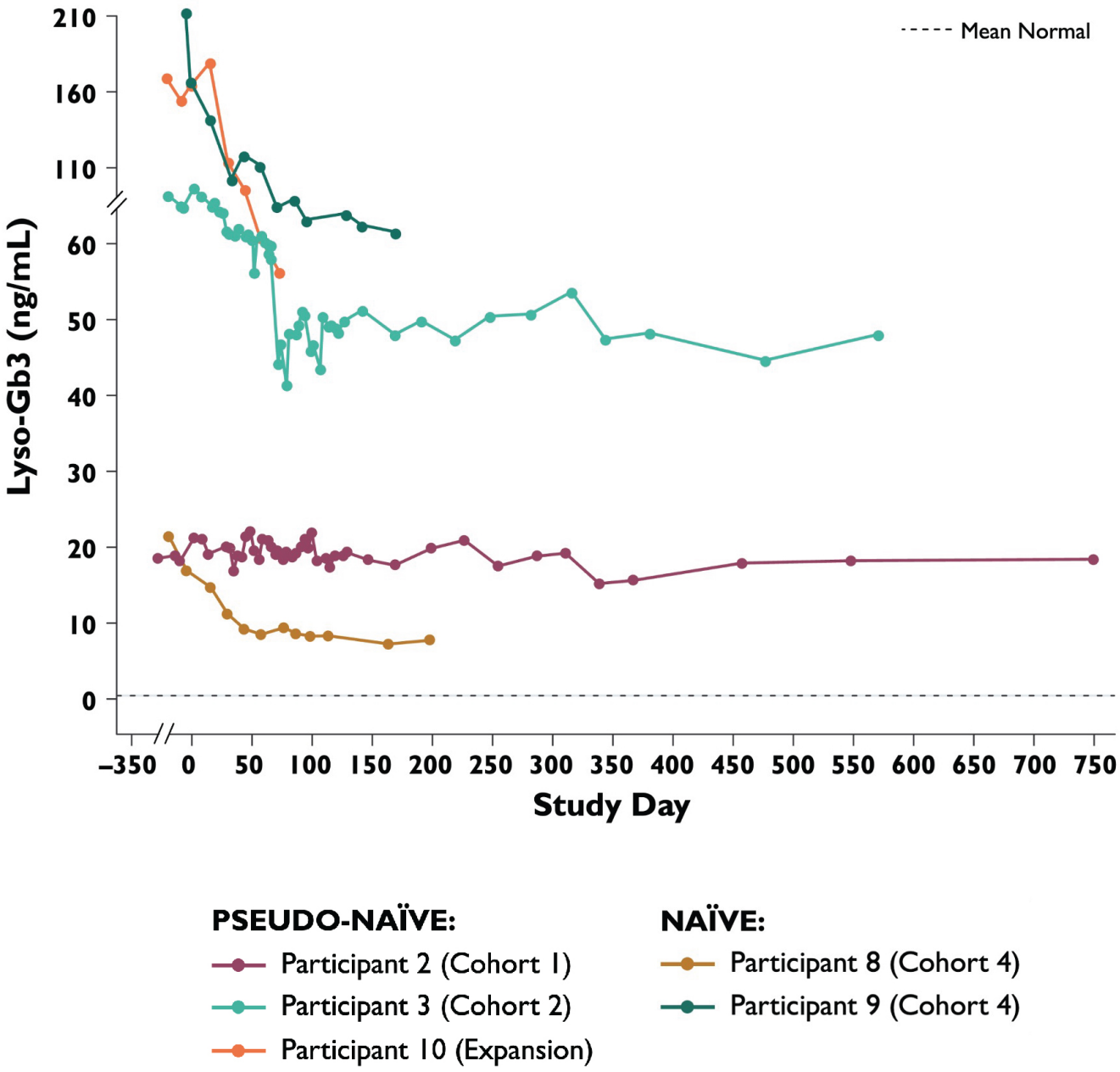


Data cut: November 15, 2022

Subject 13 (Expansion Phase): Week 6, 3.9 nmol/h/mL. α-Gal A activity measured using 3-hour reaction time. Normal range determined in healthy males.

Long Term Follow-up Data: Data points > Study Day 365. α-Gal A, alpha galactosidase A, ERT, enzyme replacement therapy

Table 5: Lyso-Gb3 in Naïve and Pseudo-naïve Patients from Dose Escalation and Expansion Phases

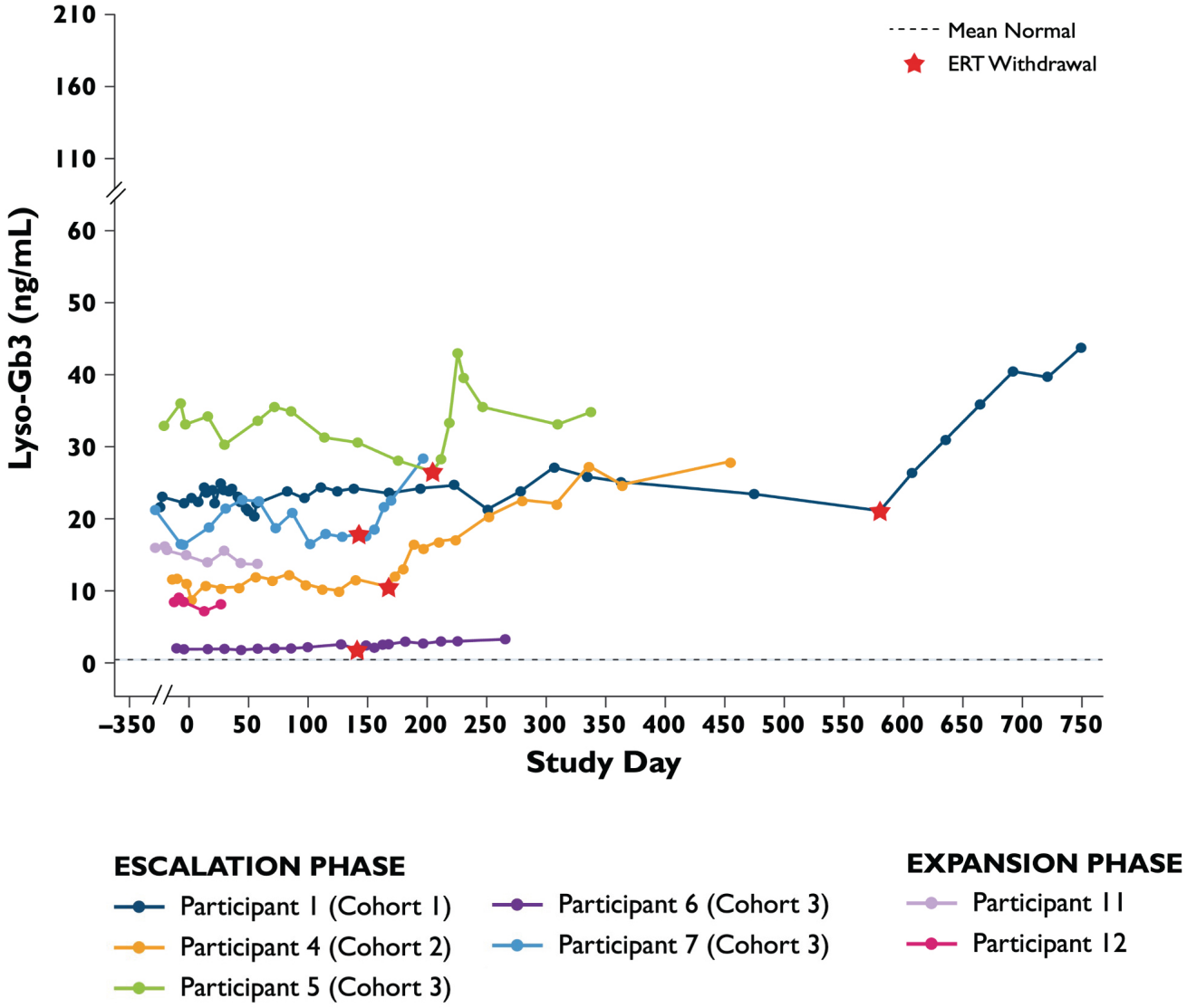


Data cut: October 20, 2022

Lyso-Gb3 normal range determined in healthy males and females. Normal range for males and females combined 0.32 to 0.63 ng/mL.

Long Term Follow-up Data: Data points > Study Day 365. Lyso-Gb3, globotriaosylsphingosine

Table 6: Lyso-Gb3 in ERT-treated Dose Escalation and Expansion Phase Patients

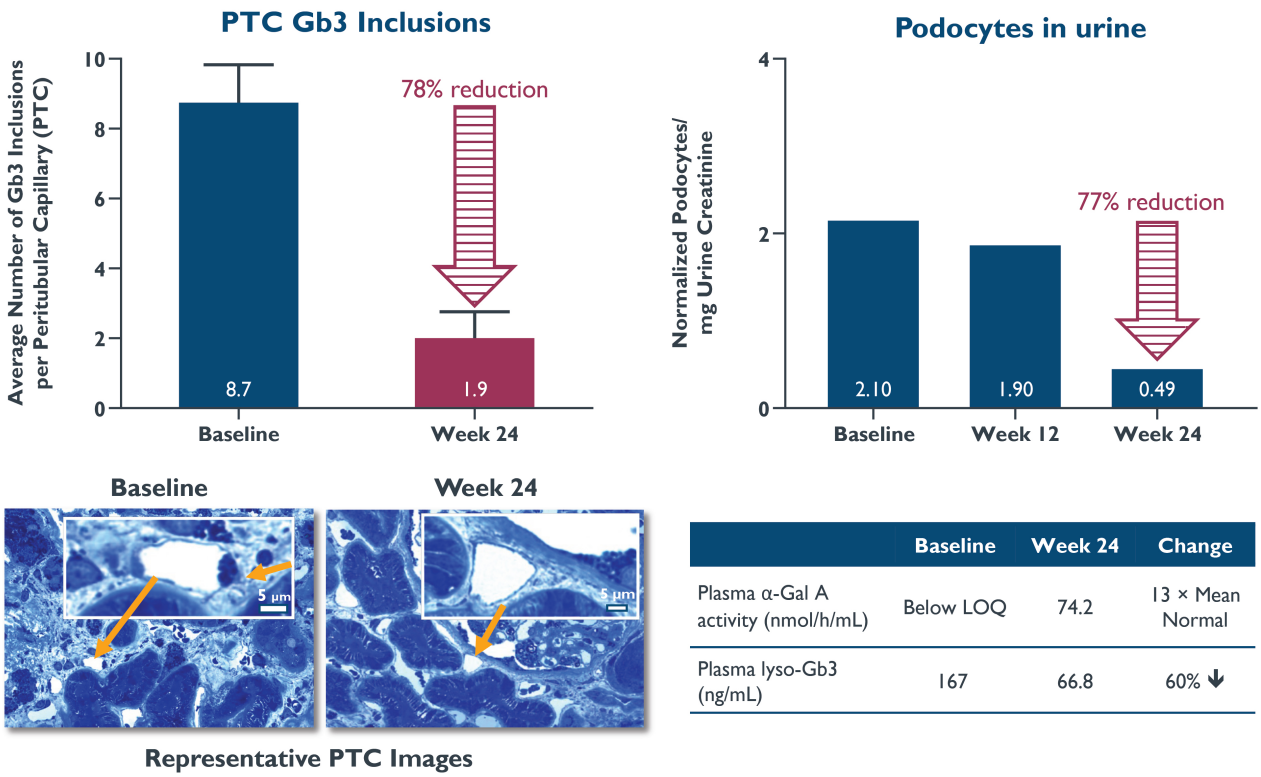


Data cut-off date: October 20, 2022

Participant 13: Week 2 34.5 ng/mL. Lyso-Gb3 normal range determined in healthy males and females. Normal range for males and females combined 0.32 to 0.63 ng/mL

Long Term Follow-up Data: Data points > Study Day 365. Lyso-Gb3, globotriaosylsphingosine; ERT, enzyme replacement therapy.

Table 7: Patient 9 PTC Gb3 Inclusions and Podocytes in Urine



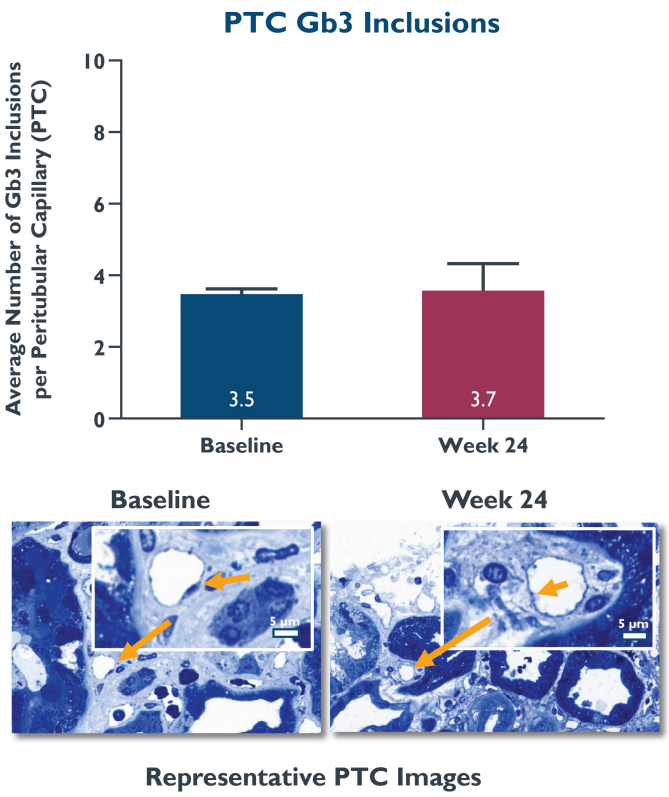
	Baseline	Week 24	Change
Plasma α-Gal A activity (nmol/h/mL)	Below LOQ	74.2	13 × Mean Normal
Plasma lyso-Gb3 (ng/mL)	167	66.8	60% ↓

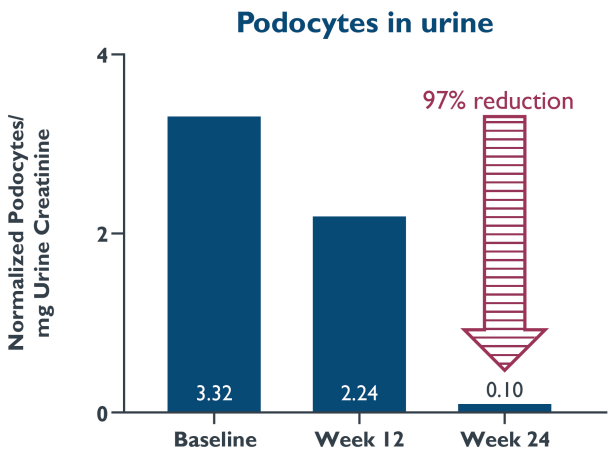
Data cut-off date: October 20, 2022

Podocyte quantification was performed via immunofluorescence with urine creatinine normalization. The Barisoni Lipid Inclusion Scoring System (BLISS) was used in a blinded manner by 3 independent pathologists to quantify PTC Gb3 inclusions. Lines above the bars indicate standard deviation.

α-Gal A, alpha-galactosidase A; ERT, enzyme replacement therapy; PTC, peritubular capillary; lyso-Gb3, globotriaosylsphingosine; Gb3, globotriaosylceramide

Table 8: Patient 8 PTC Gb3 Inclusions and Podocytes in Urine





	Baseline	Week 24	Change
Plasma α-Gal A activity (nmol/h/mL)	0.96	46.89	8 × mean normal
Plasma lyso-Gb3 (ng/mL)	16.9	7.24	57% ↓

Data cut-off date: October 20, 2022

Podocyte quantification was performed via immunofluorescence with urine creatinine normalization. The Barisoni Lipid Inclusion Scoring System (BLISS) was used in a blinded manner by 3 independent pathologists to quantify PTC Gb3 inclusions. Lines above the bars indicate standard deviation.

α-Gal A, alpha-galactosidase A; ERT, enzyme replacement therapy; PTC, peritubular capillary; lyso-Gb3, globotriaosylsphingosine; Gb3, globotriaosylceramide

TX200 – HLA-A2 Mismatched Kidney Transplant Rejection

In March 2022, we dosed the first patient in our Phase 1/2 STEADFAST clinical study evaluating TX200, our wholly-owned autologous CAR-Treg cell therapy product candidate to prevent immune-mediated rejection in HLA-A2 mismatched kidney transplantation from a living donor, with the second patient dosed in September 2022. The product candidate continues to be generally well tolerated in both patients. The third patient has received their kidney transplant and their personalized TX200 cell therapy has been manufactured, with dosing expected early in the second quarter of 2023. Dosing of this third patient would mark the completion of the first full cohort of the Phase 1/2 STEADFAST study. Manufacturing and clinical activities for the second cohort are progressing and dosing of the fourth patient is anticipated in the summer of 2023. Additional patients are in pre-screening for potential enrollment in the study. Opportunities to accelerate the dose escalation scheme are being explored with regulators.

Giroctocogene Fitelparvovec - Hemophilia A

In November 2021, following the observation of FVIII levels greater than 150% in some treated patients, we and Pfizer announced that Pfizer had voluntarily paused screening and dosing of additional patients in the Phase 3 AFFINE clinical trial of giroctocogene fitelparvovec, our investigational gene therapy for the treatment of moderately severe to severe hemophilia A, to implement a protocol amendment to provide clinical management guidance for elevated FVIII levels. Subsequently, on November 3, 2021, the U.S. Food and Drug Administration, or FDA, informed Pfizer that this trial had been placed on clinical hold while the protocol amendment and associated documents were reviewed. In March 2022, the FDA lifted the clinical hold.

In September 2022, the voluntary pause initiated by Pfizer was lifted and the trial re-opened recruitment and resumed enrollment. Dosing to support primary analysis resumed in November 2022 and is expected to be completed by the end of the

first quarter of 2023. A pivotal readout is expected in the first half of 2024, with Pfizer anticipating a biologics license application, or BLA, submission in the second half of 2024.

AFFINE is a global Phase 3, open-label, multicenter, single arm trial evaluating the efficacy and safety of a single infusion of giroctocogene fitelparvovec in more than 60 adult (ages 18-64 years) male patients with moderately severe to severe hemophilia A. The primary endpoint is impact on ABR through 12 months following treatment with giroctocogene fitelparvovec, compared to ABR on FVIII replacement therapy collected in the Phase 3 lead-in study period. We and Pfizer anticipate pivotal data readouts for this trial to be based on a full analysis of all study participants, when the first 50 patients are twelve months past reaching a steady-state of FVIII expression.

We have the potential to earn up to $240 million in future clinical, regulatory and commercial milestone payments plus tiered, escalating royalties of 14% to 20% on potential future product sales if approved for commercial sale, 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.

In December 2022, we and Pfizer presented updated follow-up data from the Phase 1/2 Alta study of giroctocogene fitelparvovec. Eleven male patients participated in the study overall, with five patients in the 3e13-vg/kg highest dose cohort. See Table 9 below for baseline patient demographics.

As of the September 6, 2022 cutoff date, all patients had been followed for 153 to 263 weeks and all patients had completed at least 35 months of follow-up. As of the September 6, 2022 cutoff date, six of the eleven patients had experienced treatment-related AEs, including four of the five patients in the highest dose cohort. The most commonly reported treatment-related AEs included elevated liver enzymes and infusion-related reactions: increased alanine aminotransferase, or ALT (5/11 (45.5%) overall; 3/5 (60.0%) in the highest dose cohort), increased aspartate aminotransferase, or AST (3/11 (27.3%) overall; 2/5 (40.0%) in the highest dose cohort), pyrexia (3/11 (27.3%) overall; 3/5 (60.0%) in the highest dose cohort), and tachycardia (2/11 (18.2%) overall; 2/5 (40.0%) in the highest dose cohort). Treatment-related SAEs were reported in one patient in the highest dose cohort who experienced Grade 3 hypotension and fever with onset approximately six hours after giroctocogene fitelparvovec infusion; the events fully resolved with treatment and did not delay post-infusion discharge the next day. See Table 10 below for more details on treatment-related AEs. As of the September 6, 2022 cutoff date, no confirmed FVIII inhibitor development occurred, and no thrombotic events, neoplastic events, abnormal alfa-fetoprotein and/or liver masses were reported.

All five patients in the highest dose cohort demonstrated FVIII activity as shown in Table 11 below through week 156. Mean FVIII activity at week 156 was 25.5% of normal as measured by chromogenic clotting assay at the central laboratory. In this highest dose cohort, the annualized bleeding rate, meaning the number of all bleeding episodes starting three weeks after infusion divided by the observation period in years, was zero for the first year post-infusion and the mean overall annual bleeding rate throughout the total duration of follow-up was 1.2 as of the September 6, 2022 cutoff date. In this highest dose cohort, two patients experienced bleeding events necessitating treatment with exogenous FVIII: one patient experienced 17 bleeding events (8 traumatic, 5 spontaneous, 4 unknown), and one patient experienced one bleeding event in a target joint, circumstances unknown. No patients in this highest dose cohort had resumed prophylaxis as of the cutoff date. Additional follow-up is required to assess durability of therapeutic effect and other long-term effects of giroctocogene fitelparvovec, such as impact on overall patient liver health.

Table 9: Baseline Patient Demographics by Giroctocogene Fitelparvovec Dose Cohort

Characteristic		Cohort 1 9e11 vg/kg	Cohort 2 2e12 vg/kg	Cohort 3 1e13 vg/kg	Cohort 4 3e13 vg/kg	All Participants
Age, years	n	2	2	2	5	11
	Mean (SD)	30.5 (9.2)	35.5 (16.3)	32.5 (0.7)	27.2 (6.1)	30.3 (7.8)
	Median	30.5	35.5	32.5	29.0	31.0
	Min, max	24, 37	24, 47	32, 33	19, 34	19, 47
Sex, n (%)	Male	2 (100)	2 (100)	2 (100)	5 (100)	11 (100)
Race, n (%)	Asian	–	1 (50)	–	–	1 (9)
	White	2 (100)	1 (50)	2 (100)	4 (80)	9 (82)
	Other	–	–	–	1 (20)	1 (9)
Ethnicity, n (%)	Hispanic or Latino	–	–	–	2 (40)	2 (18)
	Not Hispanic or Latino	2 (100)	2 (100)	2 (100)	3 (60)	9 (82)

Data cut: September 6, 2022, Max = Maximum, Min = Minimum, SD = Standard Deviation, vg = vector genomes

Table 10: Treatment-Related Adverse Events by Giroctocogene Fitelparvovec Dose Cohort

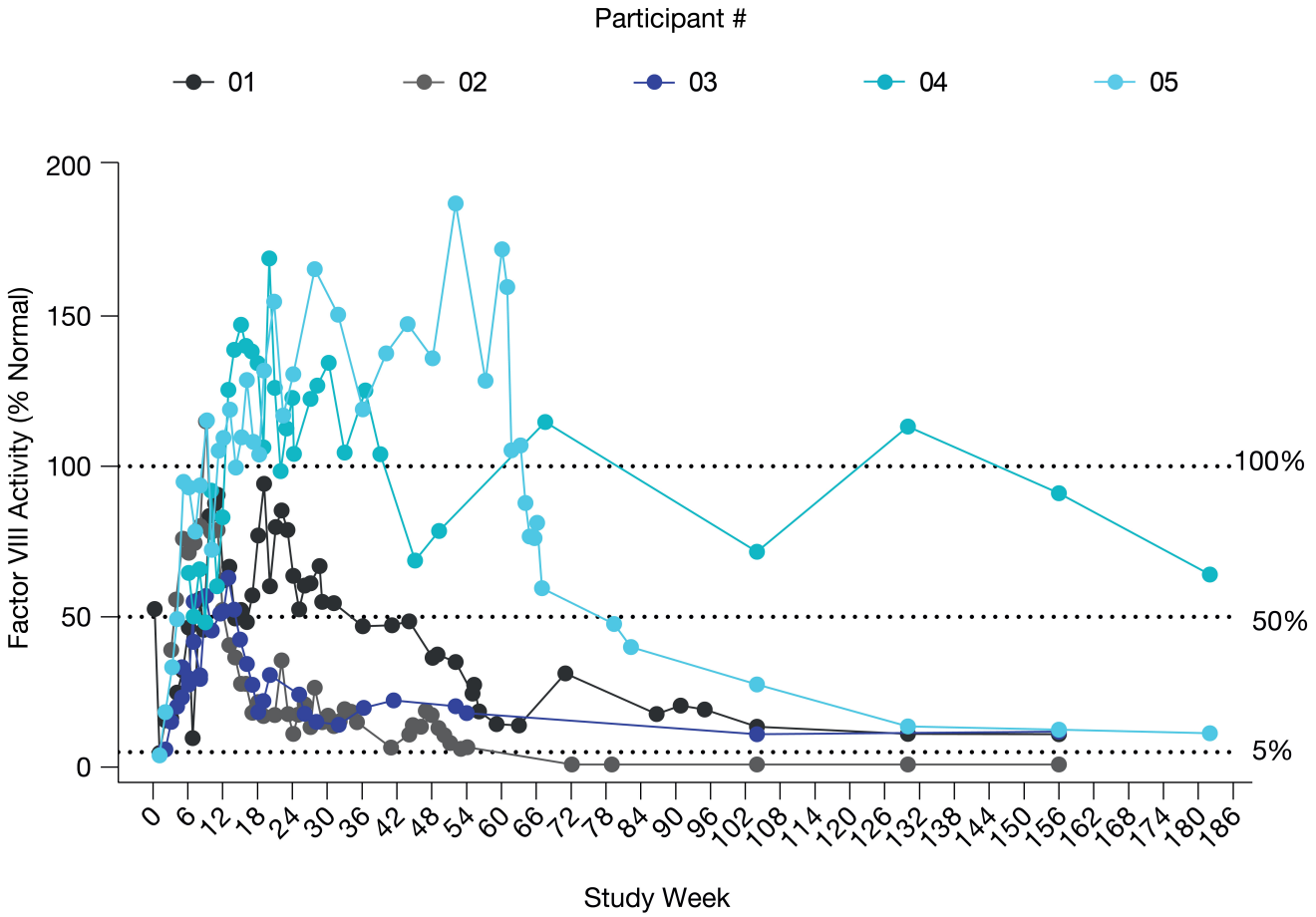
	Cohort 2: 2e12 vg/kg (n=2)		Cohort 4: 3e13 vg/kg (n=5)		All Participants (N=11)	
MedDRA Preferred Term	n	No. of Events	n	No. of Events	n	No. of Events
Any treatment-related event	2	5	4	22	6	27
Grade 3/4 AE	0	0	1[a]	1	1	1
ALT increased	2	3	3	10	5	13
AST increased	1	2	2	3	3	5
Pyrexia	0	0	3	3	3	3
Tachycardia	0	0	2	2	2	2
Myalgia	0	0	1	1	1	1
Hypotension	0	0	1	1	1	1
Fatigue	0	0	1	1	1	1
FVIII level increased	0	0	1	1	1	1

Data cut: September 6, 2022

[(a)] One patient experienced Grade 3 hypotension that was considered related to study drug and resolved with treatment

AE = Adverse Event, ALT = Alanine Transaminase, AST = Aspartate Aminotransferase, vg = vector genomes

Table 11: FVIII Activity Levels (Measured with Chromogenic Assay) for Patients in the Giroctocogene Fitelparvovec Highest Dose Cohort (3e13 vg/kg, Cohort 4)



Latest available FVIII values from September 6, 2022 data cut, FVIII = Factor VIII, vg = vector genomes

BIVV003 - Sickle Cell Disease

In January 2022, we announced that Sanofi would be transitioning its rights and obligations related to BIVV003, our ZF nuclease gene-edited cell therapy product candidate for the treatment of SCD, to us. We and Sanofi collaborated on an orderly transition, which was completed in June 2022. See "—Product Candidates in Development—Proprietary Programs—BIVV003 - Sickle Cell Disease" for additional detail concerning this transition.

In December 2022, we presented updated preliminary proof-of-concept clinical data from our Phase 1/2 PRECIZN-1 study evaluating BIVV003 at the 64th American Society for Hematology Annual Meeting and Exposition 2022, or ASH. A summary of the data is below.

Since presenting updated data at ASH in December 2022, we have progressed clinical and manufacturing activities in preparation for the dosing of patient 7 and have agreed with the FDA on a trial design for a potential Phase 3 trial and on required manufacturing processes. In addition, we have progressed additional manufacturing improvements which we believe have the potential to further strengthen clinical outcomes and reduce manufacturing costs in a potential Phase 3 trial.

We recently made the strategic decision to halt further material investments in the BIVV003 program beyond completion of the Phase 1/2 PRECIZN-1 study in order to prioritize deployment of resources to our Fabry and TX200 programs. We remain committed to completing the Phase 1/2 PRECIZN-1 study for BIVV003, and we expect to conclude the study using the funds already committed. We intend to launch a search for a potential collaboration partner who can progress this program to a potential Phase 3 trial.

Summary of Updated Preliminary Safety, Tolerability and Efficacy Results from the Phase 1/2 PRECIZN-1 Study of BIVV003 Presented at ASH on December 10, 2022

- Eligible patients underwent mobilization and apheresis with plerixafor. Autologous hematopoietic stem and progenitor cells, or HSPCs, were transfected ex vivo with ZF nuclease messenger ribonucleic acid to manufacture BIVV003. A single intravenous infusion was administered at least 72 hours after pre-conditioning with busulfan. Patients were monitored for stem cell engraftment and hematopoietic recovery, AEs, clinical and laboratory hemolysis markers, total hemoglobin, or Hb, and fetal hemoglobin, or HbF, percentage of F cells and SCD-related events post-BIVV003 infusion. Six patients achieved successful target yields of HSPCs. Five of the six patients achieving successful target yields of HSPCs had been infused with BIVV003 as of the September 30, 2022 cutoff date. Baseline characteristics of these five patients are shown in Table 12 below.
- The first four patients dosed received BIVV003 produced using the initial manufacturing process are referred to in Table 12 below as Group 1. Group 1 patients had been followed for up to 30 months post-infusion. The patient referred to in Table 12 below as Group 2 received BIVV003 manufactured using improved methods that had been shown in internal experiments to increase the number of long-term progenitor cells in the final product. As of the cutoff date, the first patient treated in Group 2, or Patient 5, had been followed for five months. A second patient in Group 2 was dosed after the September 30, 2022 cutoff date. Four of five patients in aggregate across both Groups 1 and 2 improved clinically since BIVV003 infusion through the September 30, 2022 cutoff date, as referenced in Table 13 below.

  In Group 1:

  - The effects of BIVV003 infusion on total Hb and HbF levels were maintained up to 30 months.
  - Three of the four patients had stable engraftment of ZF nuclease-modified HSPCs, resulting in sustained elevated HbF levels greater than 30% and an absence of severe vaso-occlusive crisis, or VOCs, post-BIVV003 administration.

  In Group 2:

  - Patient 5 received BIVV003 manufactured using improved methods that had been shown in internal experiments to increase the number of long-term progenitor cells in the final product.
  - The HbF level of 45% and total Hb of 12.4 g/dL at week 26 post-infusion for Patient 5 in the latest sample collected post cutoff date were greater than the levels observed in Group 1 at week 26.
- As of the September 30, 2022 cutoff date, BIVV003 was generally well tolerated, and most AEs reported in the screening, mobilization, apheresis and conditioning periods were SCD-related events. The investigator reported two SAEs of sickle cell anemia with a VOC as related to plerixafor, and one SAE of nausea as related to busulfan. Nearly half of the AEs reported after infusion of BIVV003 were related to busulfan. The investigator reported two SAEs of sickle cell anemia with a VOC nine months and 16 months after infusion in the one patient in Group 1 who had low HbF levels (11-14%). No other SCD-related SAEs were reported after infusion. No AEs related to BIVV003 were reported by the investigator or sponsor. See Table 14 below for VOCs reported before and after infusion of BIVV003.

Table 12: Baseline Characteristics of First 5 Patients Dosed

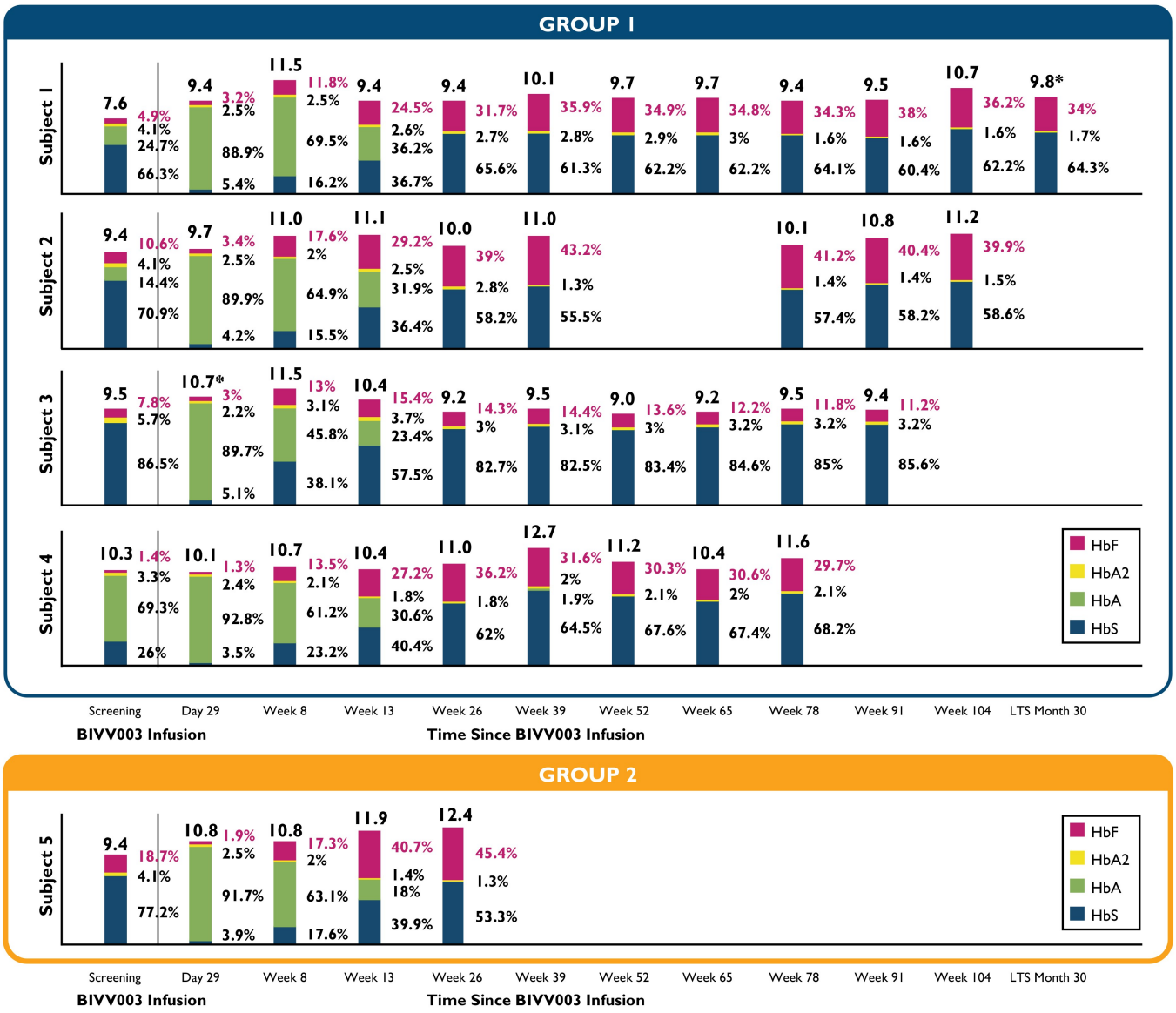
Subject	Group 1				Group 2
	Subject 1	Subject 2	Subject 3	Subject 4	Subject 5
Genotype	HbSS	HbSS	HbSS	HbSS	HbS-β^0
Gender	Female	Female	Male	Male	Male
Race	African American	African American	African American	African American	African American
Age at consent, years	35	20	18	25	27
sVOC/2 years pre-ICF	12	22	3	6	9
Hydroxyurea, Y/N	N	Y	Y	N	Y
Chronic RBC transfusion therapy, Y/N	N	Y	Y	Y	N

VOC = vaso-occlusive crisis, ICF= informed consent form, RBC = red blood cell

Group 1 includes the first four patients dosed, who received BIVV003 produced using the initial manufacturing process.

Group 2 includes patient 5 who received BIVV003 manufactured using improved methods that have been shown in internal experiments to increase the number of long-term progenitor cells in the final product.

Table 13: Total Hb and Hb Fractionation



Total hemoglobin and hemoglobin fractionation at screening and post-BIVV003 infusion over time.

HbA = adult hemoglobin, HbA2 = variant adult hemoglobin, HbF = fetal hemoglobin, HbS = sickle hemoglobin

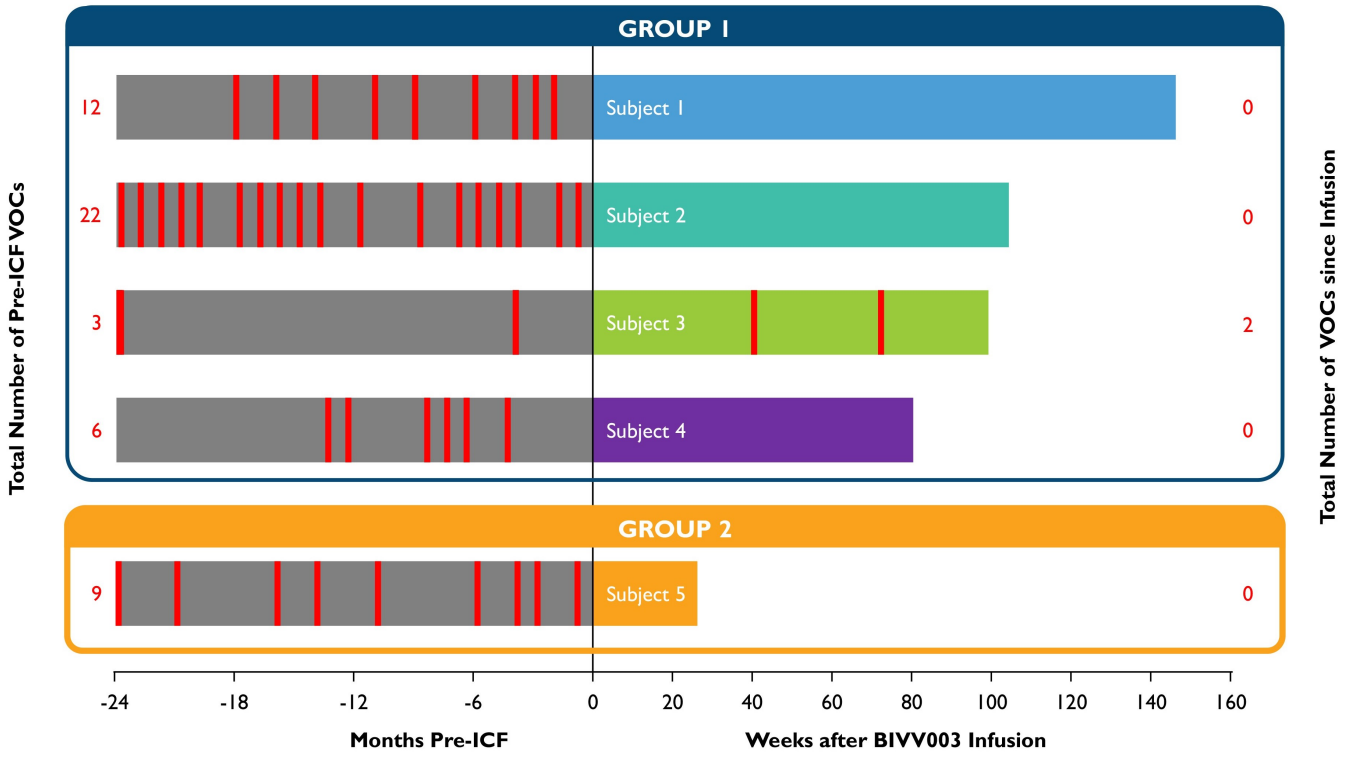
LTS= Long-term follow-up study

(*) indicates the Hb value from local lab, since the central lab value was not collected

Group 1 includes the first four patients dosed, who received BIVV003 produced using the initial manufacturing process.

Group 2 includes patient 5 who received BIVV003 manufactured using improved methods that had been shown in internal experiments to increase the number of long-term progenitor cells in the final product.

Table 14: Incidence of VOC After BIVV003 Infusion



Number of severe vaso-occlusive crises (VOCs) reported in the 24 months before signing the study informed consent form (ICF) and in the post-BIVV003 infusion period.

Red lines represent severe VOCs; two severe VOCs occurring in the same month appear as one red line

Group 1 includes the first four patients dosed, who received BIVV003 produced using the initial manufacturing process.

Group 2 includes patient 5 who received BIVV003 manufactured using improved methods that had been shown in internal experiments to increase the number of long-term progenitor cells in the final product.

OUR TECHNOLOGY

Our strategy is to translate our differentiated and versatile ZF technology platform to create product candidates with best- or first-in-class clinical potential. We believe that the versatility and flexibility of our technology platforms enable us to design therapeutic approaches to resolve the underlying genetic or cellular causes of disease, using whichever technology is best suited to deliver that treatment. Our current innovative areas of focus in preclinical studies include epigenetic regulation with our ZF technology platform in the central nervous system, or CNS, diseases and CAR-Treg cell therapy for autoimmune diseases.

ZFPs: Naturally Occurring Sequence Specific DNA Binding Proteins in Humans

ZFPs are naturally-occurring sequence-specific DNA-binding proteins in humans that recognize and bind 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 such naturally-occurring proteins in a wide range of organisms from yeast to humans. Functional domains may be added to ZFPs that enable genome editing (with enzymes such as nucleases or integrases) or epigenetic regulation (with activators and repressors) at a specific genomic site determined by the ZFP DNA-binding domain.

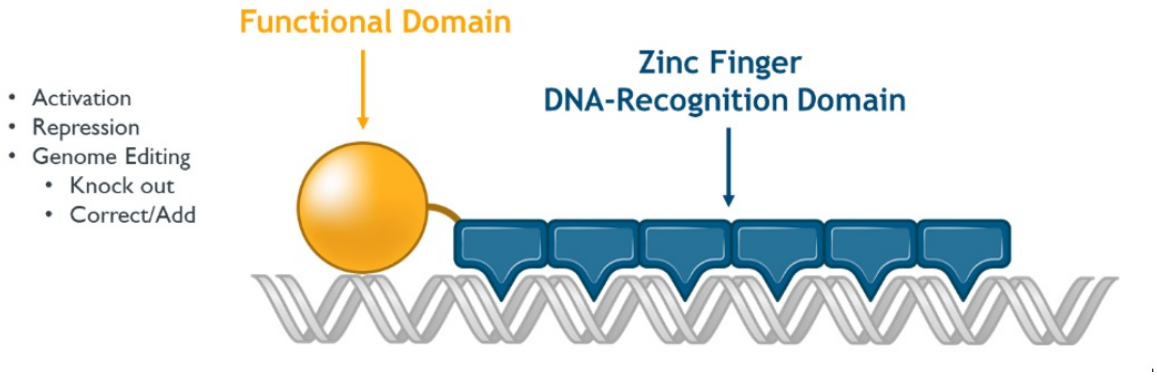


Figure 1: Schematic of the two-domain structure of a zinc finger DNA-binding domain and its functional domain

Consistent with the structure of natural ZFPs, we take a modular approach to the design of the proteins that we engineer. The DNA-recognition part of our engineered proteins 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 form a zinc finger array that recognizes longer stretches of DNA, thereby improving specificity. By modifying the amino acid sequence of ZFPs, we can engineer novel zinc finger arrays capable of recognizing the unique DNA sequences of a chosen genomic target.

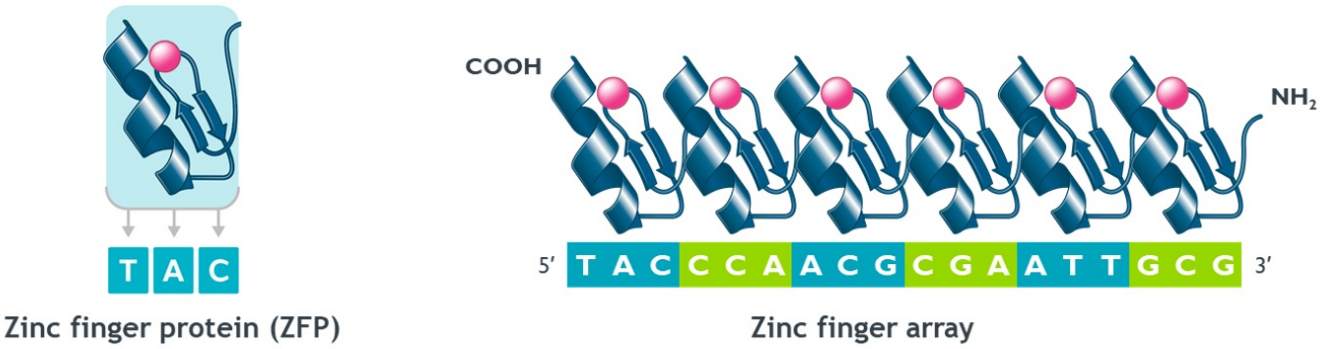


Figure 2: Schematic of a ZFP and a zinc finger array composed of 6 ZFPs

The engineered DNA-binding zinc finger array is then linked to a functional domain. The DNA-binding zinc finger array brings this functional domain to the target of interest. Our ability to use our highly specific ZFPs to precisely target a DNA sequence to a gene of interest provides us with a range of genome editing and epigenetic regulation functionalities that can be applied to multiple cell types.

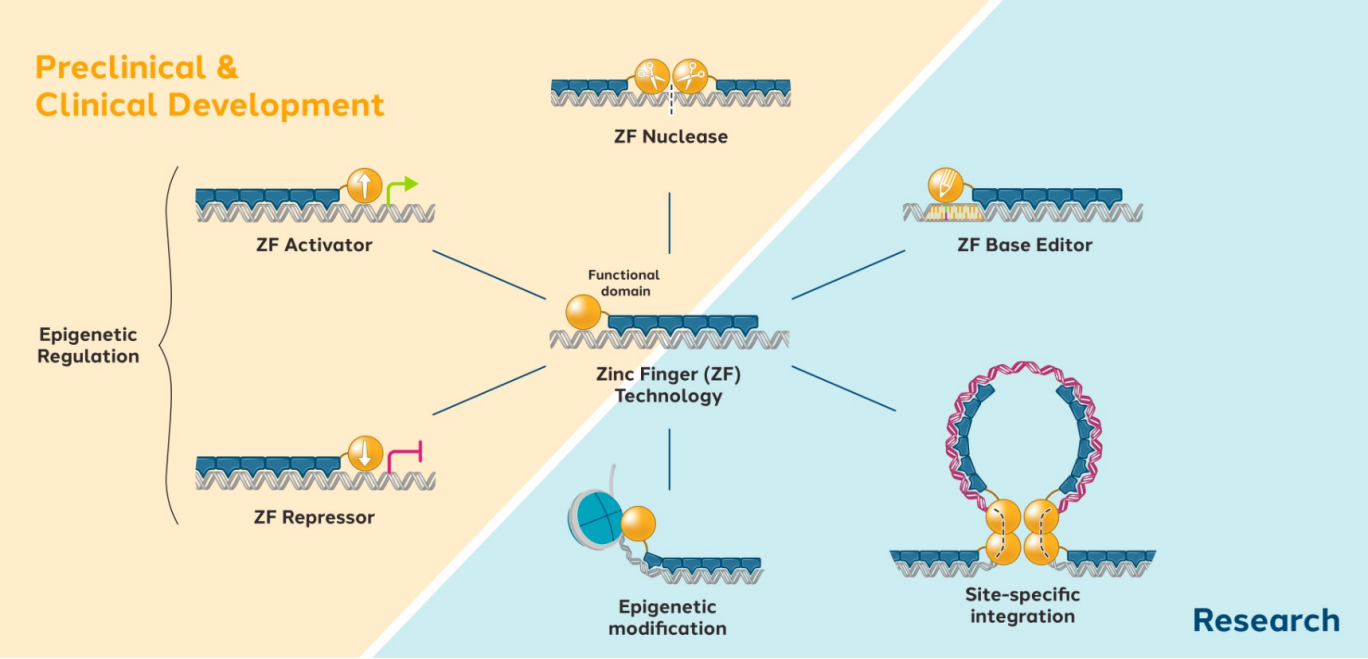


Figure 3: Examples of genome engineering tools that can be offered by our ZF platform

Our engineered zinc fingers can be attached to a cleavage domain of a restriction endonuclease, an enzyme that cuts DNA, creating a ZF nuclease. When a pair of ZF nucleases binds DNA in the correct orientation and spacing, a cut is introduced into the DNA sequence between the ZF binding sites. DNA binding by both ZF nucleases is necessary for cleavage, and the two halves of the endonuclease must be present in the correct orientation to interact with one another in order to mediate DNA cleavage. This break in the DNA triggers a natural process of DNA repair within the cell. This endogenous DNA repair process may be harnessed to achieve one of several outcomes that may be therapeutically useful (Figure 2). If cells are treated with ZF nucleases alone, the repair process joins the two ends of the broken DNA together and frequently results in the loss (deletion) or addition (insertion) of a small amount of genetic material at the site of the break. These insertions and deletion events are collectively known as "indels." These disrupt the target DNA sequence and result in the expression of a truncated or non-functional protein from the targeted gene, effectively "knocking out" the gene function. ZF nuclease-mediated genome editing can be used to disrupt genes that are involved in disease pathology. We are using ZF nuclease-mediated genome editing of the BCL11A erythroid specific enhancer, or ESE, in CD34 positive hematopoietic stem progenitor cells, or HSPCs, as the basis of a potential long-lasting and once only treatment for SCD (BIVV003).

In contrast, if cells with a mutation in a particular gene are treated not only with ZF nucleases, but also with an additional DNA sequence that encodes the correct gene sequence (referred to as a "donor" DNA) and with ZF nucleases that recognize and bind to sequences flanking the mutation, the cell's repair machinery can use the donor DNA as a template to correct the mutated gene. This ZF nucleases-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.

We are also evaluating ZF-transcription regulators, or ZF-TRs, which have the potential to regulate the expression of a target gene (Figure 4). ZF activators, or ZF-As, are created by attaching a zinc finger array to an activation domain with the aim of increasing the expression of a target gene relative to an untreated cell. Alternatively, ZF repressors, or ZF-Rs, are created by attaching a zinc finger array to a repression domain in order to down regulate or completely turn off a gene. ZF-Rs can also be designed to selectively repress expression of a mutant allele while allowing for the expression of the healthy allele. We have several preclinical programs evaluating the potential of ZF-Rs that have been designed to down regulate the expression of genes as potential treatments for CNS diseases, including a collaboration agreement with Biogen for tauopathies and Parkinson's disease, a collaboration with Takeda, for Huntington's disease and a collaboration with Pfizer for ALS. We also have a preclinical collaboration with Novartis evaluating the potential of ZF-As to upregulate expression of genes as a potential treatment for autism spectrum disorders and intellectual disability.

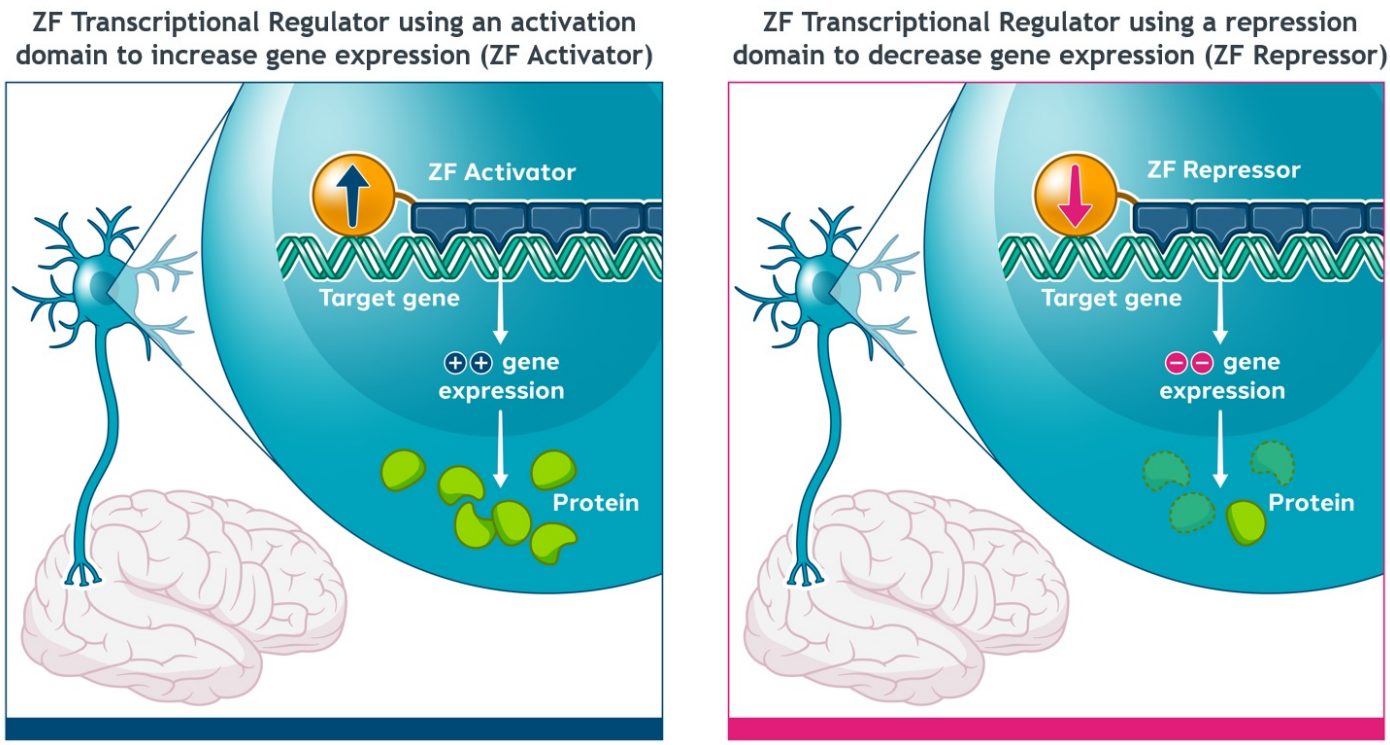


Figure 4: ZF-TRs have the potential to regulate the expression of a target gene

Multiplex cell engineering with ZF-repressors

ZF-transcriptional regulators can also be used to repress several genes in a single cell. To this aim, we engineer several ZF-Rs. The degree of regulation is tunable, offering the possibility of partial to complete knockdown. Due to their compact size, multiple ZF-Rs can be combined in a single viral construct to achieve efficient multigene modulation in a single transduction event and without the need for double-strand breaks. Delivery by lentivirus leverages a well-established method and does not require major changes to existing manufacturing processes.

As proof of concept for this novel platform, we engineered primary human T cells using multiple ZF-Rs encoded in a single lentivirus with and without a CAR, to repress expression of several allogeneic engineering targets or checkpoint inhibitors. We demonstrated that ZF-Rs act with high efficiency and specificity on target genes of choice at both the RNA and the protein level.

We believe that the ZF-R platform may be an efficient alternative, or complement, to nuclease editing approaches in T cells, with the potential to significantly expand the options for the generation of optimized T cell products.

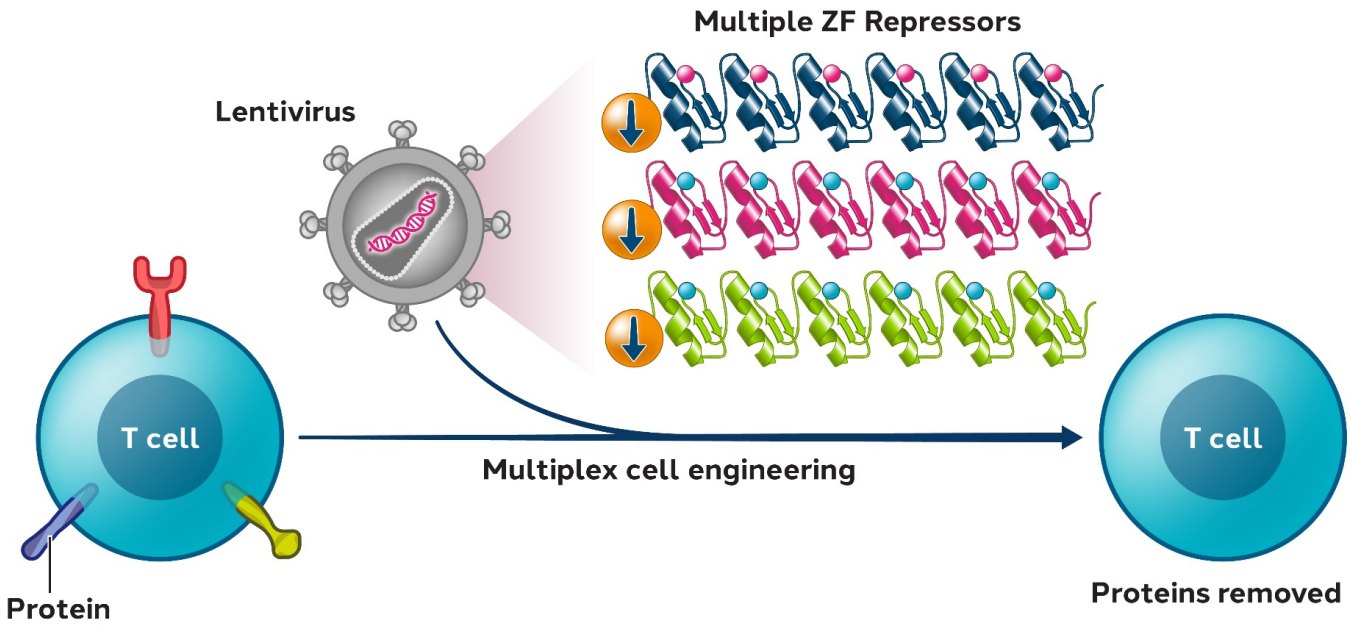


Figure 5: Multiplex cell engineering with ZF-Rs

Engineering AAVs to target the Central Nervous System (CNS)

We are evaluating several potential routes of administration for our CNS-targeted investigational therapies, as delivery of genomic medicines to the CNS is a significant obstacle to developing potential therapies treating CNS disorders.

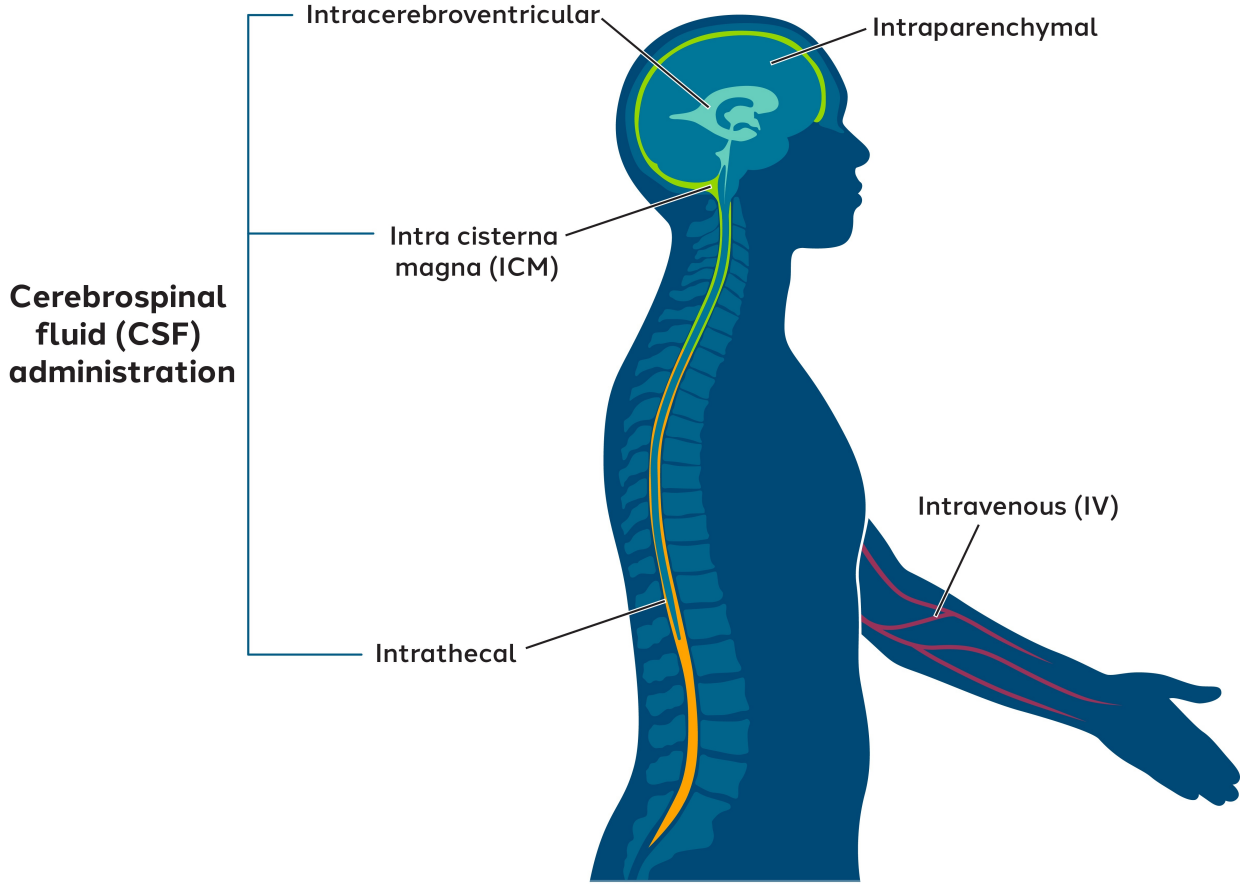


Figure 6: Potential routes of administration to target the central nervous system

Several AAV serotypes, most notably AAV9, distribute to the brain but require high doses to achieve limited expression. We have developed a proprietary AAV capsid discovery platform, SIFTER™ (Selecting In vivo For Transduction and Expression of RNA), with the aim of engineering capsids with improved CNS transduction. We are applying SIFTER™ to screen tens of millions of unique capsids in order to identify certain capsids that mediate superior delivery to the CNS. Successive rounds of screening are conducted to find capsids that reproducibly demonstrate a desired therapeutic profile.

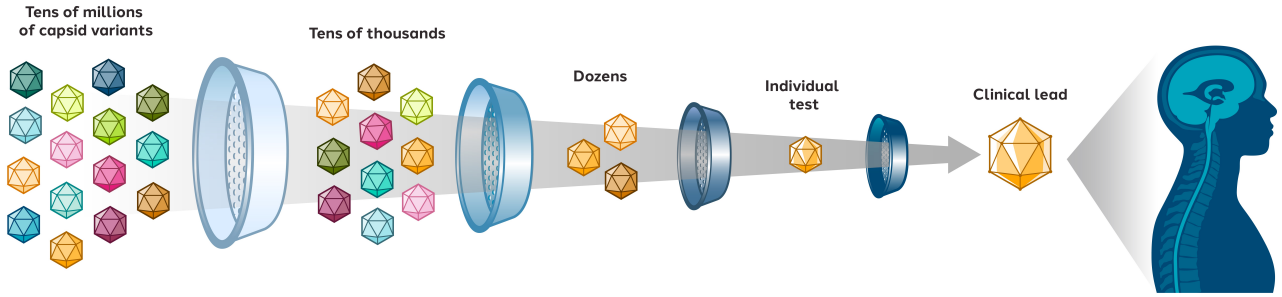


Figure 7: Sangamo's proprietary SITFER™ platform to develop novel AAV capsids targeting the CNS

In May 2022, our scientists presented results obtained with the SIFTER™ platform both for intravenous (IV) and cerebrospinal fluid (CSF) administration. This platform notably allowed us to identify new capsids exhibiting improved delivery relative to AAV9: STAC-102 and STAC-103 (STAC = Sangamo Therapeutics AAV Capsid).

Overall, we believe that improved AAV capsids with higher delivery efficiency and specificity for target tissues have strong potential to create safe and effective genomic medicines to treat CNS disorders.

Genome Engineering – Base editing

Our ZF platform can also be used to perform base editing, a novel approach in the genomic medicine space that allows for the conversion of a specific target DNA base into another DNA base without the need for double-stranded breaks. Base editing relies on the use of enzymes that can directly change the DNA sequence, such as a deaminase, which changes a specific base in a single strand of DNA.

We have developed a compact base editor architecture that can be targeted with high precision and specificity using ZFs, is small enough for packaging into relevant viral vectors, and achieves high levels of editing that are potentially suitable for therapeutic application.

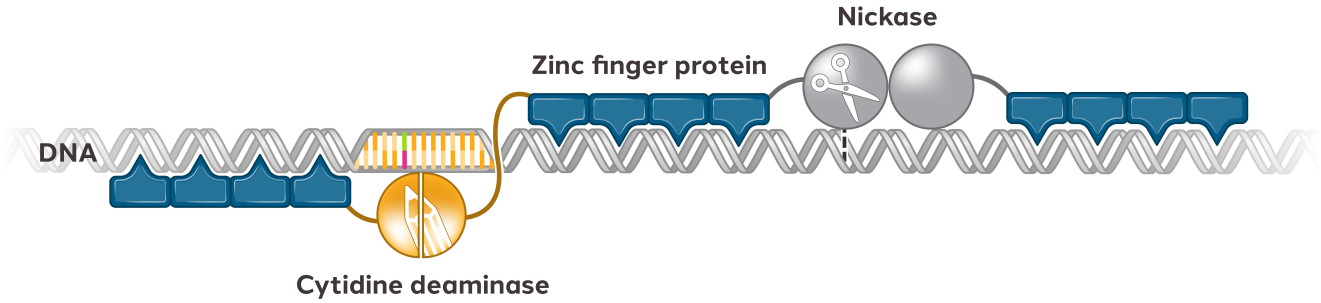


Figure 8: Compact ZF base editing architecture

ZF-base editors are well-suited to knocking out multiple genes at once due to the reduced probability of chromosomal translocation events between simultaneous DNA double-strand breaks. Notably, the compact construct architecture of our ZF-base editors makes it possible to package all three components in a single AAV vector, suggesting potential therapeutic application *in vivo*.

ZF Platform Provides Opportunity to Develop a New Class of Human Therapeutics

We believe that our ZF platform provides a unique and proprietary basis for a broad new class of drugs that have differentiated technical advantages over small-molecule drugs, protein pharmaceuticals, RNA-based therapeutics, conventional gene therapy approaches and other gene and genome editing platforms, potentially enabling us to develop therapies that address a broad range of unmet medical needs. We notably believe that our ZF genomic medicines have the potential to transform treatment strategies for severe diseases from symptom management to lasting cures.

We can generate highly specific ZF nucleases for genome editing and ZF-TRs for epigenetic regulation using a range of proprietary methods. We are developing delivery strategies to administer these therapeutics, including using mRNA, AAV, adenovirus, plasmid, lipid nanoparticles and direct injection into brain tissue or into the cerebrospinal fluid. As more genes and DNA sequences are linked to specific diseases, we believe that the clinical breadth and scope of our ZF therapeutic reagents will continue to expand.

CAR-Tregs Have Potential to Address Autoimmune and Inflammatory Diseases

A key area of focus in our preclinical pipeline is our CAR-Treg programs we are studying in autoimmune and inflammatory diseases. Tregs are a type of white blood cell and act as the key regulators of the immune system. Their natural role is to maintain immune homeostasis and prevent undesirable immune reactions to autoantigens (autoimmunity) or to antigens that are normally tolerated (food antigens, inhaled antigens, contact antigens and bacterial flora antigens). Tregs play the role of 'peacekeepers' containing other T cells before they become harmful to the organism, ensuring the immune system does not mistakenly attack healthy organs while still protecting the body from harm, e.g., from viruses and bacteria.

We are genetically re-programming Tregs *ex vivo* to add a CAR to give Tregs the ability to target a specific protein, called an antigen. CAR-Tregs are thus re-programmed to recognize and accumulate in specific tissues where the antigen is being expressed and an immune-mediated disorder is occurring. Our preclinical research shows that CAR-Tregs can inhibit overactive immune cells within the body. Moreover, they have the potential to induce long-term immune tolerance – a state of non-reactivity by the immune system to a particular auto-antigen. We aim to develop therapies that can induce and restore immune tolerance to address a wide range of inflammatory and autoimmune diseases.

CARs are composed of three main parts (see Figure 5):

- The extracellular section is composed of a single chain variable fragment, or scFv, typically derived from a monoclonal antibody and designed to recognize the target antigen, and a spacer or hinge to add spatial flexibility.
- The transmembrane domain anchors the CAR in the plasma membrane.
- The intracellular section, made of signaling and co-stimulatory domains, transmits an intracellular signal upon recognition of the antigen by the scFv.

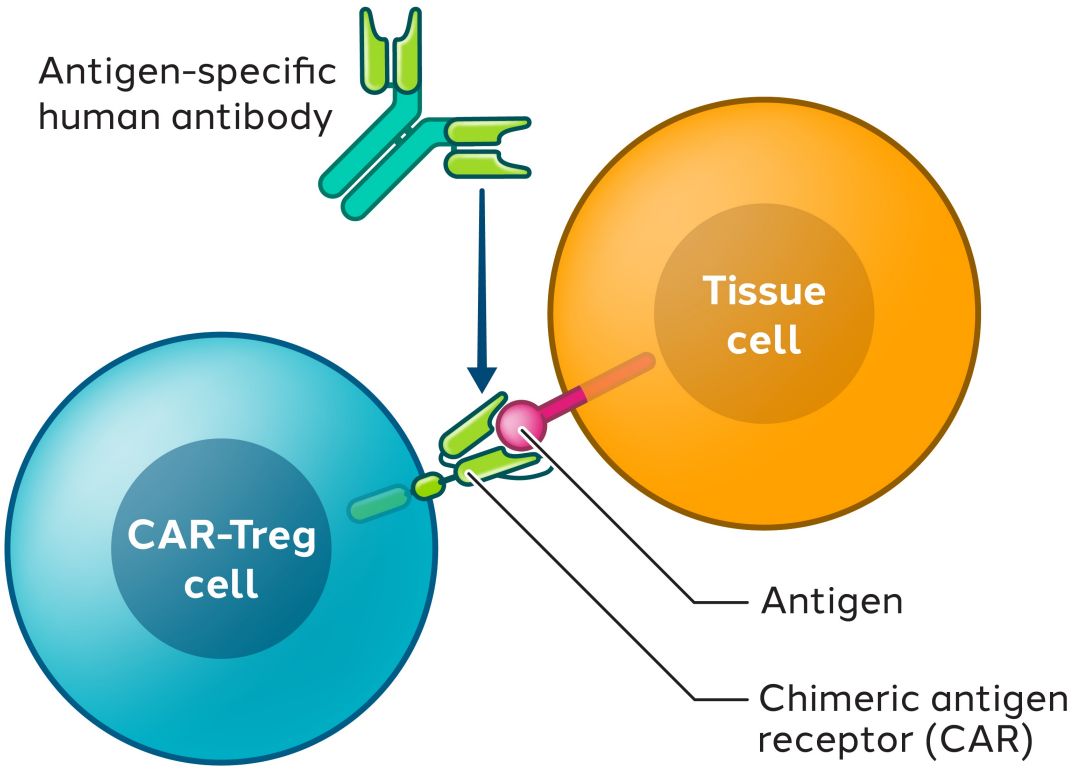


Figure 9: Schematic of CAR-Treg cell recognizing antigen on tissue cell

We carefully select the CAR target antigen for each autoimmune or inflammatory indication. Our CAR-Treg cells are designed to be active only at the site of inflammation, ensuring specific and selective action. For instance, for a CNS disease such as MS, we want to make sure that the target antigen is localized in the CNS. The target antigen may in some instances be linked to the disease etiology.

A major feature of Tregs is that they can act via multiple mechanisms to mediate suppression. Their mechanism of action can be mediated upon cell contact, through soluble factors, metabolism disruption and/or cytolysis.

- Following IV administration, CAR-Tregs are expected to migrate toward inflamed tissues due to Tregs' natural ability to migrate towards inflammatory tissues.
- Subsequently, CAR-Treg are expected to bind to their specific antigen, leading to the proliferation and activation of CAR-Treg cells.
- This activation is expected to allow Tregs to exert their natural anti-inflammatory and immuno-suppressive activities, acting through multiple molecular and cellular targets.

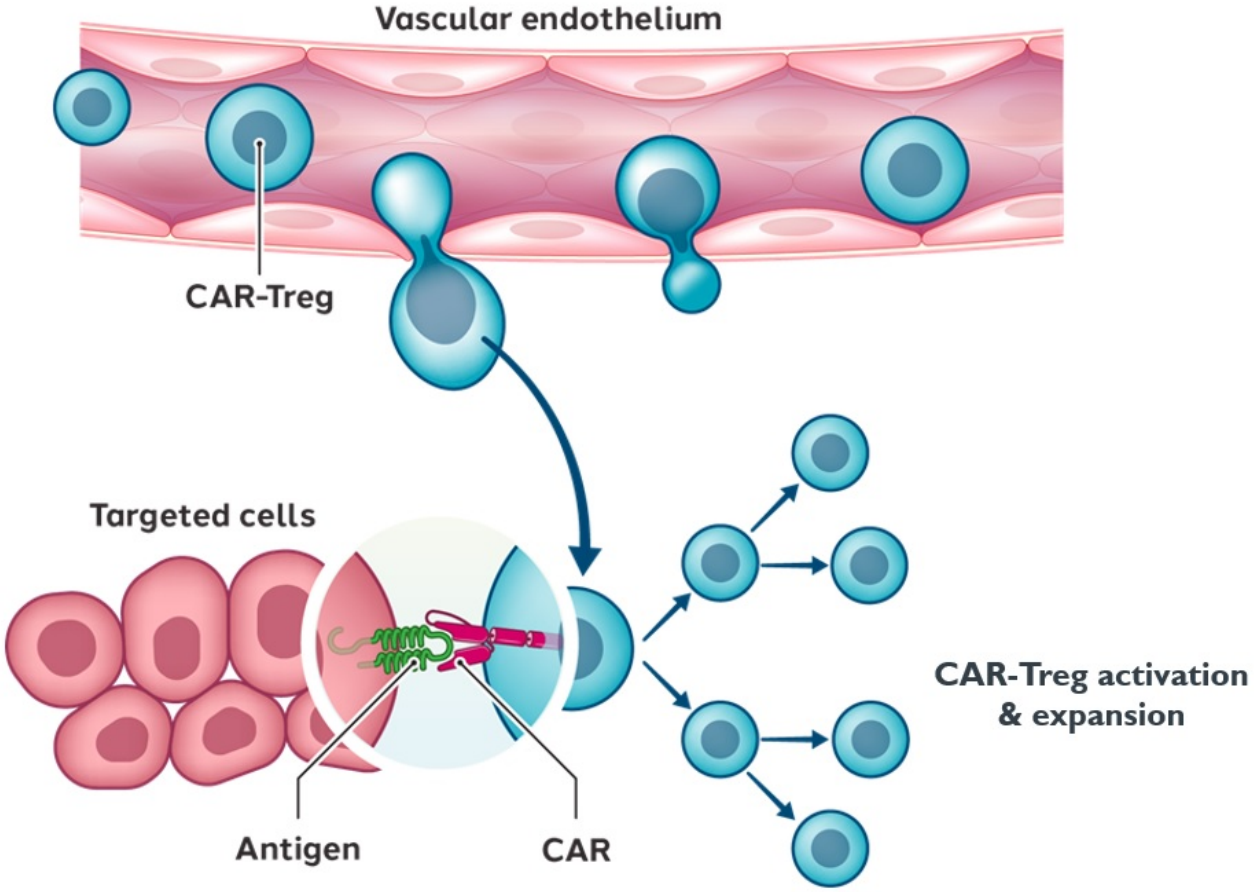


Figure 10: Expected mechanism of action of CAR-Tregs

Our most advanced CAR-Treg product candidate, TX200, is being studied for the prevention of immune-mediated rejection following HLA-A2 mismatched kidney transplantation from a living donor. TX200 is an autologous CAR-Treg cell therapy product candidate. An autologous cell therapy is made using cells from the same person as the recipient of the cells, as shown on Figure 11.

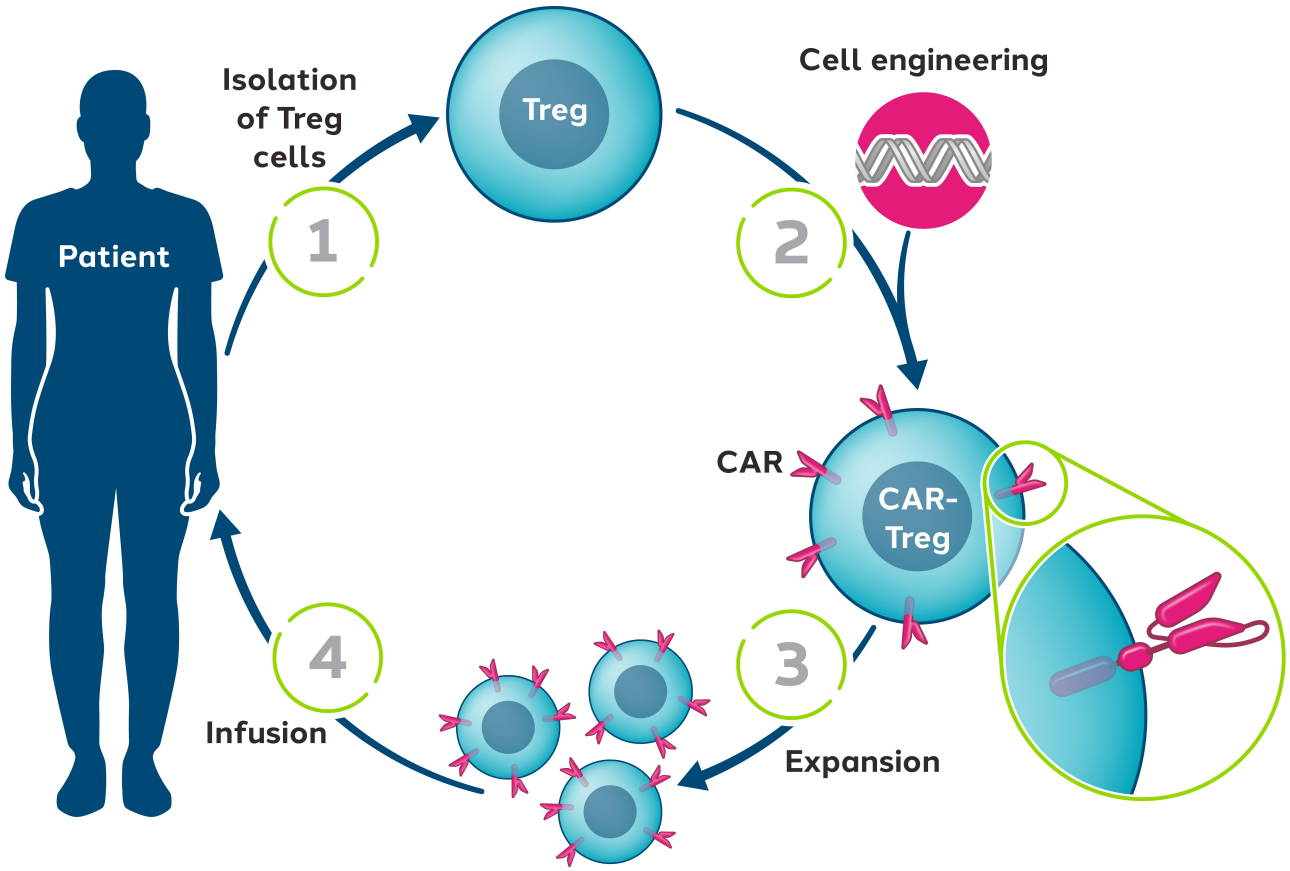


Figure 11: Schematic of our autologous CAR-Treg approach

In TX200, the patient's Tregs are collected before transplant, genetically engineered with a CAR, and then injected back into the same patient. As a result of this detailed process, we expect dosing of patients will occur several months after their enrollment. The CAR in TX200 is designed to recognize the HLA-A2 protein present on the transplanted kidney.

The first two patients have been dosed in our STEADFAST Phase 1/2 clinical study, which we expect will help us understand how CAR-Tregs work in humans and may provide broader proof of concept for genetically modified cell therapy using Tregs.

We are convinced of the fundamental impact of our CAR-Treg approach and are initiating the next step with the goal of making the approach available to a larger group of patients. Accordingly, we are developing ZF nuclease-edited allogeneic Treg therapies. Allogeneic cell therapies are donor derived, made using cells from a different person to the recipient of the cells, as opposed to autologous cell therapies. We believe that allogeneic therapies may be the future of cell therapy and could overcome the challenges of autologous approaches such as scale and manufacturing. If we are able to demonstrate proof-of-concept of autologous TX200, we anticipate follow-on autologous and allogeneic programs. There is tremendous potential from there to go into many other large autoimmune indications such as rheumatoid arthritis or diabetes.

Gene Therapy Introduces Genes into a Patient's Cells to Treat Genetic Diseases

In the process of developing our ZF technologies, we have refined our understanding of gene therapies. Gene therapy is the treatment of disease by delivery of a new gene into a patient's cells to replace an incorrect or damaged gene. Most often, gene therapy works by introducing a corrected copy of a defective gene into the patient's cells, without removing or modifying DNA. The goal of gene therapy is to treat, or potentially cure, a genetic disease by adding back a normal copy of the gene responsible for the disease.

In gene therapy, we can deliver a therapeutic gene by engineering a deactivated virus to deliver DNA for a human therapeutic protein rather than viral proteins. One virus that is commonly used in gene therapy is AAV. AAV is a naturally occurring virus that infects humans but is not known to cause disease. Engineered AAV has been used as a delivery method for gene therapy in many clinical trials in the United States and Europe and has been found thus far to be generally well-tolerated without major side effects. A gene encoding a therapeutic protein can be packaged into AAV and delivered to cells in tissues such as the liver, the eye, the brain or the heart. Once inside the cell, the gene is unpacked from the virus coat, or capsid, and

can then enable that cell to make the therapeutic protein. AAV can be manufactured at a large enough scale for use as a human therapeutic.

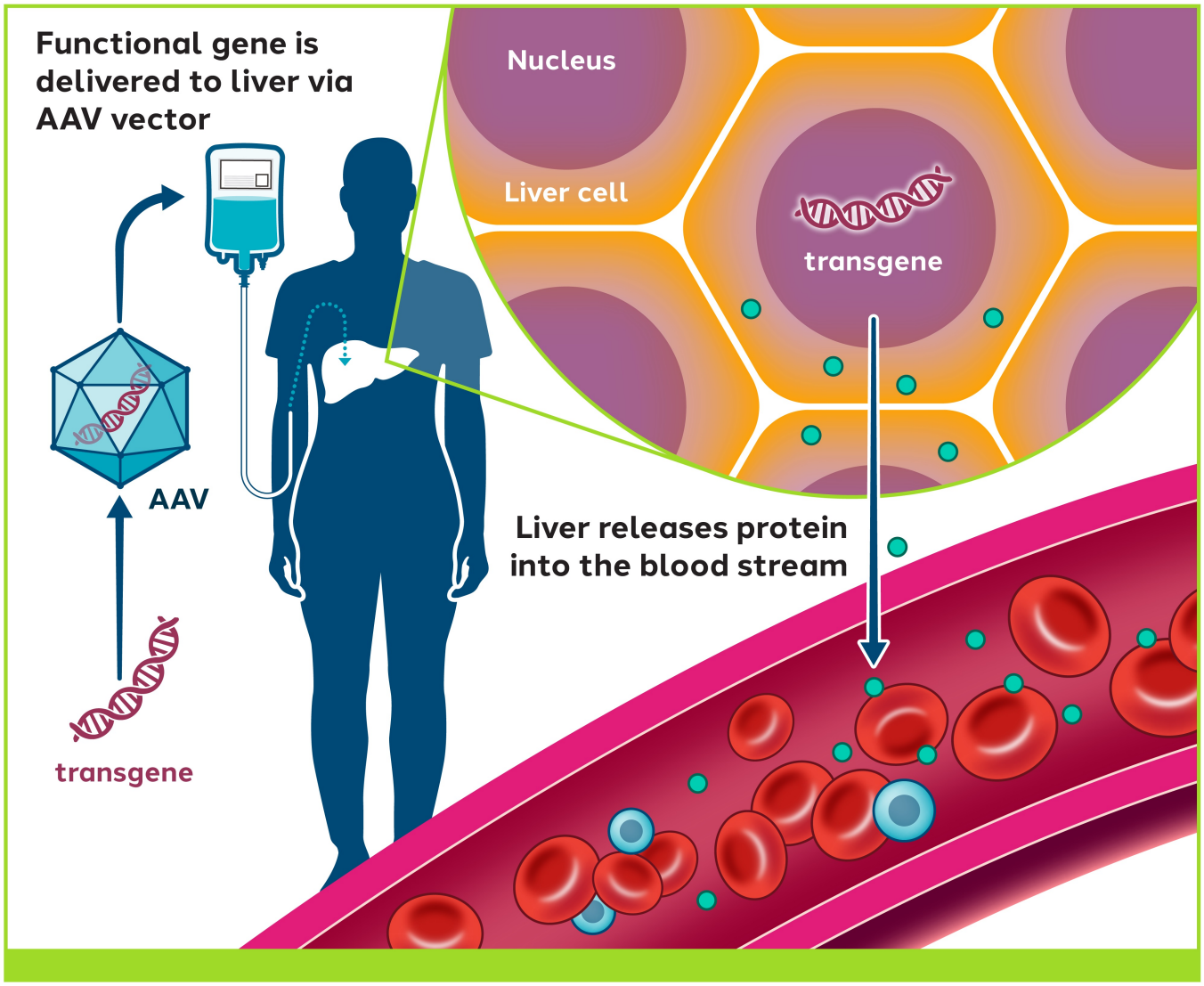


Figure 12: Our gene therapy technology

THERAPEUTIC PRODUCT CANDIDATES IN DEVELOPMENT

Proprietary Programs

Isaralgagene civaparvovec - Fabry Disease

Isaralgagene civaparvovec is our gene therapy product candidate being developed for the treatment of Fabry disease, a rare inherited metabolic disease. STAAR is an ongoing Phase 1/2 multicenter, open-label, dose-ranging clinical study designed to assess the safety and tolerability of a single infusion of isaralgagene civaparvovec in Fabry disease patients ≥ 18 years of age. Patients are infused intravenously with a single dose and followed for 52 weeks. A separate long-term follow-up study is underway to monitor the patients treated in this study for up to five years following treatment to further assess safety, durability

and efficacy. The study design provides for at least two patients to be dosed in each dose cohort, with a potential expansion in each cohort. Patients who are on stable ERT, may withdraw ERT after treatment in a controlled and monitored fashion at the discretion of the patient and the investigator.

The dose escalation phase includes males with classic Fabry disease. The study has been subsequently expanded to treat females, as well as patients with Fabry-associated cardiac or renal disease. The study's primary endpoint is the incidence of treatment-emergent adverse events. Additional safety evaluations include routine hematology, chemistry and liver tests; vital sign monitoring; electrocardiogram; echocardiogram; serial alpha-fetoprotein testing and magnetic resonance imaging, or MRI, of liver to monitor for potential formation of any liver mass. Secondary endpoints include change from baseline at specific time points over the one-year study period in α-Gal A activity, Gb3 and lyso-Gb3 levels in plasma; frequency of ERT infusion; changes in renal function and cardiac function (left ventricular mass) measured by cardiac MRI and rAAV2/6 vector clearance. Key exploratory endpoints include quality of life, Fabry symptoms and neuropathic pain scores; and immune response to AAV6 capsid and α-Gal A.

The goal of the study is to abrogate the need for ERT with a recombinant AAV2/6 vector encoding cDNA for human α-Gal A, resulting in long-term expression of α-Gal A. As a liver-directed gene therapy, isaralgagene civaparvovec is designed to be delivered by a one-time IV infusion that does not require any preconditioning regimen for patients. We believe isaralgagene civaparvovec has the potential to deliver efficacy with preserved renal function and reduced cardiac morbidity and neuropathy.

For recent updates on isaralgagene civaparvovec, please see *Business Updates* above.

CAR-Treg Cell Therapy - TX200 - HLA-A2 Mismatched Kidney Transplant Rejection

TX200 is our autologous HLA-A2 specific CAR-Treg cell therapy product candidate that we have developed for the prevention of immune mediated rejection following HLA-A2 mismatched renal transplantation. We are currently evaluating TX200 in our Phase 1/2 STEADFAST clinical study. We believe the STEADFAST study will be critical for our understanding of CAR-Treg pharmacology and biology in patients as well as establishing process development and manufacturing know-how.

TX200 has been developed for patients with end-stage renal disease or ESRD, receiving a kidney transplant, where the recipient of the kidney is HLA-A2 negative and the donor is HLA-A2 positive. A kidney transplant is considered the best treatment option for ESRD, the last stage of chronic kidney disease, when a person's kidneys are no longer working. HLA mismatch is the initial and most important barrier to successful transplantation after ABO blood types incompatibility, and approximately 21-26% of transplanted organs are HLA-A2 mismatched. In the case of an HLA-A2 positive kidney transplanted into an HLA-A2 negative patient, the recipient's immune system can recognize this mismatch and, without long-term immunosuppressive medication, will attack the new kidney carrying the HLA-A2 protein, leading to graft rejection. A lifetime of immunosuppressive therapy is associated with significant morbidity and mortality, including the development of systemic infection, malignancy and cardiovascular disease, the leading cause of death in this patient population. Therefore, the induction of immunological tolerance defined a stable and acceptable graft function without the need for immunosuppression remains a key priority in this field of medicine.

TX200 is composed of autologous Treg cells engineered to express an HLA-A2 CAR, allowing them to localize to the renal graft and activate upon recognition of the HLA-A2 antigen. We believe that TX200 has the potential to prevent kidney rejection by binding to the HLA-A2 positive kidney and inducing immune tolerance.

Similar to other genetically engineered cell therapy approaches, patients undergo a leukapheresis procedure, from which their Treg cells are isolated and engineered then cryopreserved. The HLA-A2 negative patient subsequently undergoes transplantation surgery to receive a kidney from their HLA-A2 positive living donor. Following a recovery period, the transplant recipient receives their personalized TX200 drug candidate. As a result of this detailed process, we expect dosing of patients to occur several months after their enrollment.

Our goal is that TX200 establishes the foundation for a portfolio of CAR-Tregs for major autoimmune indications, such as autoimmune hepatitis, Crohn's disease, neuromyelitis, rheumatoid arthritis, systemic sclerosis, type 1 diabetes mellitus and ulcerative colitis. We believe that allogeneic therapies may be the future of cell therapy and could overcome the challenges of autologous approaches such as scale and manufacturing. If we are able to demonstrate proof-of-concept of autologous TX200, we expect to continue to advance other autologous and allogeneic follow-on indications that are currently in preclinical development.

For recent updates on TX200, please see *Business Updates* above.

BIVV003 - Sickle Cell Disease

We are currently evaluating BIVV003, our ZF nuclease gene-edited cell therapy product candidate for SCD in the Phase 1/2 PRECIZN-1 study.

BIVV003 involves genome editing of a patient's own hematopoietic stem progenitor cells using non-viral delivery of our ZF nuclease technology designed to induce the synthesis of fetal hemoglobin. This is achieved by gene-edited knock out of the erythroid specific enhancer of the BCL11a gene, which encodes a strong repressor of the gamma globin gene. In SCD, increased fetal hemoglobin synthesis may provide the patient with functional hemoglobin and help down regulate the abnormal sickle hemoglobin that results in painful sickle cell crises and other disease features.

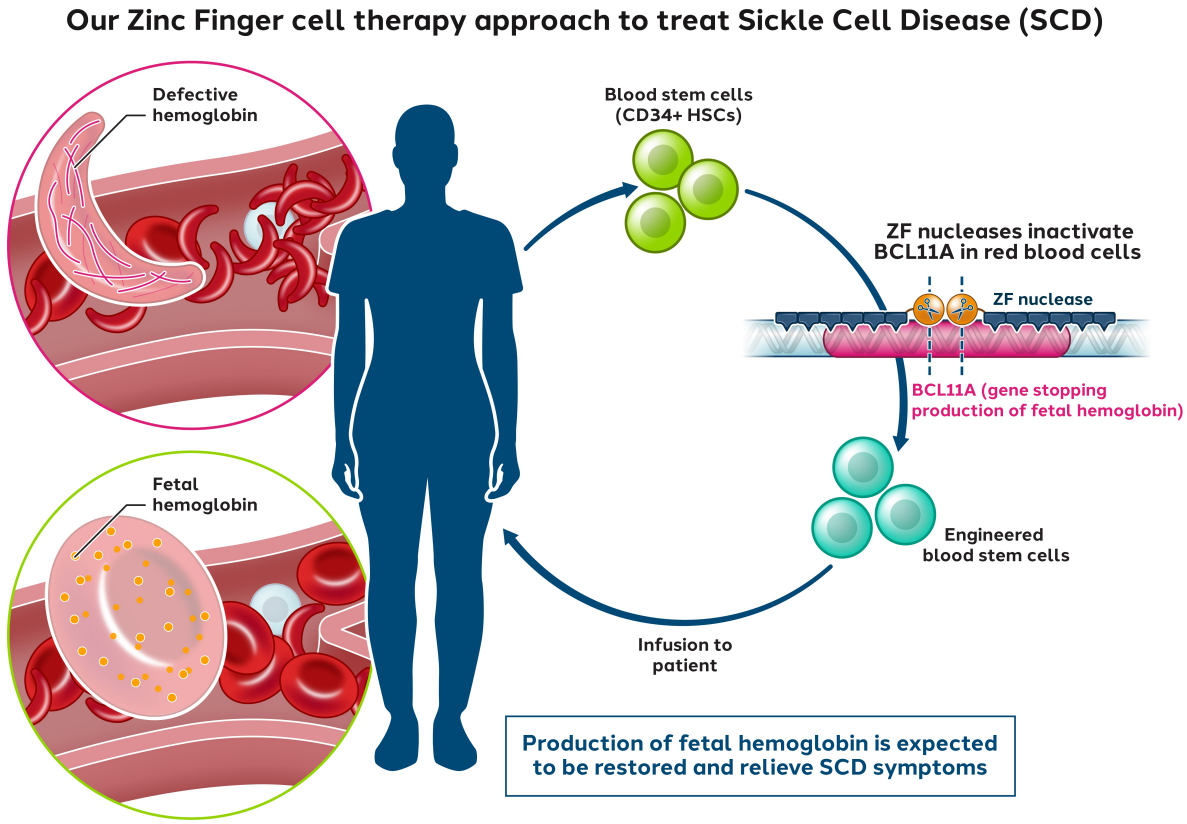


Figure 1: Our ZF cell therapy approach to treat SCD

In January 2022, we announced that we and Sanofi would be transitioning its rights and obligations related to BIVV003 back to us as of June 28, 2022, or the Termination Date. We and Sanofi collaborated on an orderly transition, which was completed and a termination and transition agreement was executed by the parties on September 6, 2022, pursuant to which Sanofi granted to Sangamo exclusive, worldwide, fully paid, royalty-free, perpetual, irrevocable licenses, with the right to grant sublicenses through multiple tiers, to certain of its intellectual property, to develop, manufacture, have manufactured, use, sell, offer to sell, import and otherwise commercialize BIVV003. We agreed to take on responsibilities for all clinical trials related to BIVV003, including completion of the ongoing clinical trial and the related long-term follow-up study. We also assumed all regulatory responsibilities related to BIVV003. Sanofi transferred and assigned to us documentation, materials, and contracts with third parties related to BIVV003, and granted us the right to use certain Sanofi-owned or leased equipment related to BIVV003.

For recent updates on BIVV003, please see *Business Updates* above.

CAR-Treg Cell Therapy - IBD

We continue to advance preclinical development of our wholly-owned CAR-Treg program to treat IBD. IBD covers debilitating disorders that involve chronic inflammation of the digestive tract, including ulcerative colitis and Crohn's disease. Our product candidate to treat IBD is composed of autologous Treg cells engineered to express a CAR designed to recognize an antigen relevant to IBD, so that it allows resulting CAR-Treg cells to localize and activate in the gut.

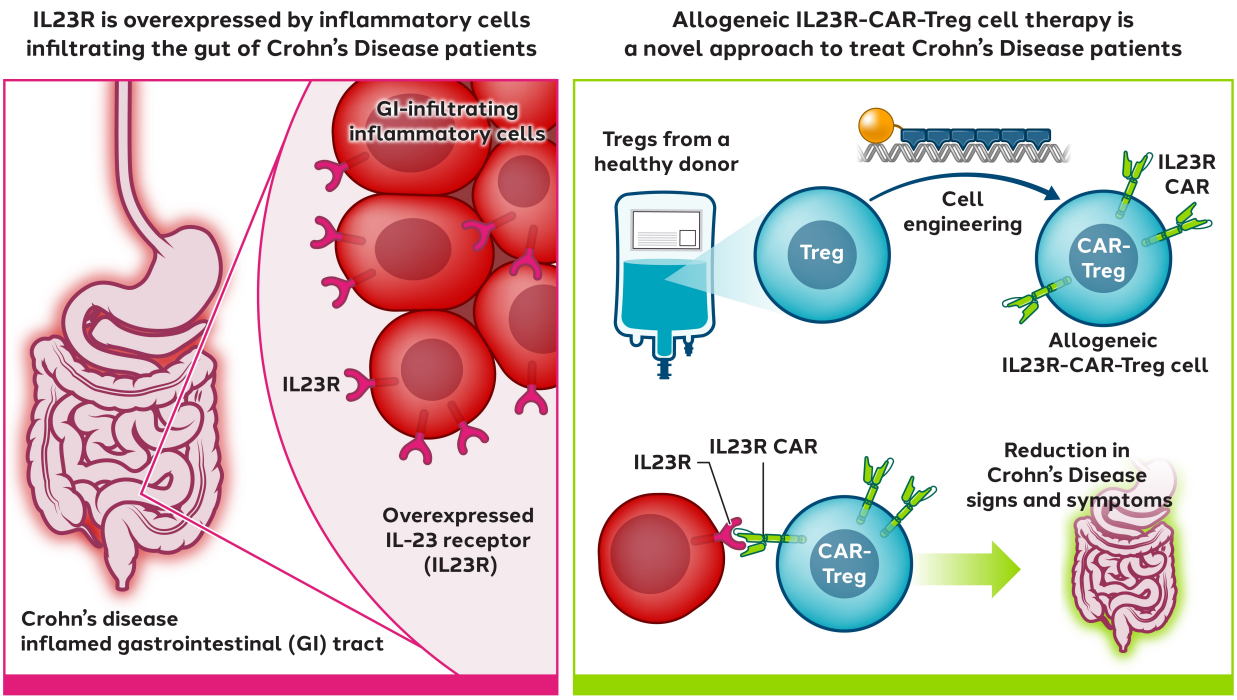


Figure 2: Our IL23R CAR-Treg candidate for Crohn's disease

CAR-Treg Cell Therapy - MS

We continue to advance preclinical development of our wholly-owned CAR-Treg program to treat MS, an autoimmune disease of the CNS. Similar to our IBD program, our product candidate to treat MS is composed of autologous Treg cells engineered to express a CAR designed to recognize an antigen relevant to MS, so that resulting CAR-Tregs can localize and activate in the CNS.

Genome Engineering - Prion Disease

We continue to advance our wholly-owned preclinical genome engineering program in prion disease, a fatal and incurable neurodegenerative disease caused by the misfolding of the prion protein encoded by the gene PRNP.

Misfolded prion protein may potentially cause other normally folded copies of prion to misfold. This may lead to a large pool of aggregated proteins that can act like a chain reaction leading to the misfolding, aggregation and spreading of further misfolded prion.

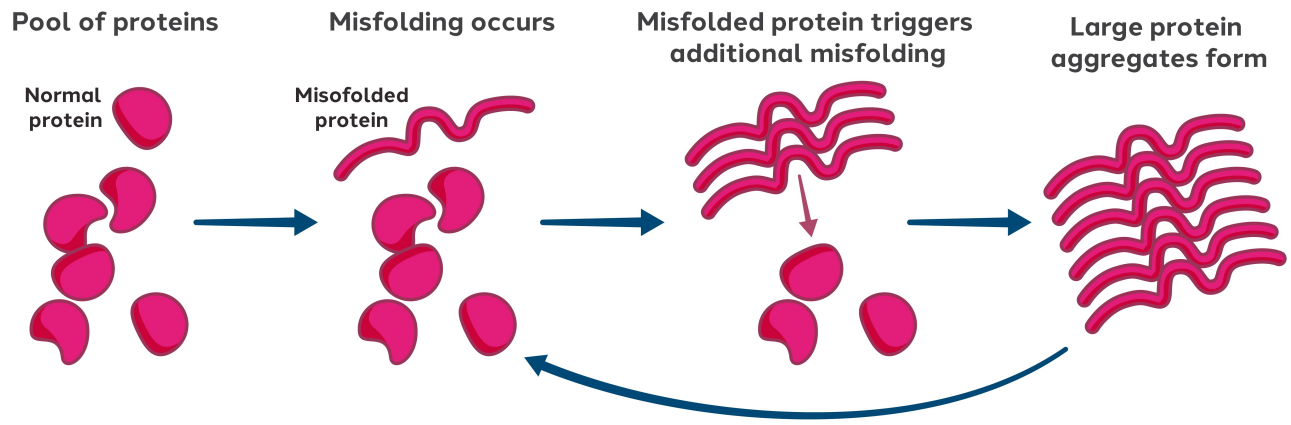


Figure 3: Misfolded prion protein aggregation chain reaction

This process is acutely toxic to neurons, and our aim is to remove a portion of prion protein from neurons to protect them from the toxicity of the misfolded prion protein. We think that this may prevent the spread and propagation of misfolded prion, and may therefore slow or halt neurodegeneration and disease progression.

To address prion disease, we are developing ZF-Rs which target the PRNP gene and have a repressor domain as their functional domain.

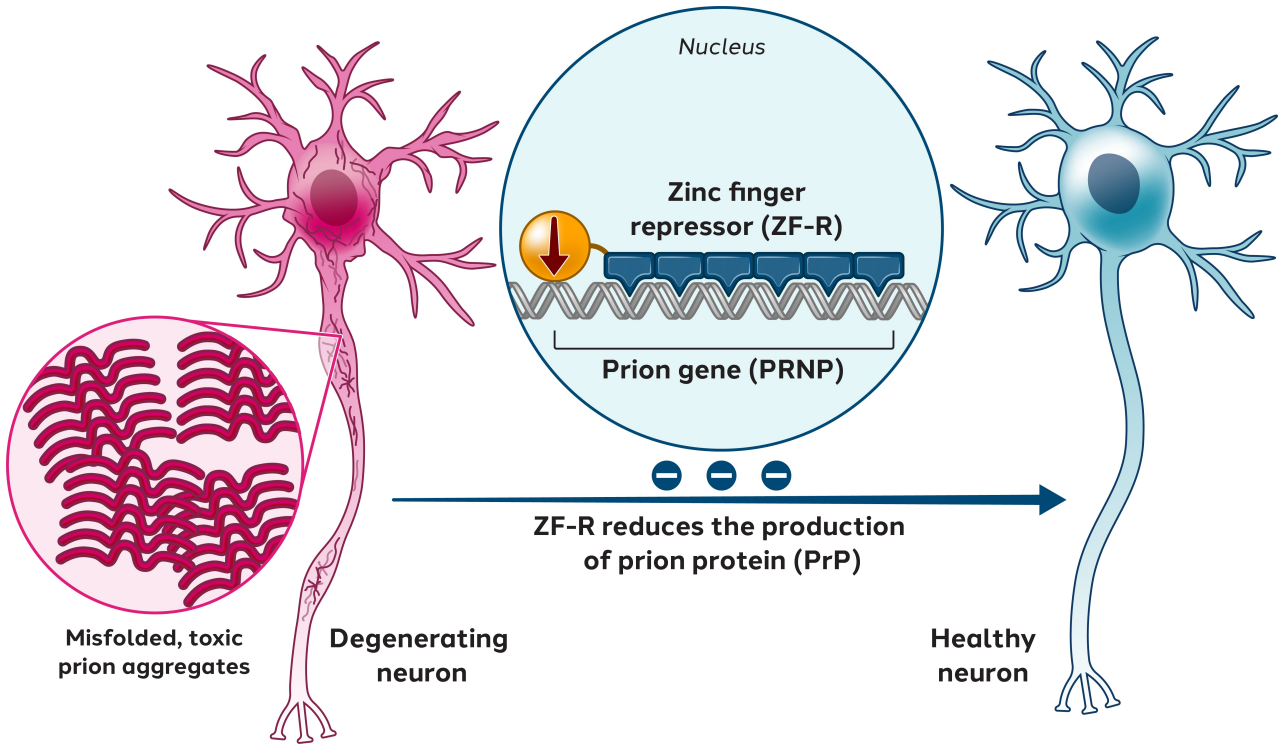


Figure 4: Our approach in prion disease using ZF-Rs

We presented the first preclinical data from this program at the Prion Conference in September 2022. We showed that our ZF-Rs specifically repressed mouse prion in vitro and in vivo, and extended survival in these inoculated mice. Overall, we believe that these early-stage preclinical data support the further development of AAV-delivered ZF-Rs for the potential treatment of prion disease, including acquired, inherited and sporadic forms.

By the end of 2023, we expect to share new data from our next wholly-owned CNS epigenetic regulation program. By the end of 2024, we anticipate submitting two new IND applications from our second wave CAR-Treg and CNS programs.

Partnered Programs

Giroctocogene Fitelparvovec - Hemophilia A

We and Pfizer continue to develop giroctocogene fitelparvovec, or SB-525. Under our collaboration agreement with Pfizer, we conducted the Phase 1/2 Alta clinical study and certain manufacturing activities, while Pfizer is responsible for subsequent worldwide development, manufacturing, marketing and commercialization, including the Phase 3 AFFINE clinical trial.

AFFINE is a global Phase 3, open-label, multicenter, single arm trial evaluating the efficacy and safety of a single infusion of giroctocogene fitelparvovec in more than 60 adult (ages 18-64 years) male patients with moderately severe to severe hemophilia A. The primary endpoint is impact on annual bleed rate, or ABR, through 12 months following treatment with giroctocogene fitelparvovec, compared to ABR on FVIII replacement therapy collected in the Phase 3 lead-in study period.

Based on initial results from the Alta study, the FDA granted regenerative medicine advanced therapy, or RMAT, designation to giroctocogene fitelparvovec. RMAT designation is granted to regenerative medicine therapies intended to treat, modify, reverse, or cure a serious condition, for which preliminary clinical evidence indicates that the medicine has the potential to address an unmet medical need. The RMAT designation includes all the benefits of the fast track and breakthrough therapy designation programs, including early interactions with the FDA. The FDA also granted giroctocogene fitelparvovec Orphan Drug and Fast Track designation, and the European Medicines Agency, or EMA, granted it Orphan Medicinal Product designation.

For recent updates on giroctocogene fitelparvovec, please see *Business Updates* above.

KITE-037 - Cancer

We and Kite Pharma, Inc., or Kite, a wholly-owned subsidiary of Gilead Sciences, Inc., continue to develop cell therapies to treat cancer using our research to design ZF nucleases and viral vectors to disrupt and insert select genes in T cells and natural killer cells, or NK-cells, including the insertion of genes that encode CARs, T cell receptors, or TCRs, and NK-cell receptors, or NKRs, directed to mutually agreed targets. Kite is responsible for all clinical development, manufacturing, marketing and commercialization. In May 2021, we announced that as part of its recent portfolio review, Kite made a decision not to submit an investigational new drug application, or IND, for KITE-037 at that time. The development program for KITE-037 remains active, and we and Kite continue to work towards the development of one or more new product candidates.

ST-501 - Tauopathies, ST-502 - Synucleinopathies and Type 1 Myotonic Dystrophy (DM1)

We and Biogen continue to develop preclinical genome engineering therapies, including our ST-501 product candidate to treat tauopathies, our ST-502 product candidate to treat synucleinopathies including Parkinson's disease and a product candidate targeting DM1, a neuromuscular disease. Biogen has also selected an undisclosed fourth neurological disease gene target under our collaboration agreement, and we have begun early research activities on therapies addressing this target. Under our collaboration agreement with Biogen, it has exclusive rights to nominate up to eight additional targets over a target selection period of five years. This collaboration leverages ZF transcriptional regulators to aim to modulate the expression of key genes involved in neurological diseases.

In March 2021, we published preclinical data in Science Advances, showing that tau-targeted ZF-transcriptional repressors selectively reduced tau messenger RNA and proteins by 50% to 80% out to 11 months without detectable off-target events.

In the first half of 2021, we presented preclinical data at the 15th International Conference on Alzheimer's and Parkinson's Diseases (AD/PD) and at the American Society of Gene & Cell Therapy (ASGCT) Annual Meeting, showing that alpha synuclein-targeted ZF-transcriptional repressors could significantly repress human alpha synuclein and were well tolerated *in vivo*.

Genome Engineering - Autism Spectrum Disorder and Neurodevelopmental Disorders

We and Novartis continue to develop preclinical genome engineering therapies for three neurodevelopmental targets, including genes linked to autism spectrum disorder and intellectual disability. The collaboration leverages our ZF-transcriptional regulators to aim to upregulate the expression of key genes involved in neurodevelopmental disorders.

Genome Engineering - ALS and Frontotemporal Lobar Degeneration

We and Pfizer have a collaboration agreement to develop preclinical genome engineering product candidates that use allele-specific ZF-transcriptional regulators to treat ALS and frontotemporal lobar degeneration, or FTLD, linked to mutations in the *C9ORF72* gene. The most frequent genetic cause of ALS is the expansion of hexanucleotide repeats, or G4C2 repeats, in the first intron of the *C9ORF72* gene. Our approach is to design ZF repressors to repress specifically pathogenic gene expression from the disease allele, while preserving expression of the healthy allele.

In September 2020, we completed our research obligations associated with this collaboration, which required us to identify, characterize and preclinically develop ZF-Rs satisfying pre-agreed criteria. Pfizer is now responsible for subsequent research and development activities as well as subsequent development, manufacturing, marketing and commercialization.

In May 2021, we presented preclinical data at the ASGCT Annual Meeting, showing that ZF-Rs were capable of selectively repressing the expression of both disease sense and antisense isoforms over a wide dose range while preserving the expression of normal isoform in patient-derived neural cells. No detectable off-target gene regulation was observed.

Takeda – Huntington's Disease

We and Takeda continue to develop potential preclinical genome engineering product candidates to treat Huntington's Disease that use a ZF-R designed to differentially down regulate the mutated disease-causing huntingtin gene, or HTT gene, while preserving the expression of the normal version of the gene.

For more information on the collaborations underlying these partnered programs, see "—Collaborations" below.

Legacy Clinical Research Programs

We have stopped development of the following clinical research programs. We continue to perform the appropriate long-term follow-up and closeout activities of the legacy studies in accordance with the study protocols.

ST-400 - Beta Thalassemia

In November 2021, we and Sanofi announced that we made a business decision to cease development of the beta thalassemia indication in order to focus resources on the SCD program. Five patients were dosed in the Phase 1/2 Thales study, an open-label, single arm clinical study to evaluate the safety and efficacy of ST-400. Results were last presented at American Society for Hematology Annual Meeting and Exposition 2021.

SB-728 - Human Immunodeficiency Virus, or HIV

SB-728 was one of the first clinical candidates to use an early generation of our ZF nuclease-mediated genome editing technology. We conducted several clinical studies evaluating SB-728, demonstrating the safety of the platform and showing immune responses from a subset of patients, however the studies did not meet our clinical expectations and we have stopped development in HIV.

SB-318 - MPS I, SB-913 - MPS II, and SB-FIX - Hemophilia B

We have stopped development of SB-318, SB-913, and SB-FIX, genome editing product candidates for the treatment of MPS I, MPS II, and hemophilia B, respectively.

COLLABORATIONS

We have entered into strategic collaborations with larger biopharmaceutical companies for several of our therapeutic programs and other partnerships for several non-therapeutic applications of our technology. We will continue to pursue further collaborations when appropriate to fund internal research and development activities and to assist in product development, manufacturing, regulatory approval and commercialization. Decisions to collaborate or not will be based on review of our internal resources, institutional knowledge and commercial considerations.

Novartis

In July 2020, we entered into a collaboration and license agreement with Novartis for the research, development and commercialization of gene regulation therapies to treat three neurodevelopmental disorders. Under the agreement, we granted to Novartis an exclusive, royalty bearing and worldwide license, under our relevant patents and know-how, to develop, manufacture and commercialize certain of our ZF-transcriptional regulators targeted to three undisclosed genes that are associated with neurodevelopmental disorders, including autism spectrum disorder and intellectual disability. We perform early research activities over the collaboration period for each gene target and manufacture the ZF-transcriptional regulators required for such research, costs of which are funded by Novartis. Novartis is responsible for additional research activities, IND-enabling studies, clinical development, regulatory approvals, manufacturing of preclinical, clinical and approved products, and global commercialization. Subject to certain exceptions set forth in the agreement, we are prohibited from developing, manufacturing or commercializing any therapeutic product targeting any of the three genes that are the subject of the collaboration. Novartis also has the option to license certain of our proprietary AAVs for the sole purpose of developing, manufacturing and commercializing licensed products arising from the collaboration.

Under the agreement, Novartis paid us a $75.0 million upfront license fee payment in August 2020. In addition, we are eligible to earn from Novartis up to $420.0 million in development milestones and up to $300.0 million in commercial milestones. We are also eligible to earn from Novartis tiered high single-digit to sub-teen double-digit royalties on potential net commercial sales of licensed products arising from the collaboration. These royalty payments are subject to reduction due to patent expiration, loss of market exclusivity and payments made under certain licenses for third-party intellectual property. The agreement continues, on a product-by-product and country-by-country basis, until the expiration of the applicable royalty term. Novartis has the right to terminate the agreement, in its entirety or on a target-by-target basis, for any reason after a specified notice period. Each party has the right to terminate the agreement on account of the other party's bankruptcy or material, uncured breach.

Biogen

In February 2020, we entered into a global licensing collaboration agreement with Biogen for the research, development and commercialization of gene regulation therapies for the treatment of neurological diseases which became effective in April 2020. Our collaboration aims to leverage our proprietary ZF technology delivered via AAV to modulate expression of key genes involved in neurological diseases. Concurrently with the execution of the collaboration agreement, we also entered into a stock purchase agreement with Biogen MA, Inc., pursuant to which Biogen MA, Inc. purchased 24,420,157 shares of our common stock, or the Biogen Shares, for an aggregate purchase price of $225.0 million.

Under the collaboration agreement, Biogen paid us an upfront license fee payment of $125.0 million. We are also eligible to earn research, development, regulatory and commercial milestone payments that could total up to approximately $2.4 billion if Biogen selects all of the targets allowed under the agreement and all the specified milestones set forth in the agreement

are achieved, which includes up to $925.0 million in pre-approval milestone payments and up to $1.5 billion in first commercial sale and other sales-based milestone payments. In addition, we are also eligible to receive tiered high single-digit to sub-teen royalties on potential net commercial sales of licensed products arising from the collaboration. 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.

Under the collaboration agreement, we granted to Biogen an exclusive, royalty bearing and worldwide license, under our relevant patents and know-how, to develop, manufacture and commercialize certain ZF and/or AAV-based products directed to certain neurological disease gene targets selected by Biogen. Biogen has already selected four of these: our ST-501 product candidate to treat tauopathies, our ST-502 product candidate to treat synucleinopathies including Parkinson's disease, a third product candidate targeting DM1, a neuromuscular disease, and a fourth undisclosed neurological disease gene target. Biogen has exclusive rights to nominate up to seven additional targets over the remainder of the five-year period from the effective date of the collaboration agreement (i.e., through April 2025). For each gene target selected by Biogen, we perform early research activities, costs for which are shared by the companies, aimed at the development of the combination of proprietary CNS delivery vectors and ZF-TRs (or potential other ZF products) targeting therapeutically relevant genes. Biogen has assumed responsibility and costs for the IND-enabling studies, clinical development, related regulatory interactions, and global commercialization. We are primarily responsible for manufacturing activities for the initial clinical trials for the first three products of the collaboration and plan to leverage our in-house manufacturing capacity, where appropriate, which is currently in development. Biogen is responsible for manufacturing activities beyond the first clinical trial for each of the first three products. Our research activities for any targets will be performed over the period not to exceed seven years from the effective date of the collaboration agreement (i.e., through April 2027). Subject to certain exceptions set forth in the collaboration agreement, we are prohibited from developing, manufacturing or commercializing any therapeutic product directed to the targets selected by Biogen.

The collaboration agreement continues, on a product-by-product and country-by-country basis, until the expiration of all applicable royalty terms. Biogen has the right to terminate the collaboration agreement, in its entirety or on target-by-target basis, for any reason after a specified notice period, and also has the right to replace up to eight targets. Each party has the right to terminate this agreement on account of the other party's bankruptcy or material, uncured breach. In addition, we may terminate the collaboration agreement if Biogen challenges any patents licensed by us to Biogen.

Pursuant to the terms of the stock purchase agreement, Biogen has agreed not to, without our prior written consent and subject to specified conditions and exceptions, directly or indirectly acquire shares of our outstanding common stock, seek or propose a tender or exchange offer or merger between the parties, solicit proxies or consents with respect to any matter, or undertake other specified actions related to the potential acquisition of additional equity interests in us. Such standstill restrictions expire on the earlier of the three-year anniversary of the effectiveness of the collaboration agreement and the date that Biogen beneficially owns less than 5% of our common stock.

The stock purchase agreement also provides that, subject to certain limitations, upon Biogen's request, we must register for resale any of the Biogen Shares on a registration statement to be filed with the SEC, until such time as all remaining Biogen Shares may be sold pursuant to Rule 144 promulgated under the Securities Act during any 90-day period.

Kite

In February 2018, we entered into a collaboration and license agreement with Kite, which became effective in April 2018 and was amended and restated in September 2019, for the research, development and commercialization of engineered cell therapies for cancer. Kite is responsible for all clinical development and commercialization of any resulting products.

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 ZF nuclease and final vectors (i.e., AAVs, RVVs) 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 are 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 are 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 $150.0 million upfront payment from Kite when the agreement became effective in April 2018. In addition, Kite reimburses our direct costs to conduct the joint research program, and Kite is responsible for all subsequent development, manufacturing and commercialization of any licensed products. We are also eligible to earn contingent development- and sales-based milestone payments that could total up to $3.0 billion if all the specified milestones set forth in this agreement are achieved. Of this amount, approximately $1.3 billion relates to the achievement of specified research, clinical development, regulatory and first commercial sale milestones, and approximately $1.8 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 10 times that the associated milestone event is achieved, regardless of the number of licensed products that may achieve such milestone event. In addition, we are 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 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.

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

We have two separate collaboration agreements with Pfizer:

Giroctocogene Fitelparvovec Collaboration

In May 2017, we entered into an exclusive, global collaboration and license agreement with Pfizer for the research, development and commercialization of giroctocogene fitelparvovec, also known as SB-525, our gene therapy product candidate for hemophilia A, and closely related products, which we amended in December 2019.

Under this agreement, we were responsible for conducting the Phase 1/2 clinical study and certain manufacturing activities for giroctocogene fitelparvovec, while Pfizer is responsible for subsequent worldwide development, manufacturing, marketing and commercialization of giroctocogene fitelparvovec. We may also collaborate in the research and development of additional AAV-based gene therapy products for hemophilia A.

We received an upfront license fee of $70.0 million, achieved a $25.0 million milestone in December 2019 upon completion of the transfer of the IND for giroctocogene fitelparvovec to Pfizer, and achieved a $30.0 million milestone in October 2020 upon the dosing of the first patient in our pivotal Phase 3 AFFINE trial. We are eligible to earn further development milestone payments on the achievement of specified clinical development, intellectual property, regulatory and first commercial sale milestones for giroctocogene fitelparvovec 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 giroctocogene fitelparvovec 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 14% - 20% of the annual worldwide 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 giroctocogene fitelparvovec 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 are 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) 15 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 giroctocogene fitelparvovec and related products automatically terminate. Upon termination by us for cause or by Pfizer in any country or countries, Pfizer is

required to automatically grant us an exclusive, royalty-bearing license under certain technology controlled by Pfizer to develop, manufacture and commercialize giroctocogene fitelparvovec in the terminated country or countries.

C9ORF72 Collaboration

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 ZF-transcriptional regulators 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 ZF-transcriptional repressors 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 achieved a $5.0 million milestone payment in September 2020 associated with the completion of all of our research activities for the *C9ORF72* collaboration. We are eligible to earn 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 of 14% - 20% 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 is responsible for the cost of its performance of the research program. Pfizer is 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, worldwide, royalty-bearing, license under our relevant patents and know-how to develop, manufacture and commercialize gene therapy products that use resulting ZF-transcriptional regulators that satisfy pre-agreed criteria. During a specified period, neither we 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) 15 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, either party will not be permitted to research, develop, manufacture or commercialize ZFPs that specifically bind to the *C9ORF72* gene for a period of time.

Sanofi

In January 2014, we entered into an exclusive worldwide collaboration and license agreement, or the 2014 Collaboration Agreement to develop therapeutics for hemoglobinopathies, focused on beta thalassemia and SCD. The 2014 Collaboration Agreement was originally signed with Biogen MA, Inc., who subsequently assigned it to Bioverativ Inc., which was later acquired by Sanofi. Under the 2014 Collaboration Agreement, we were originally jointly conducting two research programs: a beta thalassemia program, which was discontinued in the third quarter of 2021, and the SCD program, which resulted in the development of SAR445136 (now known as BIVV003), a ZFN, gene-edited cell therapy product candidate for the treatment of SCD. In December 2021, Sanofi notified us of its termination for convenience, effective as of the June 28, 2022 Termination Date, of the 2014 Collaboration Agreement. A Termination and Transition Agreement was executed by the parties on September 6, 2022, pursuant to which Sanofi granted us exclusive, worldwide, fully paid, royalty-free, perpetual, irrevocable licenses, with the right to grant sublicenses through multiple tiers, to certain of its intellectual property, to develop, manufacture, have manufactured, use, sell, offer for sale, import and otherwise commercialize BIVV003, the product candidate in development under the SCD program. We have agreed to take on responsibilities for all clinical trials related to BIVV003, including completion of the ongoing clinical trial and the related long-term follow-up study. We also assumed all regulatory responsibilities related to BIVV003. Sanofi transferred and assigned to us documentation, materials and contracts with third parties related to BIVV003, and the right to use certain Sanofi-owned or leased equipment related to BIVV003.

Sanofi has also agreed to reimburse the costs of conducting the ongoing clinical trial of BIVV003 and the costs of the long-term follow-up study through December 31, 2023, up to $7.0 million. In addition, should we elect not to continue the development of BIVV003 past December 31, 2023, Sanofi will become obligated to reimburse us for the costs of the long-term follow-up study incurred after 2023, up to $5.3 million. Sanofi's reimbursement obligations will terminate upon certain triggering events, including if we enter into a contract with a third party for collaboration, partnership, sale, licensing, or divestiture of BIVV003, or if the FDA permits early closure of the clinical trial and/or the long-term follow-up study.

Takeda

In January 2012, we entered into a collaboration and license agreement with Shire International GmbH, a wholly-owned subsidiary of Takeda, which we amended and restated in September 2015, to research, develop and commercialize human therapeutics and diagnostics for monogenic diseases based on our ZF technology. We received an upfront license fee of $13.0 million in 2012 and achieved a $1.0 million milestone in 2014. Pursuant to the amended and restated agreement, Takeda has an exclusive, worldwide license to ZF therapeutics for treating Huntington's disease.

Under the amended and restated agreement, Takeda has full control over, and full responsibility for the costs of, the Huntington's disease program, subject to certain obligations, including the obligation to retain us to perform ZF design, optimization and assessment services and to reimburse us for the costs of such services. Takeda 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 ZF 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 Takeda, subject to certain diligence obligations. We also granted Takeda a right of first negotiation to obtain a license to such programs under certain circumstances. Should we proceed to commercialize the specific hemophilia A and B programs returned to us by Takeda, we will be required to pay single digit percentage royalties to Takeda, up to a specified maximum cap, on commercial sales of therapeutic products from the programs returned to us. We do not have any obligations under the amended and restated agreement to make milestone payments to Takeda.

The amended and restated agreement may be terminated by (i) us or Takeda, in whole or in part, for the uncured material breach of the other party, (ii) us or Takeda for the bankruptcy or other insolvency proceeding of the other party and (iii) Takeda, 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 Corteva AgriScience, formerly known as Dow AgroSciences LLC, or DAS, Sigma-Aldrich Corporation (now MilliporeSigma in the United States and Merck KGaA outside the United States), Genentech, Inc., Open Monoclonal Technology, Inc. (now Ligand Pharmaceuticals Inc.) and F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc.

INTELLECTUAL PROPERTY

Patents, trade secrets, know-how and licensed technologies are important to our business. Our strategy includes filing, obtaining, maintaining, licensing, and when necessary, defending our patents and patent applications to protect technologies, inventions, and improvements to inventions that we consider important for the research, development, and commercialization of our technologies and our product candidates. We have filed numerous patent applications with the U.S. Patent and Trademark Office, or USPTO, and with patent offices in multiple foreign jurisdictions. Our proprietary intellectual property includes methods relating to the design of zinc finger proteins, 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, Treg cell therapy platforms, and viral vector delivery platforms, enabling technologies related to our platform and the use of genome editing across a variety of applications. We rely on a combination of patents, copyrights, trademarks, proprietary know-how, continuing technological innovations and trade secret protections, 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 in relevant fields certain intellectual property directed to the design, selection, and use of ZFPs, ZF nucleases and ZF-transcriptional repressors for genome editing and epigenetic regulation from numerous academic institutions. Although no individual in-license is material to our overall protection of our ZFP and ZF nuclease platforms, we believe that these in-licenses, in combination with our own know-how, patent applications and patents, protect us from unauthorized third parties who might try to copy or use our products or technologies.

In addition, with respect to our cell therapy products, our subsidiary, Sangamo France, has a license agreement with the University of British Columbia pursuant to which it exclusively licensed in relevant fields the right to the CAR for use in our TX200 product candidate. This license includes one patent family, which is expected to expire in September 2038, absent any patent term adjustment, or PTA, patent term extension, or PTE, or disclaimers.

Our Intellectual Property

In addition to our in-licensed patent portfolio, we have numerous issued patents and pending patent applications comprising approximately 170 patent families that are directed to the design, compositions and uses of ZFPs, ZF nucleases, ZF-transcriptional repressors, TALE proteins and CRISPR/Cas editing systems, Treg cell therapy platforms, viral vector delivery platforms, and other technologies related to our programs.

Given our over two-decade history with zinc finger technology, some of the earliest zinc finger patents in our portfolio began expiring in 2015. 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 ZF technology. Additionally, patents that may be issued from our pending applications will extend the patent exclusivity of our patent estate.

We believe that our in-licensed and our owned patents and patent applications, in combination with our know-how and trade secrets, in the aggregate, will provide us with substantial protection of and exclusivity around the commercial development of our gene therapy, cell therapy and genome engineering programs. In this regard, patents issued to us, applied for by us, or exclusively and non-exclusively licensed to us, cover our commercially relevant technologies, including the following types of inventions, processes and products:

- *ZFP and ZF nuclease design, engineered nucleases, and compositions (multiple patents issued with expected expiration dates ranging from 2029 to 2036), absent any PTA, PTE or disclaimers):* These patents cover inventions including 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 (multiple patents issued with expected expiration dates ranging from 2028 to 2031, absent any PTA, PTE or disclaimers):* These patents cover inventions including 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 (multiple patents issued with expected expiration dates ranging from 2031 to 2036, absent any PTA, PTE or disclaimers):* These patents cover inventions including treatments for HIV, beta thalassemia and SCD, hemophilia inherited metabolic diseases, 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 (multiple patents issued with expected expiration dates ranging from 2028 to 2035, absent any PTA, PTE or disclaimers):* These patents cover inventions including 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 biopharmaceutical companies, 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 administrative, judicial, and regulatory interpretation and refinement. Obtaining, maintaining, and enforcing patent protection in the United States and other countries remains uncertain and depends, in part, upon decisions of the patent offices, courts, administrative bodies and lawmakers in these countries. It is also possible that we may develop proprietary products or technologies in the future that are not patentable. 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. It is possible that, under certain circumstances, patent applications will be rejected and we subsequently abandon them. It is possible that we may decide that an issued patent or pending patent application may provide us with little or no competitive advantage in view of its associated costs, in which case we may abandon or allow to lapse such patent or patent applications. 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. It is possible that our current patents, or patents which we may later acquire, may be successfully challenged, invalidated in whole or in part, or deemed unenforceable. The laws of some foreign countries may not protect our proprietary rights to the same extent as do the laws of the United States.

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 USPTO 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 USPTO 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. 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. 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. Ultimately, patent protection must be sought on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Accordingly, we may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries.

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 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. Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In some countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations, and prospects may be adversely affected.

In the future, third parties may assert patent, copyright, trademark, and other intellectual property rights to technologies that are important to our business. The outcome following any potential legal assertions of infringement, 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 biopharmaceutical collaborators are leaders in the research and development of gene therapies, cell therapies and genome engineering therapies using ZF DNA-binding proteins.

We are aware of several other 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 ZF genome engineering technologies. The fields of gene therapy, cell therapy and genome engineering are highly competitive, and we expect competition to persist and intensify in the future from a number of different sources, including other biopharmaceutical companies; academic and research institutions; and government agencies that will seek to develop ZFs as well as technologies that will compete with our ZF technology platform, such as TALE proteins and the CRISPR-Cas editing system.

Accordingly, our competitors may succeed in obtaining patent protection, receiving FDA approval or commercializing competitive products before we do. 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 F. Hoffman-LaRoche Ltd., Protalix Biotherapeutics, Inc., Sanofi S.A. and numerous other biopharmaceutical firms.
- Gene therapy companies developing gene-based products in clinical trials such as BioMarin Pharmaceutical, Inc., F. Hoffman-LaRoche Ltd. through their wholly-owned subsidiary Spark Therapeutics, Freeline Therapeutics Holdings plc and 4D Molecular Therapeutics, Inc. and numerous other gene therapy companies.
- Cell therapy companies developing cell-based products, including Abata Therapeutics, Inc., Allogene Therapeutics, Inc., AZTherapies, Inc., Beam Therapeutics, Inc., Bluebird bio, Inc., Cellectis S.A., Cellenkos, Inc., Cova Therapeutics, Inc., CRISPR Therapeutics AG, Editas Medicines, Inc., GentiBio, Inc., Graphite Bio, Inc., Kyverna, Inc., Precision BioSciences, Inc., Sonoma Biotherapeutics, Inc., TeraImmune, Inc., Quell Therapeutics, Inc., Vertex Pharmaceuticals and numerous other cell therapy companies.
- Nuclease and base editing technologies under development for therapeutic applications of genome modification including companies such as Caribou Biosciences, Inc., CRISPR Therapeutics AG, Editas Medicine, Inc., Intellia Therapeutics, Inc. and Beam Therapeutics developing the CRISPR/Cas editing system, Cellectis S.A. developing TALE nucleases and meganucleases, bluebird bio, Inc. developing Homing Endonucleases and MegaTALs and Precision BioSciences, Inc. developing meganucleases and numerous other gene editing companies.
- Antisense therapeutics and RNA interference technology, including RNAi and microRNA, which are technologies that may compete with ours 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., Moderna, Inc., Regulus Therapeutics Inc., Voyager Therapeutics, Inc., Wave Life Sciences, Inc. and numerous other companies.
- Small molecules in development by pharmaceutical companies such as Biogen, Inc., Pfizer, Inc.,Vertex Pharmaceuticals, Inc. and numerous other companies.

We expect to face intense competition from other companies for collaborative arrangements with biopharmaceutical 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 currently rely heavily on 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, supply chain,

project management, and manufacturing to facilitate appropriate oversight of our CMOs, support of our regulatory filings and execution of clinical trials.

We believe that in-house manufacturing capability can provide a competitive advantage. To this end, we have commenced AAV cGMP manufacturing in our Brisbane, California facility designed to manufacture Phase 1/2 clinical study supplies for our gene therapy pipeline. We have also completed cell therapy manufacturing qualification runs in Brisbane, California and initiated qualification activities for cell therapy manufacturing in our Valbonne, France facility.

We intend to continue to rely on CMOs for the manufacture of our product candidates for any Phase 3 clinical trials, and if approved, for commercial supply. We believe this balanced approach to manufacturing, investing in internal capacity and capabilities while strengthening our commitment with external capacity, will enable us to meet our anticipated pipeline needs.

We currently leverage three distinct manufacturing platforms: AAV vector production for our genome engineering and gene therapy product candidates, HSPC modification for some of 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 ZF nuclease. The manufacturing process for our HSPC cell therapy product candidates utilizes the patient's own HSPCs. These HSPCs are transfected using mRNA to produce ZF nucleases that target specific DNA sites, resulting in modified HSPCs. The third platform utilizes our ZF nuclease technology to transform CAR-Tregs for autologous and allogeneic cell therapies. We believe we have capabilities to manufacture regulatory T cells in therapeutic quantities to be used to treat inflammatory and autoimmune disorders.

GOVERNMENT REGULATION

We operate within the heavily regulated biopharmaceutical industry 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, the European Commission, national competent authorities of the European Union, or EU, Member States and the UK Medicines and Healthcare Products Regulatory Agency, or MHRA.

Product Regulation

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. FDA approval also must be obtained before marketing of biologic products. In the EU, approval from the competent authorities of EU Member States must be obtained before commencing clinical trials. In addition, medicinal products can only be marketed if a marketing authorization, or MA, from the competent regulatory agencies has been obtained.

The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes, regulations and applicable guidance require the expenditure of substantial time and financial resources and we may not be able to obtain the required regulatory approvals.

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 IND application, 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 Good Clinical Practice, or 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;

- preparation and submission to the FDA of a BLA for marketing approval that includes substantial evidence of safety and efficacy from results of nonclinical testing and clinical trials and payment of user fees, if applicable;
- 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 inspection of the nonclinical and clinical trial sites that generated the data in support of the BLA; 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 additional preclinical testing, that may include 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 National Institutes of Health, or 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 various phases of preclinical and clinical research in the EU are subject to significant regulatory controls. 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, or MAA. All studies should be conducted in accordance with GLP and all applicable EMA, European Commission and European Pharmacopoeia guidelines related to 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 1 (first-in-human clinical trials) through to Phases 2 and 3, which are quality, safety and efficacy studies. Similar restrictions and requirements apply as in the United States regarding preclinical data to support trials using viral vectors. The preclinical tests should establish parameters such as toxicity, pharmacodynamics and pharmacokinetic properties, as well as the quality of the gene therapy medicinal products. Due to the particular nature of gene therapy medicinal products, it is recognized 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

Clinical trials involve the administration of the biologic product candidate to 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 and cell 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 efficacy 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, national competent authorities of EU Member States 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 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 safety 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 up to a 15-year period.

In the EU, clinical trials are governed by the Clinical Trials Regulation (EU) No 536/2014, or the CTR, which entered into application on January 31, 2022. The CTR is intended to harmonize and streamline clinical trial authorizations, simplify adverse-event reporting procedures, improve the supervision of clinical trials and increase clinical trial transparency. Specifically, the CTR, which is directly applicable in all EU Member States, introduces a streamlined application procedure through a single-entry point, the Clinical Trials Information System, or CTIS, which is a single set of documents to be prepared and submitted for the application, as well as simplified reporting procedures for clinical trial sponsors. A harmonized procedure for the assessment of applications for clinical trials has been introduced and is divided into two parts. Part I assessment is led by the competent authorities of a reference Member State selected by the trial sponsor and relates to clinical trial aspects that are considered to be scientifically harmonized across EU Member States. This assessment is then submitted to the competent authorities of all the concerned Member States in which the trial is to be conducted for their review. Part II is assessed separately by the competent authorities and ethics committees in each concerned EU Member State. Individual EU Member States retain the power to authorize the conduct of clinical trials in their territory. The extent to which ongoing clinical trials will be governed by the CTR will depend on the duration of the individual clinical trial. If a clinical trial continues for more than three years after January 31, 2022, the CTR will begin to apply to the clinical trial after expiry of this three-year period. The CTR will apply to clinical trials from an earlier date if the clinical trial has already transitioned to the CTR framework.

If the medicinal product is considered to be a genetically modified organism, or GMO, then GMO approval may also be required from the national GMO competent authorities of EU Member States. There is no harmonization between EU Member States regarding the approach to and timelines of GMO approval, which may result in diverging requirements between EU Member States. In addition, the submission of applications for approval of GMOs to national competent authorities of EU Member States is not made in tandem with applications for the approval of clinical trials that must be submitted via CTIS. As a result, sponsors of clinical trials that include GMOs requiring separate approval cannot benefit from submission of a single application dossier for the approval of a clinical trial and the subsequent synchronized response from EU Member States. This may impact study initiation in a given country.

The conduct of clinical trials should follow the approved clinical trial protocol, informed consents requirements, including patient informed consents, procedures and controls designed and approved for such studies, accepted standard medical and scientific research procedures and be conducted in accordance with the relevant principles of GCP and all applicable laws and regulations. Gene therapy medicinal products are in addition subject to the rules of GCP for ATMPs, which outline specific additional safeguards and requirements. Record retention requirements are increased for ATMPs as there are relevant long-term follow-up and human safety and traceability requirements.

Compliance with cGMP Requirements

Manufacturers of biologics must comply with applicable current Good Manufacturing Practices, or 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, as well as foreign authorities including the competent authorities of the EU Member States. Both domestic and foreign manufacturing establishments must register and provide additional information to the FDA, as well as foreign authorities including the competent authorities of the EU Member States, 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 or authorization for clinical trial, 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 and foreign authorities including the competent authorities of the EU Member States will not approve a BLA unless they determine 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 develop additional information about the physical and biological characteristics of the 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.

For a product candidate that is also a human cellular or tissue product, the FDA also requires compliance with current Good Tissue Practices, or cGTPs. These are FDA and EU regulations that govern the methods used in, and the facilities and controls used for, the manufacture of human cells, tissues and cellular and tissue-based products, or HCT/Ps, which are human cells or tissue intended for implantation, transplant, infusion, or transfer into a human recipient. The primary intent of the GTP requirements is to ensure that cell and tissue-based products are manufactured in a manner designed to prevent the introduction, transmission and spread of communicable disease. FDA and EU regulations also require tissue establishments to register and list their HCT/Ps with the FDA or the competent authorities of the EU Member States and, when applicable, to evaluate donors through screening and testing.

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 or for a product indication for orphan diseases.

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 effective, for its intended use 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

In the EU, medicinal products can only be commercialized after a related MA, has been granted. To obtain an MA for a product in the European Economic Area, or EEA (which is comprised of the 27 Member States of the EU plus Norway, Iceland and Liechtenstein), an applicant must submit a MAA, either under a centralized procedure administered by the EMA or one of the procedures administered by competent authorities in the EU Member States (decentralized procedure, national procedure or mutual recognition procedure). An MA may be granted only to an applicant established in the EU.

The centralized procedure provides for the grant of a single MA by the European Commission that is valid for all EU Member States. Pursuant to Regulation (EC) No 726/2004, the centralized procedure is compulsory for specific products, including for (i) medicinal products derived from biotechnological processes, (ii) products designated as orphan medicinal products, (iii) ATMPs and (iv) products with a new active substance indicated for the treatment of HIV/AIDS, cancer, neurodegenerative diseases, diabetes, autoimmune and other immune dysfunctions and viral diseases. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, authorization through the centralized procedure is optional on related approval.

Under the centralized procedure, the EMA's Committee for Medicinal Products for Human Use, or CHMP, conducts the initial assessment of a product. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing MA. The maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated assessment may be granted by the CHMP in exceptional cases. If the CHMP accepts a request for accelerated assessment, the time limit of 210 days will be reduced to 150 days (excluding clock stops). The CHMP can, however, revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment.

Unlike the centralized authorization procedure, the decentralized MA procedure requires a separate application to, and leads to separate approval by, the competent authorities of each EU Member State in which the product is to be marketed. This application is identical to the application that would be submitted to the EMA for authorization through the centralized procedure. The reference EU Member State prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. The resulting assessment report is submitted to the concerned EU Member States that, within 90 days of receipt, must decide whether to approve the assessment report and related materials. If a concerned EU Member State cannot approve the assessment report and related materials due to concerns relating to a potential serious risk to public health, disputed elements may be referred to the Heads of Medicines Agencies' Coordination Group for Mutual Recognition and Decentralised Procedures – Human for review. The subsequent decision of the European Commission is binding on all EU Member States.

The mutual recognition procedure allows companies that have a medicinal product already authorized in one EU Member State to apply for this authorization to be recognized by the competent authorities in other EU Member States. Like the decentralized procedure, the mutual recognition procedure is based on the acceptance by the competent authorities of the EU Member States of the MA of a medicinal product by the competent authorities of other EU Member States. The holder of a national MA may submit an application to the competent authority of an EU Member State requesting that this authority recognize the MA delivered by the competent authority of another EU Member State.

An MA has, in principle, an initial validity of five years. The MA may be renewed after five years on the basis of a reevaluation of the risk-benefit balance by the EMA or by the competent authority of the EU Member State in which the original MA was granted. To support the application, the MA holder must provide the EMA or the competent authority with a consolidated version of the electronic Common Technical Document providing up-to-date data concerning the quality, safety and efficacy of the product, including all variations introduced since the MA was granted, at least nine months before the MA ceases to be valid. The European Commission or the competent authorities of the EU Member States may decide on justified grounds relating to pharmacovigilance to proceed with one further five-year renewal period for the MA. Once subsequently

definitively renewed, the MA shall be valid for an unlimited period. Any authorization which is not followed by the actual placing of the medicinal product on the EU market (for a centralized MA) or on the market of the authorizing EU Member State (for a decentralized MA) within three years after authorization ceases to be valid (the so-called sunset clause).

Innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the Priority Medicines, or PRIME, designation. Products eligible for PRIME must target conditions for which there is an unmet medical need and demonstrate the potential to address the unmet medical need by introducing new methods of therapy or improving existing ones. Benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements and potentially accelerated MAA assessment once a dossier has been submitted.

In the EU, a "conditional" MA may be granted in cases where all the required safety and efficacy data are not yet available. The European Commission may grant a conditional MA for a medicinal product if it is demonstrated that all of the following criteria are met: (i) the benefit-risk balance of the medicinal product is positive, (ii) it is likely that the applicant will be able to provide comprehensive data post-authorization, (iii) the medicinal product fulfils an unmet medical need and (iv) the benefit of the immediate availability to patients of the medicinal product is greater than the risk inherent in the fact that additional data are still required. The conditional MA is subject to conditions to be fulfilled for generating the missing data or ensuring increased safety measures. It is valid for one year and must be renewed annually until all related conditions have been fulfilled. Once any pending studies are provided, the conditional MA can be converted into a traditional MA. However, if the conditions are not fulfilled within the timeframe set by the EMA and approved by the European Commission, the MA will cease to be renewed.

An MA may also be granted "under exceptional circumstances" where the applicant can show that it is unable to provide comprehensive data on efficacy and safety under normal conditions of use even after the product has been authorized and subject to specific procedures being introduced. These circumstances may arise in particular when the intended indications are very rare and, in the state of scientific knowledge at that time, it is not possible to provide comprehensive information, or when generating data may be contrary to generally accepted ethical principles. Like a conditional MA, an MA granted in exceptional circumstances is reserved to medicinal products intended to be authorized for treatment of rare diseases or unmet medical needs for which the applicant does not hold a complete data set that is required for the grant of a standard MA. However, unlike the conditional MA, an applicant for authorization in exceptional circumstances is not subsequently required to provide the missing data. Although the MA "under exceptional circumstances" is granted definitively, the risk-benefit balance of the medicinal product is reviewed annually, and the MA will be withdrawn if the risk-benefit ratio is no longer favorable.

Manufacturing Regulation in the EU

Various requirements apply to the manufacturing and placing on the EU market of medicinal products. The manufacturing of medicinal products in the EU requires a manufacturing authorization, and import of medicinal products into the EU requires a manufacturing authorization allowing for import. The manufacturing authorization holder must comply with various requirements set out in the applicable EU laws, regulations and guidance, including EU cGMP standards. Similarly, the distribution of medicinal products within the EU is subject to compliance with the applicable EU laws, regulations and guidelines, including the requirement to hold appropriate authorizations for distribution granted by the competent authorities of EU Member States. Marketing authorization holders and/or manufacturing and import authorization, or MA holders and/or distribution authorization holders may be subject to civil, criminal or administrative sanctions, including suspension of manufacturing authorization, in case of non-compliance with the EU or EU Member States' requirements applicable to the manufacturing of medicinal products.

Post-approval Requirements

Rigorous and extensive FDA and EU 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. Failure to comply with the FDA's post-approval regulations can result in withdrawal of product approval and licensure.

A sponsor also must comply with the FDA's or EMA's, European Commission's and/or the applicable EU Member States' competent regulatory authorities' 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 (or Summary of Product Characteristics in the EU) (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 and RMAT Designation

Products that are intended for treating rare conditions that affect fewer than 200,000 people in the United States, or that affect more than 200,000 persons but are not expected to recover the costs of developing and marketing a treatment drug, may qualify for orphan designation. In the EU, these rare conditions are defined as either having a prevalence of no more than five in every 10,000 people in the EU or that the medicinal product to treat such condition, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify the necessary investment in developing the medicinal product. 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 United States and for up to 10 years in the EU. 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.

Regenerative medicine advanced therapy, or RMAT, designation is intended to expedite review of a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products, intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition and for which preliminary clinical evidence indicates the potential to address unmet medical needs for such a disease or condition.

RMAT designation provides potential benefits that include more frequent meetings with the FDA to discuss the development plan for the product candidate, and eligibility for rolling review and priority review of the related BLA. Products granted RMAT designation may also be eligible for accelerated approval on the basis of a surrogate or intermediate endpoint reasonably likely to predict long-term clinical benefit, or reliance upon data obtained from a meaningful number of sites, including through expansion to additional sites. However, RMAT designation does not change the FDA's standards for product approval. Additionally, RMAT designation can be revoked if the criteria for eligibility cease to be met as clinical data emerges.

Clinical Trial Data Disclosure

Many jurisdictions have mandatory clinical trial information obligations incumbent on sponsors. In the EU, transparency requirements relating to clinical trial information are established in the CTR, which establishes a general principle according to which information contained in CTIS shall be made publicly accessible unless confidentiality is justified on grounds of protecting personal data or commercially confidential information, protecting confidential communications between EU Member States in relation to the preparation of an assessment report or ensuring effective supervision of the conduct of a clinical trial by EU Member States. This confidentiality exception may be overruled if there is an overriding public interest in disclosure. The publication of data and documents in relation to the conduct of a clinical trial will take place in accordance with specific timelines. The timelines are established by the EMA and are determined based on the documents and the categorization of the clinical trial. In addition, sponsors of clinical trials may apply for deferral of publication of certain documents at the time of submission of the initial clinical trial application. The application for deferral of publication should be based on justified grounds and include a reasoned proposed deferral period. Applications for deferral of publication are subject to the approval of concerned EU Member States.

In addition, Regulation No. 1049/2001 on access to documents, or the ATD Regulation, and the related EMA policy 0043 on access to documents provide for a wide right for EU-based interested parties to submit an access to documents request to the EMA to access certain information held by the EMA. 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 these data are in the public domain.

Regulation of Our Operations

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:

- the federal healthcare Anti-Kickback Statute, which prohibits, among other things, persons and entities 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, including the federal False Claims Act, and civil monetary penalty laws, which prohibit, 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, which 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, which 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 as well as covered subcontractors;
- the federal Physician Payments Sunshine Act created under the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the ACA, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare and Medicaid Services, or CMS, information related to payments and other transfers of value to physicians (currently defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physician assistants and nurse practitioners) 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, marketing expenditures; or drug pricing; and/or ensure the registration of sales 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.

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 significant penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs, 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. 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.

Healthcare Reform

The U.S. 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 ACA, 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. The ACA 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 now agree to offer 70% 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.

There have been legal and political challenges to certain aspects of the ACA, as well as efforts to repeal or replace certain aspects of the ACA. For example, on June 17, 2021, the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. Further, on August 16, 2022, President Biden signed the Inflation Reduction Act of 2022, or the IRA, into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost through a newly established manufacturer discount program. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how additional challenges and the healthcare reform measures of the Biden administration will impact the ACA.

Other legislative changes have been proposed and adopted in the United States since the ACA 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 2031 unless additional Congressional action is taken. However, pursuant to COVID-19 pandemic relief legislation, these Medicare sequester reductions are suspended from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic. Under current legislation, the actual reduction in Medicare payments will vary from 1% in 2022 to up to 4% in the final fiscal year of this sequester. Additionally, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024. In January 2013, the American Taxpayer Relief Act of 2012, or the ATRA, was signed into law, 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. Further, Congress is considering additional health reform measures.

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 Presidential executive orders, 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. Additionally, in July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, the U.S. Department of Health and Human Services, or HHS, released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. No legislation or administrative actions have been finalized to implement these principles. It is unclear whether these or similar measures will be implemented in the future. In addition, the IRA, among other things, (1) directs HHS to negotiate the price of certain single-source drugs and biologics covered under Medicare and (2) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. These provisions will take effect progressively starting in fiscal year 2023, although they may be subject to legal challenges. It is currently unclear how the IRA will be implemented but is likely to have a significant impact on the pharmaceutical industry. Further, the Biden administration released an additional executive order on October 14, 2022, directing HHS to submit a report within ninety (90) days on how the Center for Medicare and Medicaid Innovation can be further leveraged to test new models

for lowering drug costs for Medicare and Medicaid beneficiaries. It is unclear whether this executive order or similar policy initiatives will be implemented in the future. 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, designed to encourage importation from other countries and bulk purchasing.

In the United States, the EU 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 EU 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. Further, it is possible that additional governmental action is taken in response to the COVID-19 pandemic.

Pricing, Coverage and Reimbursement

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.

In the EU, pricing and reimbursement schemes vary widely from country to country. EU Member States may approve a specific price for a product, or they may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other EU Member States allow companies to fix their own prices for products but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the EU have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures. The Health Technology Assessment, or HTA, process is the procedure according to which the assessment of the public health impact, therapeutic impact and the economic and societal impact of use of a given medicinal product in the national healthcare systems of the individual country is conducted. The outcome of HTA regarding specific medicinal products will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU Member States. In December 2021, the EU HTA Regulation was adopted, which will enter into application in 2025 and is intended to harmonize the clinical benefit assessment of HTA across the EU. See "Risk Factors—*Even if we are able to commercialize any approved products, such 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 them, which could harm our business*."

Environmental Regulation

U.S. federal and state laws regarding safe working conditions, environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservancy and Recovery Act and the Toxic Substances Control Act, affect our business. These and other laws govern our use, handling and disposal of various biological, chemical and radioactive substances used in, and wastes generated by, our operations. We may incur significant costs to comply with such laws and regulations now or in the future. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. We believe that we are in material compliance with applicable environmental laws and regulations that continued compliance therewith will not have a material effect on our business. We cannot predict, however, how changes in these laws and regulations may affect our future operations.

Privacy Regulation

We are, or may become, subject to numerous privacy and data security laws and regulations in the United States and in other foreign jurisdictions, including, as applicable, the Federal Trade Commission Act, the EU General Data Protection Regulation, or EU GDPR, the EU GDPR as it forms part of the United Kingdom's law by virtue of Section 3 of the European Union (Withdrawal) Act 2018, as amended, or UK GDPR, and the California Consumer Privacy Act of 2018, or CCPA.

The collection, use, disclosure, transfer or other processing of personal data regarding individuals in the EEA, including personal health data, is subject to the EU GDPR. The EU GDPR, which is wide-ranging in scope, imposes several requirements on us relating to, among other things, the control over personal data by individuals to whom the personal data relates, notice we must provide to individuals regarding our processing of their personal data, 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 EU GDPR also imposes strict rules on the transfer of personal data to countries that the European Commission does not consider to provide an adequate level of privacy and data security (including the United States). While the European Commission recently issued a decision that allows transfers of personal data from the EEA to the United Kingdom to occur without restriction for a period of four years ending June 27, 2025, this decision could be withdrawn or not renewed, which would require us to implement additional mechanisms to continue making such transfers. The EU GDPR authorizes the imposition of large penalties and other corrective actions for noncompliance, including potential fines of up to €20 million or 4% of the annual global revenue of the noncompliant company, whichever is greater, definitive bans on data processing or private litigation related to processing of personal data brought by classes of data subjects or consumer protection organizations authorized at law to represent their interests. The EU GDPR requirements related to international data transfers apply not only to third-party transactions, but also to transfers of information between us and our subsidiaries such as Sangamo France, including employee information. The EU GDPR has increased our responsibility and potential liability in relation to personal data that we process compared to prior EU law, particularly in light of our acquisition of Sangamo France, and we may be required to put in place additional mechanisms to ensure compliance with the EU GDPR, which could divert management's attention and increase our cost of doing business.

In the United States, federal, state and local governments have enacted numerous privacy and data security laws, including laws on data breach notification, personal data privacy and consumer protection. For example, the CCPA requires businesses to provide detailed disclosures in privacy notices and honor requests of California residents to exercise certain privacy rights related to their personal data (including the right to delete their personal data and to opt out of the sale of their personal data). The CCPA provides for civil penalties of up to $7,500 per violation and allows private litigants affected by certain data breaches to recover significant statutory damages. Although the CCPA exempts some data processed in the context of clinical trials, the CCPA may increase compliance costs and potential liability with respect to other personal data we may maintain about California residents. The California Privacy Rights Act of 2020, or CPRA, which became operative on January 1, 2023, expanded the CCPA's requirements to apply to personal information of business representatives and employees, and established a new regulatory agency, the California Privacy Protection Agency, to implement and enforce the law and impose administrative fines. Other states, such as Virginia, Colorado, Utah and Connecticut, have also passed comprehensive privacy and data security laws, and similar laws are being considered in several other states, as well as at the federal and local levels. These developments may further complicate compliance efforts, and may increase legal risk and compliance costs for us and the third parties upon whom we rely.

Compliance with these and any other applicable privacy and data security laws and regulations is a rigorous and time-intensive process, and we may be required to put in place additional mechanisms ensuring compliance with the new data protection rules. If we fail to comply with any such laws or regulations, we may face significant fines and penalties that could adversely affect our business, financial condition and results of operations. Furthermore, the laws are not consistent, and compliance in the event of a widespread data breach is costly. See "Risk Factors—*Our current and future relationships with healthcare providers, customers and third-party payors subject us to applicable anti-kickback, fraud and abuse, privacy, data security and other healthcare laws and regulations. If we fail to comply with such regulations, we could face regulatory investigations or actions, litigation, and substantial fines and penalties, and our business, reputation, results of operations, financial condition and prospects could be adversely affected.*"

HUMAN CAPITAL MANAGEMENT

Our Mission and Our Employees

At Sangamo, we are committed to translating ground-breaking science into genomic medicines that transform patients' lives. We are a passionate group of biotechnology professionals based in the United States, France and the United Kingdom with years of experience and technical expertise, committed to developing best-in-class genomic medicines. We embrace collaboration, discipline and efficiency while welcoming fresh ideas and stimulating personal development. We encourage and

embrace diversity, equity and inclusion, and believe it enhances our work towards one common goal: to transform the lives of the patients we aim to serve.

We view our employees as one of our most valuable assets in serving our mission. We compete in the highly competitive biotechnology industry, and attracting, retaining and developing a diverse group of talented employees is crucial to our strategy and our ability to compete effectively. We are committed to the development and retention of our workforce to support our research, product development, manufacturing and regulatory efforts and our plans for commercializing our wholly-owned product candidates if and when approved. There continues to be a shortage of skilled individuals with substantial experience discovering, developing and manufacturing genomic medicines, which is likely to continue. As a result, there continues to be competition between biopharmaceutical companies and academic institutions for individuals with these skills.

Our Values

We believe success comes when we align our core values with our mission to deliver genomic medicines that replace today's symptomatic treatments and transform patients' lives. Our core values are:

- Doing what's right for patients:
  - We collaborate with purpose and are driven by results that benefit patients.
  - We strive to put patient safety and quality of care first.
  - Patient needs drive our sense of urgency to deliver medicines.
  - We embrace our responsibility to pioneer the field of genomic medicine bioethically.
  - We take an inclusive approach to guide our drug development.
- Succeeding through teamwork:
  - We are driven by our shared vision that genomic medicine will transform the lives of patients and the field of healthcare.
  - We are a passionate and dedicated group of individuals who collaborate proactively and openly to execute and progress our business forward.
  - We define our priorities clearly, communicate them, and take collective accountability to deliver results for all stakeholders.
  - We are resilient and determined to succeed together because patients are depending on us.
- Innovating through smart decisions:
  - We courageously, relentlessly, and urgently pursue the journey of innovation to succeed in the field of genomic medicine.
  - We mine scientific possibilities with the goal of unlocking new treatment solutions for serious diseases.
  - We strive to achieve our business goals through agile, inclusive and efficient decision making.
  - We learn and grow from decades of scientific experience to develop therapies at the cutting edge of medicine.
  - We learn from failure, and seek to continuously improve performance, as part of the journey to achieve breakthroughs.
- Fostering belonging:
  - We develop shared goals that create a sense of belonging.
  - We are a company where diverse individuals can flourish, grow and develop their expertise while bringing their authentic selves to work.
  - We feel connected to our local communities, the environment in which we live and the patient communities we serve.
  - We come together to understand our scientific learnings and progress the evolution of our business.
  - We embrace diversity, equity and inclusion.
  - We are committed to nurturing diverse and inclusive environments to advance healthcare equity.

Our Management of Human Capital

Our Chief People Officer leads our human resources function with a focus on attraction and recruitment of candidates, leadership training and development, diversity and inclusion efforts, total rewards packages consisting of compensation and benefits, and employee engagement and retention. As of December 31, 2022, our global human resources function was comprised of 12 full time human resources professionals.

As of December 31, 2022, we had 478 full time employees located in the United States, France and the United Kingdom. Of these employees, 375 were located in the United States, primarily in the San Francisco Bay Area, 94 were located in Valbonne, France and the remaining nine were located near London, United Kingdom. Of these employees, 206 were primarily engaged in research and development activities, 176 were primarily engaged in technical operations and manufacturing and 96 were primarily engaged in general and administrative activities. We also engage the services of independent contractors and consultants as needed for special or temporary projects or specific expertise.

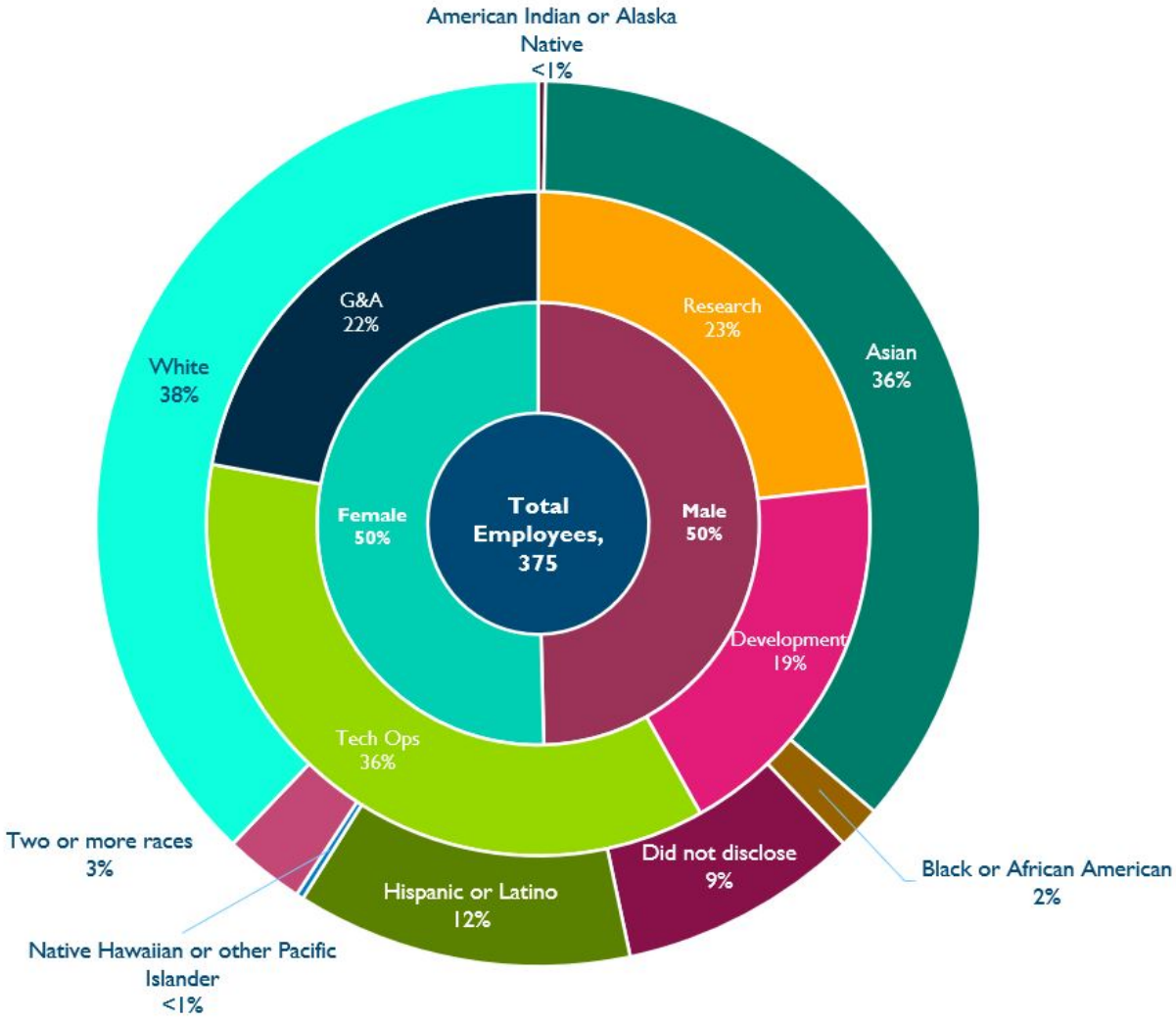
To manage our human resources, we track and report internally on key talent metrics including headcount by business unit and country, historical headcount growth, turnover, new hires and terminations, open roles and employee demographics including gender, race and ethnicity. Our senior executives use these metrics to assist with resource planning, recruitment and retention initiatives and the design of our compensation and benefits programs. We share these metrics quarterly with the Compensation Committee of our Board of Directors to assist it in fulfilling its duties to establish our enterprise compensation philosophy, administer our compensation and benefit plans, evaluate the performance of our executive officers and key employees and review and monitor management development and succession plans.

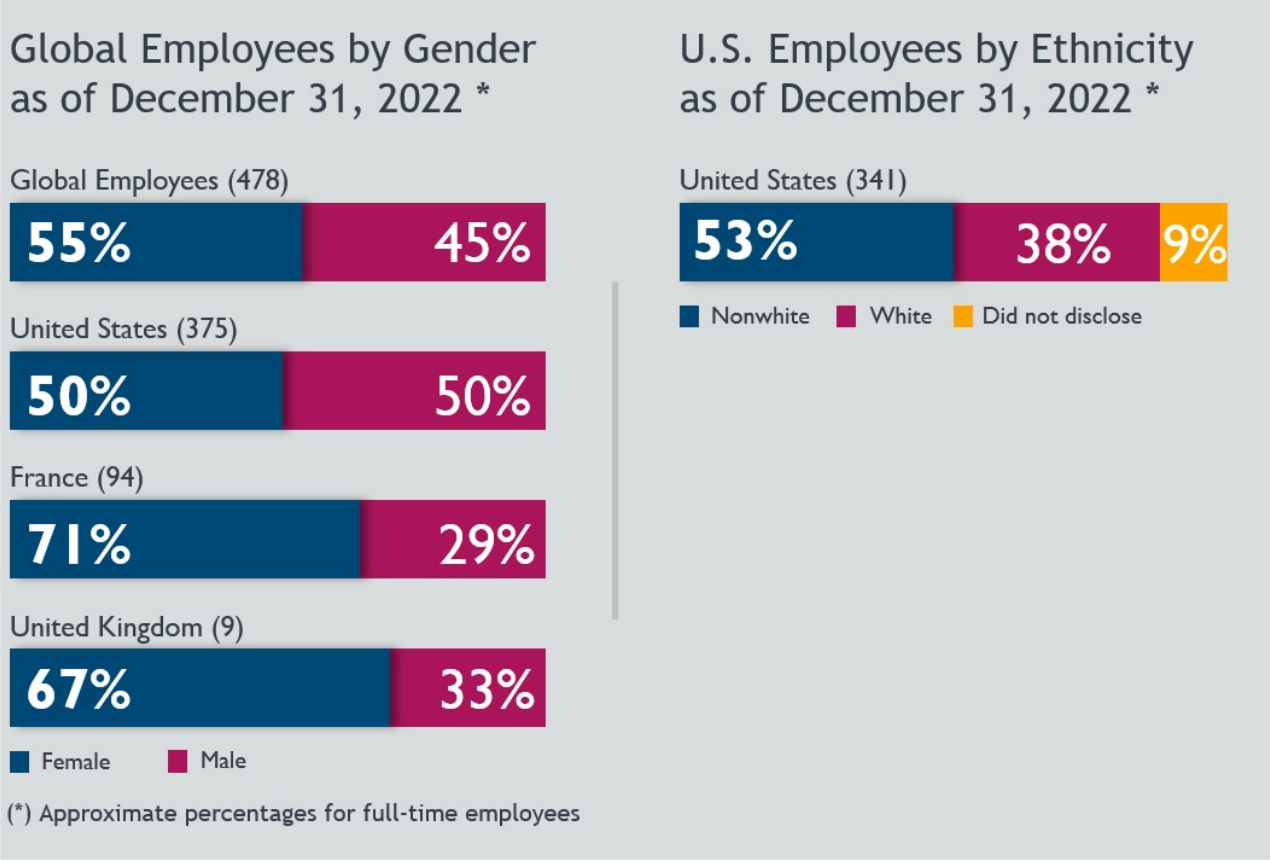
Our employees participate in a biannual employee engagement survey. The results of this survey continue to help us better understand the culture, work dynamics and overall commitment of our employees and to also identify areas of focus that will increase overall employee engagement. We were pleased with our participation rate of 74%, demonstrating favorable levels of employee engagement and commitment.

Our Commitment to Diversity, Equity and Inclusion

We strongly believe in a diverse workplace where all Sangamo employees can thrive in an inclusive environment free from discrimination, harassment, bias and prejudice. We aim to treat all individuals with respect and dignity and to provide all Sangamo employees with equal opportunity and fair treatment based on merit. By embracing diversity and inclusion, we create an organization committed to working together to develop innovative solutions in support of the Sangamo mission consistent with our values. At Sangamo, we cultivate a culture and environment where different backgrounds and perspectives are not only respected and heard, but also embraced and celebrated. Not only is a diverse, equitable and inclusive mindset and culture critical to an engaged and committed workplace, but it is also imperative in delivering innovative solutions for our patients.

The following depicts Sangamo's United States employee demographics, based on self-identification, as of December 31, 2022:





Within the human resources team, we have a Senior Program Manager whose time is fully dedicated to leading our Diversity, Equity and Inclusion, or DEI, efforts in partnership with our Chief People Officer and Chief Operations Officer. There is also a working group who identifies key areas of focus for the company to implement diversity initiatives. We have six employee resource groups, or ERGs, that are led by employees in partnership with an executive sponsor, and we have dedicated budgets for each of these ERGs so that they can make a specific impact in the areas of building and reinforcing community, leadership development and talent attraction. We are working on various partnerships with Life Science Cares, a non-profit organization with a mission of leveraging the resources of life science companies to help reduce the effects of poverty, and our Chief Operating Officer, D. Mark McClung, serves as a board member. We have also participated in the Bloomberg Gender Equality Index to better align our investments and initiatives with our employees.

Our Compensation and Benefits

Given the highly competitive nature of our industry and the importance of recruitment and retention to our success, we strive to provide our employees with what we believe is a very competitive and comprehensive total rewards package of compensation, benefits and development opportunities. This package includes at or above-market pay; healthcare benefits for employees and family members; a health savings account for eligible U.S. employees with above market employer contributions; generous paid time off benefits; family leave; bereavement leave; flexible work schedules; contributions to retirement and/or pension plans; a supplemental long term disability plan; mental health benefits and onsite gym access. In addition, we offer a monthly stipend for employees to spend on health and well-being. We also offer every full-time employee globally the benefit of equity ownership in Sangamo through stock option grants and/or restricted stock units. Our U.S. employees are also eligible to participate in an employee stock purchase plan, which offers the opportunity to purchase our common stock at a discount of at least 15%.

The COVID-19 Pandemic

Employee safety and wellbeing is of paramount importance to us in any year and continued to be of particular focus in 2022 in light of the continuing COVID-19 pandemic. In response to the pandemic, we have supported our employees and government efforts to curb the COVID-19 pandemic through safety and communication efforts and resources. These efforts will continue as needed pending shifts in the external and internal environments as a result of the pandemic.

Environment

Sangamo is headquartered in Brisbane, California, with research facilities in Richmond, California and European facilities in Valbonne, France and the United Kingdom. In house manufacturing operations are located within the Brisbane and Valbonne facilities. Sangamo's headquarters in Brisbane is LEED certified, meaning it meets the requirements of a green building set by the U.S. Green Building Council.

Trademarks and Tradenames

SANGAMO® and Better Therapeutics By Design® are our registered trademarks in the United States and Sangamo Therapeutics™ and SIFTER™ are our trademarks. All other trademarks or trade names referred to in this Annual Report on Form 10-K are the property of their respective owners.

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 Securities and Exchange Commission, or 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. In addition, the SEC maintains a website at www.sec.gov that contains reports, proxy and information statements and other information regarding issuers that file electronically with the SEC.

ITEM 1A – RISK FACTORS

Our business involves significant risks, some of which are described below. Before making investment decisions regarding our common stock, you should carefully consider these risks, as well as the other information in this Annual Report on Form 10-K, including our financial statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations." The occurrence of any of the events or developments described below could have a material adverse effect on our business, results of operations, financial condition, prospects and stock price. In such event, the market price of our common stock could decline, and you could lose all or part of your investment. In addition, there are additional risks not described below that either are not presently known to us or that we currently deem immaterial, and these additional risks could also materially impair our business, operations or market price of our common stock.

Risks Relating to Research, Development, Regulatory Approval and Commercialization of Our Product Candidates and Technologies

Our success depends substantially on clinical trial results demonstrating safety and efficacy of our product candidates to the satisfaction of regulatory authorities. We may be unable to obtain positive clinical trial results and regulatory approvals for any of our product candidates.

We are a clinical-stage biotechnology company with no approved products and no product revenues. We have ongoing clinical trials evaluating product candidates that use our platform technologies in gene therapy and cell therapy and we anticipate initiating additional clinical trials in the future on other product candidates. We are substantially dependent on the results of these clinical trials, and there is no guarantee that final results of clinical trials conducted on our product candidates now or in the future will demonstrate the safety and efficacy of any of our product candidates. In addition, none of our product candidates have obtained regulatory approval. Obtaining positive clinical trial results and regulatory approvals is expensive, lengthy, challenging and unpredictable and may never occur for any of our product candidates. If we fail to obtain positive clinical trial results and regulatory approvals for our product candidates, our anticipated revenues from our product candidates and our prospects for profitability would be adversely affected, which would likely cause the market price of our common stock to significantly decline.

Conducting clinical trials and obtaining regulatory approvals is complex and exposes our business to numerous risks, including potential unexpected costs and delays.

We must conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates to the satisfaction of regulatory authorities in order to obtain regulatory approvals necessary for commercialization. We have limited experience in conducting later stage clinical trials and may not possess the necessary resources and expertise to complete such trials. Clinical trials are expensive, lengthy and unpredictable. 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. Events that may delay or prevent successful or timely completion of clinical development and regulatory approval include, among others:

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

- delays in reaching agreement on acceptable terms with prospective clinical research organizations, or CROs, and clinical trial sites;
- delays in opening clinical trial sites or obtaining required institutional review board, or IRB, ethics committee or national competent authority approval at each clinical trial site, such as the delays we have experienced opening the clinical trial sites in the United Kingdom for our Phase 1/2 STAAR clinical study evaluating isaralgagene civaparvovec, our wholly-owned gene therapy product candidate for the treatment of Fabry disease, due to the COVID-19 pandemic;
- delays or interruptions in recruiting, screening and enrolling suitable patients to participate in our clinical trials and dosing enrolled patients, such as (i) the delays we have experienced in recruiting, screening and enrolling patients and experienced and continue to experience in dosing patients for our Phase 1/2 STAAR clinical study evaluating isaralgagene civaparvovec due to challenges related to the COVID-19 pandemic, including due to patients testing positive for COVID-19, patients reconsidering their participation in the study and the limited number of screening sites, among other reasons and (ii) the pause in dosing of additional patients in the Phase 3 AFFINE trial of giroctocogene fitelparvovec implemented by Pfizer in March 2022 and lifted in September 2022;
- the imposition of clinical holds by regulatory authorities on our clinical trials or those of our collaborators, such as the clinical hold imposed by the FDA on the Phase 3 AFFINE trial of giroctocogene fitelparvovec imposed in November 2021 and lifted in March 2022;
- delays in clinical trial activities due to the COVID-19 global pandemic, including delays associated with certain patients testing positive for COVID-19 prior to enrollment or dosing in the study, which have previously impacted clinical trial timelines for our Fabry and TX200 programs;
- delays or difficulties we may experience in enrolling and dosing the final patients in our Phase 1/2 PRECIZN-1 study evaluating BIVV003, our ZFN gene-edited autologous cell therapy product candidate for the treatment of sickle cell disease;
- failure by us, any CROs we engage or any other third parties to adhere to clinical trial requirements;
- failure to perform in accordance with the Good Clinical Practice and Good Laboratory Practice regulations of the FDA, or applicable comparable foreign regulations in the EU 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, or as a result of manufacturing or formulation changes to our product candidates;
- delays in having patients complete participation in a trial or return for post-treatment follow-up;
- clinical trial sites or patients dropping out of a trial;
- selections of clinical endpoints that require prolonged periods of clinical observation or analysis of the resulting data;
- occurrences of serious adverse events or other safety concerns associated with product candidates that are viewed to outweigh their potential benefits, result in approval delays or other regulatory restrictions, or harm our reputation;
- occurrences of serious adverse events or other safety concerns in clinical trials of the same class of agents conducted by other sponsors;
- failures to demonstrate that product candidates are safe and effective for their proposed indication;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- unexpected costs and expenses and lack of sufficient funding to develop our product candidates; and
- losses of licenses to critical intellectual properties.

We have not yet reached agreement with regulatory authorities on the complete development pathway for certain product candidates, and such authorities have the ability to change decisions or guidance with respect to approvable endpoints, particularly as the technology continues to develop in these areas. For example, we are aware of another company developing a gene therapy to treat hemophilia A that the FDA recommended complete its Phase 3 study and submit two-year follow-up safety and efficacy data on all study participants notwithstanding the company's contention that it and the FDA had previously agreed on the extent of data necessary to support a biologics license application, or BLA. While we and Pfizer anticipate pivotal data readouts for our Phase 3 AFFINE trial to be based on full analyses of all study participants, when the first 50 patients are twelve months past reaching a steady-state of FVIII expression, the FDA or other comparable foreign regulatory authorities

could determine that we need to treat more patients in this trial than expected or follow patients for longer than expected to generate the required data, or that we need to make other modifications to the trial, any of which could negatively impact the ability to complete the trial and seek regulatory approvals for giroctocogene fitelparvovec, which could in turn materially and adversely affect its competitive position and commercial viability and therefore our business, prospects and market price of our stock.

Due to the novelty of certain product candidates and their technologies, the endpoints needed to support regulatory approvals will likely be different from those originally anticipated. Any inability to successfully complete preclinical and clinical development of our product candidates, or complete such trials in the timeframes anticipated, could result in additional costs to us or impair our ability to generate revenues from product sales or achieve regulatory and commercialization milestones and royalties, or shorten any periods during which we may have exclusivity.

Even if a product candidate successfully obtains 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. Also, any regulatory approval of our product candidates, once obtained, may be withdrawn, varied or suspended. If we are unable to obtain and maintain regulatory approvals for our product candidates in one or more jurisdictions, or if any approval contains significant limitations, we would not be able to generate anticipated revenues and may struggle to become profitable, which would have an adverse effect on our business operations and financial condition.

Success in research and preclinical studies or early clinical trial results may not be indicative of results obtained in later trials. Likewise, preliminary, initial or interim data from clinical trials may be materially different from final data.

Results from research and preclinical studies or early clinical trials are not necessarily predictive of future clinical trial results, and preliminary, initial 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 trials despite demonstrating positive results in preclinical studies or having successfully advanced through initial clinical trials or preliminary stages of clinical trials. From time to time, we have and may in the future publish or report preliminary, initial or interim data. Preliminary, initial or interim data from our clinical trials and those of our collaborators 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. In this regard, such data may show initial evidence of clinical benefit, but as patients continue to be followed and more patient data becomes available, there is a risk that any therapeutic effects will not be durable in patients and/or will decrease over time, or cease entirely. Preliminary, initial or interim data also remain subject to audit and verification procedures that may result in the final data being materially different from such preliminary, initial or interim data. As a result, preliminary, initial or interim data should be considered carefully and with caution until the final data are available. For example, there can be no assurance that the FVIII levels shown in the updated data announced in December 2022 by Pfizer and us from the Phase 1/2 Alta study of giroctocogene fitelparvovec will persist in future follow-up or any other data from the Alta study or the Phase 3 AFFINE trial. Mean FVIII levels shown in the Alta study, after an initial peak, have trended downward from the time of treatment through each week of follow up. We cannot anticipate whether and to what extent this trend will continue downward over time. Similarly, there can be no assurance that the sustained elevated α-Gal A levels or the reduction of lyso-Gb3 levels observed in patients treated in the STAAR study will persist in future follow-up or in any other data from the STAAR study, or that such patients or any other future patients in the study, who are withdrawn from ERT will remain off ERT. In addition, patients in the STAAR study may experience more serious AEs, or SAEs. For this reason and potentially other reasons, giroctocogene fitelparvovec and isaralgagene civaparvovec may not ultimately demonstrate a durable, safe and effective clinical benefit to the satisfaction of regulatory authorities in the final results of the Alta study, the Phase 3 AFFINE clinical trial or Phase 1/2 STAAR study, as applicable, and even if satisfactory to regulatory authorities, such benefit may not be sufficient to yield a commercially-viable product.

There is no guarantee that any of our pending clinical trials will be successful. Many of our product candidates currently use our ZF technology platform, including ZF nuclease and ZF-transcriptional regulator-technologies, which has not yet yielded any approved therapeutic products. Moreover, many of our product candidates are preclinical and have never demonstrated any clinical benefit. In addition, our viral delivery systems continue to evolve and have not been used in any approved products. If our product candidates using our ZF technology platform and viral delivery systems are not able to demonstrate the safe, effective and durable results we are hoping to see in clinical trials, we may be forced to suspend or terminate development of some or all of our product candidates or seek alternative technologies to develop or deliver product candidates.

In addition, there is a high failure rate for product candidates proceeding through clinical trials. Many companies in the biopharmaceutical industry 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. Any such setbacks could adversely affect our business, financial condition, results of operations and prospects.

Our product candidates are subject to a lengthy and unpredictable regulatory approval process in each jurisdiction where approval is sought.

A regulatory authority such as the FDA, the European Commission or comparable foreign regulatory authorities must approve any human therapeutic product before it can be marketed in the jurisdiction it governs. The process for receiving regulatory approval is lengthy and unpredictable, and a product candidate may not withstand the rigors of testing under the process. Before commencing clinical trials in humans in the United States, we must submit an 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 EU, for example, an application for the approval of a clinical trial must be submitted for each clinical trial to each national competent authority and relevant ethics committee of EU Member States in which sponsor wishes to conduct the clinical trial. Only after an IND becomes effective and/or the clinical trial authorization has been obtained may clinical trials begin. See "Business—Government Regulation" for details regarding the regulatory approval processes applicable to our product candidates. While there is some overlap, the regulatory requirements to conduct clinical trials and seek marketing approval vary by jurisdiction. There is no guarantee that the safety studies and other data generated will be sufficient to permit us to conduct clinical trials in all jurisdictions where planned, or once generated, that such clinical trial data will be sufficient to obtain marketing approval in all jurisdictions in which we intend to seek such approval. If we are not able to obtain the necessary regulatory approvals to conduct our clinical trials and commercialize our product candidates, or if such approvals are delayed or suspended, our business, prospects and market price of our common stock would be adversely affected.

We may not be able to identify, qualify and enroll sufficient patients for our clinical trials or complete our clinical trials in a timely manner, which could delay or prevent us from proceeding with the development of our product candidates.

Identifying, qualifying and enrolling patients in clinical trials of our product candidates, and completing these clinical trials, is critical to our success. Patient enrollment and trial completion is affected by factors including:

- size of the patient population and process for identifying patients;
- design of the trial protocol;
- eligibility and exclusion criteria;
- perceived risks and benefits of the product candidate under study;
- perceived risks and benefits of genomic approaches to treatment of diseases;
- availability of competing therapies and clinical trials;
- potential additional delays related to the COVID-19 global pandemic, including the impact of certain patients testing positive for COVID-19 prior to enrolling or dosing in the study;
- delays or interruptions related to voluntary pauses of our clinical trials or those of our collaborators, such as the prior voluntary pause in March 2022 in enrolling and dosing additional patients in the Phase 3 AFFINE trial of giroctocogene fitelparvovec, which pause was lifted in September 2022, and the activation of trial sites;
- the imposition of clinical holds by regulatory authorities on our clinical trials or those of our collaborators, such as the prior clinical hold imposed by the FDA on the Phase 3 AFFINE trial of giroctocogene fitelparvovec, which hold has since been lifted, and the potential inability of Sangamo and our collaborators to lift clinical holds imposed by regulatory authorities in a timely manner or on acceptable terms, or at all;
- delays or difficulties we may experience in enrolling and dosing additional patients in our Phase 1/2 PRECIZN-1 study;
- severity of the disease under investigation;
- availability of genetic testing for potential patients;
- proximity and availability of clinical trial sites for prospective patients;
- required and desired characteristics of patients;
- ability to obtain and maintain patient consent;
- risk that enrolled patients will drop out before completion of the trial;
- patient referral practices of physicians; and
- ability to monitor patients adequately during and after treatment.

The timing of our clinical trials depends on our ability to recruit patients to participate as well as completion of required follow-up periods. There are also a number of other product candidates in development by our competitors, who compete for the same limited patient populations. If we are not able to enroll the necessary number of patients in a timely manner, we may not be able to complete our clinical trials on our desired timelines or at all, which could negatively impact the competitive position and commercial viability of our product candidates or delay or reduce the product revenues, milestone payments or royalty payments we expect to earn from our product candidates. For example, we have experienced delays and challenges in recruiting, screening, enrolling and dosing patients for our Phase 1/2 STAAR clinical study evaluating isaralgagene civaparvovec, our wholly-owned gene therapy product candidate for the treatment of Fabry disease, due to challenges related to the COVID-19 pandemic, patients testing positive for COVID-19, patients reconsidering their participation in the study and the limited number of screening sites, among other reasons. Our Phase 1/2 STEADFAST clinical study evaluating TX200 has experienced similar delays and challenges.

In addition, we and Pfizer also previously announced that some of the patients treated in the Phase 3 AFFINE trial of giroctocogene fitelparvovec have experienced FVIII activity greater than 150% following treatment, and that Pfizer had decided to voluntarily pause screening and dosing of additional patients in this trial to implement a proposed protocol amendment intended to provide guidelines for the clinical management of elevated FVIII levels. Subsequent to the voluntary pause, the FDA put this trial on clinical hold, which was subsequently lifted in March 2022. While the voluntary pause initiated by Pfizer was lifted, the trial re-opened, and recruitment, enrollment and dosing resumed, we cannot assure you that the dosing will be completed in a timely manner, or at all, or that the presentation of data from such trial will be published in a timely manner, if at all. Continued delays or additional pauses to the Phase 3 AFFINE trial could negatively impact the projected timelines for conducting and completing the trial and seeking regulatory approvals for giroctocogene fitelparvovec, which could in turn materially and adversely affect giroctocogene fitelparvovec's competitive position and commercial viability and therefore our business, prospects and market price of our common stock.

In addition, if fewer patients are willing to participate in our clinical trials because of negative publicity from adverse events related to genomic medicines, competitive clinical trials for similar patient populations or for other reasons, the timelines for conducting clinical trials of our product candidates and presenting clinical data may be delayed. These delays could result in increased costs, limitation or termination of clinical trials, and delays in product development timelines. If we are forced to expand to additional jurisdictions to address these challenges, it could impose additional costs, delays and risks. If we are not successful in conducting our clinical trials as planned, it would have an adverse effect on our business, financial condition, results of operations, prospects and market price of our common stock.

We may encounter difficulties in advancing product candidates from research programs to preclinical and clinical development.

We intend to advance our product candidates from research programs through preclinical development and to submit new INDs, applications for clinical trial approval and equivalent filings in other jurisdictions necessary to conduct human clinical trials evaluating our product candidates. The preparation and submission of applications to conduct clinical trials requires us to conduct rigorous and time-consuming preclinical testing and studies and prepare documentation relating to, among other things, the toxicity, safety, manufacturing, chemistry and clinical protocols 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 a product candidate and may fail to demonstrate consistency in the formulation of a product candidate. Our preclinical tests may produce negative or inconclusive results, which may lead us to decide, or which may lead regulators to require us, to conduct additional preclinical testing. If we cannot obtain positive results in preclinical testing, we may decide to abandon a product candidate altogether. In addition, our ability to complete and submit such applications to conduct clinical trials may depend on the support of our collaborators and the timely performance of their obligations under relevant collaboration agreements. If our collaborators are not able to perform such obligations or if they choose to slow down or delay the development of a product candidate, we may not be able to submit the clinical trial applications on a timely basis or at all. Furthermore, the submission of applications to conduct clinical trials involves significant cost and labor, and we may not have sufficient resources and personnel to complete the filing of all intended applications, which may force us to scale back the number of applications or forego potential applications that we believe are promising. Any delay, suspension or reduction of our efforts to pursue our preclinical and clinical development strategy could have an adverse effect on our business and cause the market price of our common stock to decline.

Special regulatory designations, such as RMAT or orphan drug designations, may not be available for our product candidates or may not lead to a faster development or regulatory review or approval process.

We have received RMAT designation for our product candidate to treat severe hemophilia A. Additionally, some of our product candidates, including our product candidate to treat Fabry disease, have also been granted Orphan Drug Designation by the FDA, and some have also been designated Orphan Medicinal Products by the EMA. Regulatory authorities in some jurisdictions, including the United States and the EU, may designate drugs for relatively small patient populations as

orphan drugs. For additional information regarding these special regulatory designations, see "Business—Government Regulation."

If we request such designations for our other current or future product candidates, there can be no assurances that the FDA, the European Commission or comparable foreign regulatory authorities will grant any of our product candidates such designations. Additionally, such designations do not guarantee that any regulatory agency will accelerate regulatory review of, or ultimately approve, those product candidates, nor does it limit the ability of any regulatory agency to grant such designations to product candidates of other companies that treat the same indications as our product candidates prior to our product candidates receiving marketing approval. Such designations can also be revoked. RMAT designation can be revoked if the criteria for eligibility cease to be met as clinical data emerges. Orphan drug exclusivity may be revoked if any regulatory authority 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.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the approved indications or 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 a product candidate has side effects or causes 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. For example, one patient in the STAAR study expansion phase experienced a Grade 3 SAE of shoulder enthesopathy in December 2022 requiring hospitalization that occurred 14 days following infusion of isaralgagene civaparvovec. The Principal Investigator and the Safety Monitoring Committee for the study assessed the SAE as possibly related to the isaralgagene civaparvovec treatment, and the SAE was reported to regulatory authorities. While the Safety Monitoring Committee has since determined that the study may proceed without modification, the patient remains enrolled in the STAAR study, and this event was reported to other investigators for awareness, possible adverse side effects in this or other studies, including additional SAEs, could develop in the future, which could delay or halt any further development or potential commercialization of the applicable product candidate.

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 payors 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 approved product may not gain market acceptance among physicians, healthcare payors, patients or the medical community. Market acceptance of approved products depends on a number of factors, including:

- the efficacy and safety of the product as demonstrated in clinical trials;
- the clinical indications and patient populations for which the product is approved;
- acceptance by physicians, treatment centers and patients of the product as a safe and effective treatment;
- the adoption of novel genomic therapies by physicians, hospitals and third-party payors;
- the potential and perceived advantages of the product over alternative treatments;
- the safety of the product seen in a broader patient group, including its use outside the approved indications;
- any restrictions on product use together with other medications;
- the prevalence and severity of any side effects;
- product labeling or product insert requirements of the FDA or other comparable foreign regulatory authorities;
- the timing of market introduction of the product as well as competitive products;
- the development of manufacturing and distribution processes for the product;

- 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 from the approved product, which would compromise our ability to become profitable.

Even if we are able to commercialize any approved products, such 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 them, 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. 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, which can affect demand for, or the price of, any approved product. Given the nature of the product candidates that we are developing, some patients may require treatment only one-time (e.g., single dose administration), and there is substantial uncertainty about the pricing structure for such products, and the level of coverage and reimbursement that will be available for a shift to single-dose treatment as compared to chronic therapy over a patient's lifetime. If other companies establish a new pricing structure or business model, including payment based on demonstration of long-term efficacy, our ability to price or obtain reimbursement for our products may be adversely affected. If such pricing structure or business model do not adequately fund the costs of our research and development, manufacturing and commercialization efforts, our business may be adversely affected.

In addition to uncertainty about the potential pricing structure for certain of our product candidates, cost containment is a recurrent trend in the healthcare industry. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for certain medications. 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. If reimbursement is not available or is available only at limited levels, we may be unable to successfully commercialize any product candidate for which we obtain regulatory approval. 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 an adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Many EU Member States periodically review their reimbursement procedures for medicinal products, which could have an adverse impact on reimbursement status. We expect that legislators, policymakers and healthcare insurance funds in the EU Member States will continue to propose and implement cost-containing measures, such as lower maximum prices, lower or lack of reimbursement coverage and incentives to use cheaper, usually generic, products as an alternative to branded products, and/or branded products available through parallel import to keep healthcare costs down, particularly due to the financial strain that the COVID-19 pandemic has placed on national healthcare systems of the EU Member States. These measures could include limitations on the prices we would be able to charge for product candidates that we may successfully develop and for which we may obtain regulatory approval or the level of reimbursement available for these products from governmental authorities or third-party payors. Further, an increasing number of EU and other foreign countries use prices for medicinal products established in other countries as "reference prices" to help determine the price of the product in their own territory. Consequently, a downward trend in prices of medicinal products in some countries could contribute to similar downward trends elsewhere.

Moreover, in order to obtain reimbursement for our products in some European countries, including some EU Member States, we may be required to compile additional data comparing the cost-effectiveness of our products to other available therapies. HTA of medicinal products is becoming an increasingly common part of the pricing and reimbursement procedures in some EU Member States, including those representing the larger markets. The outcome of an HTA will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU Member States. The extent to which pricing and reimbursement decisions are influenced by the HTA of the specific medicinal product currently varies between EU Member States. In December 2021, the EU HTA Regulation was adopted, which will enter into application in 2025 and is intended to harmonize the clinical benefit assessment of HTA across the EU. However, individual EU Member States will continue to be responsible for assessing non-clinical (e.g., economic, social and ethical) aspects of health technologies and making decisions on pricing and reimbursement. If we are unable to maintain favorable pricing and reimbursement status in EU Member States for product candidates that we may successfully develop and for which we may

obtain regulatory approval, any anticipated revenue from and growth prospects for those products in the EU could be negatively affected.

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. Also, there has been heightened governmental scrutiny recently over biopharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent Presidential executive orders, 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 biopharmaceutical products. 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. For a discussion of health reform activity and the current pricing framework, see "Business—Government Regulation—Healthcare Reform" and "Business—Government Regulation—Pricing, Coverage and Reimbursement."

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.

In addition, the policies of the FDA, the competent authorities of the EU Member States, the EMA, the European Commission and other comparable regulatory authorities with respect to clinical trials may change, and additional government regulations may be enacted. For instance, the regulatory landscape related to clinical trials in the EU recently evolved. The CTR, which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each EU Member State along with a harmonized assessment procedure, leading to a single decision for each EU Member State. Compliance with the CTR requirements by us and our third-party service providers, such as CROs, may impact our developments plans. It is currently unclear to what extent the UK will seek to align its regulations with the EU in the future. A decision by the UK not to closely align its regulations with the new approach that will be adopted in the EU may have an effect on the cost of conducting clinical trials in the UK as opposed to other countries and/or make it harder to seek a marketing authorization in the EU for our product candidates on the basis of clinical trials conducted in the UK.

If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may be impacted.

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 competent 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 required to comply with FDA rules and is subject to FDA review and periodic inspections, in addition to other potentially applicable federal and state laws, to ensure compliance with cGMP and adherence to commitments made in the BLA.

If we or a regulatory authority 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, product labeling, advertising and promotion for any approved product will be subject to regulatory requirements and continuing regulatory review. Failure to comply with such requirements, when and if applicable, could subject us to a number of actions ranging from warning letters to product seizures or significant fines, among other actions.

Any government investigation of alleged violations of laws or regulations 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 comply with EU and EU Member State laws that apply to the conduct of clinical trials, manufacturing approval, marketing authorization of medicinal products and marketing of such products, both before and after grant of the marketing authorization, or with other applicable regulatory requirements may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials, or to grant marketing authorization, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the marketing authorization, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties.

See "Business—Government Regulation—Post-approval Requirements" for more information.

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

We are exposed to the risk of fraud or other misconduct by our employees and contractors, 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. Misconduct by our employees and contractors 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 such 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, or comparable foreign programs, 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.

We may use our financial and human resources to pursue a particular research program or product candidate and fail to capitalize on other programs or product candidates that may be more profitable or for which there is a greater likelihood of success.

We have limited resources and may forego or delay pursuit of certain research programs or product candidates that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities or pursue collaborations rather than retain sole responsibility for development. Our current and future research and development programs for product candidates may not yield any commercially viable products. The evaluation of the commercial potential or target market for a particular product candidate is forward-looking and based upon assumptions involving, for example and not limited to, market evolution, advances in disease standard of care, competition and reimbursement. This reliance on assumptions means that, if our assumptions prove to be inaccurate or incomplete, we may pursue opportunities that end up having a number of competitors that are more advanced than our product candidates, or we may relinquish valuable rights to a product candidate through strategic collaboration, licensing or other royalty arrangements in cases where it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. For example, we recently made the strategic decision to halt further material investments in the BIVV003 program beyond completion of the Phase 1/2 PRECIZN-1 study in order to prioritize deployment of resources to our Fabry and TX200 programs. While we intend to launch a search for a collaboration partner who can progress this program to a potential Phase 3 trial, we may not be successful in doing so in a timely manner, on acceptable terms or at all, and as a result, we could miss valuable opportunities to capitalize on the potential of the BIVV003 program. We

may also allocate internal resources to a product candidate in a therapeutic area in which it would have been more advantageous to enter into a collaboration or that does not prove to have viable commercial opportunities. Any failure to use our financial and human resources efficiently could harm our business and operations.

ZF technology is novel and has never been used to develop any approved, commercially viable therapeutic products.

Our ZF technology is a novel technology which to date has not yielded any approved commercially viable therapeutic products, and there can be no guarantee that our product development efforts using ZF technology will be fruitful. We have invested heavily in development of this technology, and our failure to develop approved, commercially viable products using ZF technology would significantly limit our business and prospects and would adversely impact the market value of our common stock.

Risks Relating to Manufacturing

We recently completed the construction of several facilities for clinical trial supplies. We have limited experience manufacturing biopharmaceutical products, and there can be no assurance that we will be able to maintain compliant manufacturing facilities, build additional facilities and manufacture our product candidates as intended.

We expect to use both contract manufacturing organizations, or CMOs, and our own facilities to meet our projected needs for clinical trial supply. We operate an AAV manufacturing facility in Brisbane, California to manufacture Phase 1/2 clinical study supplies for our gene therapy product candidates, and in 2021 we completed construction of cell therapy manufacturing facilities in Brisbane, California and Valbonne, France to manufacture supplies for our cell therapy product candidates. Operationalizing these new facilities requires us to transition manufacturing processes and know-how of our product candidates from our CMOs to our own facilities. 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 evaluations intended to demonstrate the comparability of material previously produced by CMOs with that generated by our facilities. Although some of our employees have experience in the manufacturing of biopharmaceutical products from prior employment at other companies, we, as a company, have no prior experience in biopharmaceutical product manufacturing, and operating these facilities will require us to comply with complex regulations and to continue to hire and retain experienced scientific, quality control, quality assurance and manufacturing personnel. In addition, government approvals are required for us to operate manufacturing facilities and are time-consuming to obtain and maintain. As a manufacturer of biopharmaceutical products, we also will 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 will 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 facilities in compliance with cGMP, regulatory or other applicable requirements, resulting in potential negative consequences, including regulatory actions, which could undermine our ability to use these facilities 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.

The manufacture, storage and transport of our product candidates is complex, expensive, highly regulated and risky, which could hamper their commercial viability.

There are significant risks associated with manufacturing, storing and transporting our product candidates including, among others, cGMP compliance, cost overruns, technical problems with process scale-up, specialized facilities, process reproducibility, stability issues, lot consistency, yields and timely availability of highly specific raw materials. Even though product batches released for use in clinical trials undergo sample testing, some defects may only be identified following release. In addition, process deviations or unanticipated effects of approved process changes may result in these intermediate products not complying with stability requirements or specifications. Also, our product candidates must be stored and transported at temperatures within a certain range. If these environmental conditions deviate, our product candidates' remaining shelf-lives could be impaired or their efficacy and safety could be adversely affected, making them no longer suitable for use. Moreover, product candidates that are biologics involve complex processes, including the development of cell lines or cell systems to produce the biologic, with the challenge of significant variability. 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.

Moreover, manufacturing, storing and transporting our product candidates is subject to strict regulatory standards, which adds additional production risk. Even if efficacy and safety data from our clinical trials would otherwise support

regulatory approval of a product candidate, there is no assurance that we or our CMOs will be able to manufacture our product candidates to specifications at levels necessary to support or maintain regulatory approval by the FDA or other comparable foreign regulatory authorities.

Thus, there is no guarantee we will be successful in establishing a larger-scale commercial manufacturing process for our product candidates or obtaining the needed manufacturing capacity. Due to these manufacturing challenges, there is risk that some of our product candidates could be subject to inventory outages, reputational damage and product liability risks, and result in additional expense and delays to clinical trials and commercialization. Supply interruptions or shortages could result in potential negative impacts to our business, prospects and market price of our common stock.

If we use chemical, biological or 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 comply with these laws and regulations could result in fines, penalties and additional liabilities and restrictions on our operations.

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 in large part upon third-party CMOs to manufacture and supply drug product for our preclinical studies and clinical trials. Although we have in-house manufacturing facilities in Brisbane, California and Valbonne, France, these facilities will only manufacture limited quantities of our product candidates for our early-stage clinical trials. We intend to continue to rely on third parties for the manufacture of product candidates for later stage clinical trials, and for commercial-scale manufacturing for any approved product. The manufacture of biopharmaceutical products in compliance with the FDA's cGMP, or comparable foreign GMP regulations, requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of biopharmaceutical 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 conduct later-stage clinical trials could be jeopardized. Any delay or interruption in the supply of clinical trial materials could delay the completion of our clinical trials, increase the costs associated with developing our product candidates and, depending upon the period of delay, require us to commence new clinical trials at significant additional expense or terminate the clinical trials completely.

We and our CMOs must comply with cGMP requirements enforced by the FDA through its facilities inspection program and comparable foreign regulatory authorities. These requirements include, among other things, quality control, quality assurance and the maintenance of records and documentation. We and our CMOs may be unable to comply with these cGMP requirements and with other FDA, state and comparable 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, variation 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 trials, regulatory submissions, approvals or commercialization of our product candidates, entail higher costs or impair our reputation.

Our current agreements with our CMOs do not provide for the entire supply of the drug product necessary for all anticipated clinical trials or for full scale commercialization. If we and our CMOs 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 manufacturer is identified, which could also delay the development of, and impair our ability to commercialize our product candidates.

The number of third-party CMOs 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 CMOs, which could have an adverse effect on our business. New manufacturers 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 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 and third parties on which we rely may be adversely affected by natural disasters and catastrophic or other events outside of our control, and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster or event.

Natural disasters could severely disrupt our operations and our facilities, including our current manufacturing facilities in Brisbane, California and Valbonne, France and the manufacturing facilities of our CMOs, and any disruption would likely have a negative impact on our business, financial condition, results of operations and prospects. If a natural disaster, pandemic or epidemic, including the COVID-19 pandemic, political crisis, power outage or any other event that is out of our control occurred that prevented us or third parties on which we rely from using all or a significant portion of our or their facilities, that damaged critical infrastructure or that otherwise disrupted our or their operations, it may be difficult or, in certain cases, impossible for us to continue our business and operations 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 an adverse effect on our business, financial condition, results of operations and prospects. Such disasters or events occurring at facilities of third parties on which we rely could also negatively impact our business and operations.

Risks Relating to our Industry

Our product candidates are based on novel genomic medicine 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 genomic medicine, consisting of gene therapy, gene-edited cell therapy and genome engineering. 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.

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, or comparable foreign regulatory authorities, will require us to submit follow-up data regarding our clinical trial patients 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, or comparable foreign regulatory authorities, may revoke their 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 genomic medicines conducted by others may cause the FDA or other comparable foreign regulatory authorities to change the requirements for approval of our product candidates. The FDA and European Commission have only very recent and limited experience in the approval of in vivo gene therapy products. 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.

If we or our competitors develop, acquire, or market technologies or products that are more effective than ours, our financial condition and ability to successfully market or commercialize our product candidates or be profitable would be adversely affected.

The biopharmaceutical industry is highly competitive and subject to significant and rapid technological change. We are aware of several companies focused on other methods for editing cells, editing genes and regulating gene expression and a

growing number of commercial and academic groups pursuing the development of genome engineering technology. The field of genomic medicine is highly competitive, and we expect competition to persist and intensify in the future from a number of different sources, including biopharmaceutical companies, academic and research institutions, and government agencies that will seek to develop competing products as well as technologies that will compete with our ZF technology platform. For example, in genome engineering and gene therapy products, competing proprietary technologies with our product development focus include but are not limited to, recombinant proteins, other gene therapy/cDNAs, nuclease and base editing technologies, antisense therapeutics and RNA interference technologies, siRNA, RNAi and microRNA approaches, exon skipping, small molecule drugs, monoclonal antibodies, CRISPR/Cas technology and TALE proteins, meganucleases, and MegaTALs. A growing number of companies are also developing rival cell therapy technologies and product candidates. See "Business—Competition" for more information on the competition we may face.

Any products that we or our collaborators or strategic partners develop 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. ZF nucleases and ZF-TRs 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.

In addition to possessing competing technologies, our competitors include biopharmaceutical 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. Even if our product candidate is more effective, it may be disadvantaged if it is not first to market. In addition, any products that we develop may compete with existing products or services that are well established in the marketplace. Further, some of our product candidates in development are designed for use once. Any success in developing one-time use therapeutics could cause us to lose potential recurring revenues from therapeutics that are designed to be taken over a patient's lifetime.

The COVID-19 pandemic has adversely impacted and could continue to adversely impact our business and operations and the business and operations of our collaborators, manufacturers and other business partners.

We have experienced and continue to experience impacts from the COVID-19 pandemic on our business and operations and could continue to experience these or potentially more severe impacts as the pandemic evolves in the United States, France, the United Kingdom and locations of our clinical studies and trials, including the new sites for our STAAR study in Canada, Italy and Australia. For example, we have experienced periodic short-term disruptions to our onsite operations while addressing positive cases of COVID-19 in clinical trial patients, and our operations could experience longer term disruptions in the future in the event of a significant outbreak of COVID-19 among clinical trial patients. Moreover, from time to time, we have been required to reorganize and prioritize our resources to mitigate moderate supply constraints due to the impact of COVID-19. If our programs encounter longer-term disruptions, it could impact our ability to support our biopharmaceutical partners as contemplated in our collaboration agreements and could result in adjustments to our timelines, although we do not believe that the short-term disruptions to date have resulted in any such impacts.

Additionally, our Phase 1/2 STAAR clinical study previously experienced delays in its timeline due in part to COVID-19 impacts and the diversion of healthcare resources to fight the pandemic. For example, the April 2021 opening of the first clinical trial site in the United Kingdom for this study experienced a delay of approximately one year due to the significant prevalence of COVID-19 in the United Kingdom. Additionally, we have experienced delays in recruiting, enrolling and dosing patients for this study, due in part to the hesitation of patients to travel by plane to trial sites not within driving distance and to enter medical facilities during the pandemic and also due in part to trial sites prioritizing COVID-19 clinical care over research activities such as the STAAR study. The study has also experienced delays when certain patients have decided to take the COVID-19 vaccine or tested positive for COVID-19 prior to enrollment or dosing in the study. Moreover, we previously experienced some short-term delays in sourcing the necessary raw materials to manufacture supplies for the STAAR study and transporting clinical trial materials due to COVID-19 impacts. We estimate that these challenges set back our 2021 STAAR study timelines by approximately three to six months. Clinical timelines for this study could be revised again if COVID-19 impacts to our recruitment, screening, enrollment and dosing of patients and to our sourcing of raw materials for this study intensify because of vaccination delays, new COVID-19 variants or unexpected events.

In addition, our STEADFAST study had previously experienced delays in its timeline due to COVID-19 impacts related to manufacturing and technology transfer challenges with our CMOs and due to patients and donors testing positive for COVID-19. We estimate that these challenges set back our overall clinical study timeline in total by approximately three months. COVID-19 impacts may affect guidance on future dosing timelines.

With respect to our partnered programs, the timelines for the studies and trials managed by our collaborators are also subject to potential delay in the future if these studies and trials experience similar challenges that we have experienced and continue to experience in our STAAR and STEADFAST studies.

The extent to which the COVID-19 pandemic will impact our business, operations and financial condition, either directly or indirectly, will also depend on future developments that remain highly uncertain at the present time. These developments include the ultimate duration and severity of the pandemic, the impacts of new COVID-19 variants, travel restrictions, public health restrictions in the United States, France, the United Kingdom, Australia, Taiwan and other countries, business closures or business disruptions and the effectiveness and timeliness of actions taken in the United States, France, the United Kingdom, Australia, Taiwan and other countries to contain and treat the disease, including the effectiveness of vaccination programs. The surge of new variants of the virus has resulted and may in the future result in new or the return of prior orders and restrictions. Disruptions to our operations, and possibly more severe disruptions in the future that could arise due to the restrictions applicable in the places we operate or our industry generally or to us and our facilities specifically, could impede our ability to conduct research in a timely manner, comply with our research obligations to our collaborators and advance the development of our therapeutic programs. These delays and disruptions could result in adverse material impacts to our business, operating results and financial condition. As our understanding of events evolves and additional information becomes available, we may materially change our guidance relating to our revenues, expenses and timelines for manufacturing, clinical trials and research and development.

In addition, to the extent the COVID-19 pandemic continues to adversely affect our business and results of operations, it may also have the effect of heightening many of the other risks and uncertainties described in this "Risk Factors" section.

Negative public opinion and increased regulatory scrutiny of genomic medicines 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.

Genetically modified products are currently subject to public debate and heightened regulatory scrutiny. Gene therapy remains a novel technology, with only two *in vivo* gene therapy products approved for a genetic disease to date in the United States and only a few *in vivo* gene therapy products for genetic diseases approved to date in the EU. 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. For example, 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, whether or not the specific company was involved with retroviral gene transfer, or whether the specific company's clinical trials were placed on hold in connection with these events. Other adverse events could occur in the field of genomic medicine that could result in increased regulatory scrutiny, potential regulatory delays or negative impact on public perception genomic medicines, which could cause our stock price to decline.

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.

Even if the regulatory approval for genetically modified products developed using our technology is obtained, our success will also depend on public acceptance of the use of genetically modified products including medicines, 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. 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.

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

Healthcare providers, including 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. 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, transparency, health privacy and security and patients' rights and comparable foreign legislation are and will be applicable to our business. Outside the United States, interactions between pharmaceutical companies and health care professionals are also governed by strict laws, such as national anti-bribery laws of EU Member States, national sunshine rules, regulations, industry self-regulation codes of conduct and physicians' codes of professional conduct. If we fail to comply with these, or to comply with these adequately or appropriately, we could be subject to significant penalties.

For details regarding the restrictions under applicable federal and state healthcare laws and regulations that may affect our ability to operate see "Business—Government Regulation—Additional Regulation."

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. Scrutiny has also increased, 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. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. If our operations or 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 or applicable regulations, we and they could be subjected to significant civil, criminal and administrative enforcement actions, see "Business—Government Regulation—Additional Regulation."

Further, we are required to comply with domestic and international privacy and data security laws, such as the EU GDPR and the CCPA, which apply to the collection, use, disclosure, transfer, or other processing of personal data, including data we collect about trial participants in connection with clinical trials. Other states, such as Virginia, Colorado, Utah and Connecticut, have also passed comprehensive privacy and data security laws, and similar laws are being considered in several other states, as well as at the federal and local levels. Certain jurisdictions have enacted data localization and cross-border data transfer laws, which could make it more difficult to transfer information across jurisdictions. Existing mechanisms that may facilitate cross-border transfers of personal data may change or be invalidated. In particular, the EEA and the UK have significantly restricted the transfer of personal data to the United States and other countries whose privacy and data security laws they believe to be inadequate. If we are unable to implement a legal mechanism to ensure that our transfers of personal data from the EEA or the UK are lawful, we could face adverse consequences, including increased exposure to regulatory actions, substantial fines and injunctions against processing or transferring personal data, and could be required to increase our data processing capabilities in the EEA, the UK or elsewhere at significant expense. Restrictions on our ability to transfer personal data from the EEA, the UK or elsewhere could impact our clinical trial activities in the EEA or the UK and limit our ability to collaborate with CROs and other third parties. For more information regarding these regulations, see "Business—Government Regulation—Privacy Regulation."

Our obligations related to privacy and data security are quickly changing and becoming increasingly stringent, creating regulatory uncertainty. These obligations may be subject to differing applications and interpretations, which may be inconsistent or in conflict among jurisdictions. Preparing for and complying with these obligations requires us to devote significant resources. These obligations may also necessitate changes to our information technologies, systems and practices and those of third parties upon which we rely. Moreover, despite our efforts, our personnel or third parties upon which we rely may fail to comply with such obligations, which could negatively impact our business operations and compliance posture.

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 or our third-party partners to comply with laws, regulations, policies, legal or contractual obligations, industry standards or regulatory guidance relating to privacy or data security, may result in significant consequences. These consequences may include, but are not limited to, governmental investigations and enforcement actions, litigation (including class-related claims), additional reporting requirements and/or oversight, fines and penalties, bans on processing personal data, orders to destroy or not use personal data, civil and criminal liability and adverse publicity. Any of these events could have a material adverse effect on our reputation, business or financial condition, including but not limited to interruptions or stoppages in business operations (including clinical trials), inability to process personal data

or to operate in certain jurisdictions, limited ability to develop or commercialize our products, expenditure of time and resources to defend any claim or inquiry or revision 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 inherent risks of product liability exposure related to the testing of our product candidates in human clinical trials and will face even greater product liability risks if we commercially sell any approved products. 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 clinical trial 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.

Unfavorable global economic conditions could have a negative impact on our operations, which could materially and adversely affect our business, financial condition, results of operations, prospects and market price of our common stock.

Financial instability or a general decline in economic conditions in the United States and other countries caused by political instability and conflict, including the ongoing conflict between Russia and Ukraine, and economic challenges caused by general health crises such as the COVID-19 pandemic have led to market disruptions, including significant volatility in commodity prices, credit and capital market instability and supply chain interruptions, which have caused record inflation globally. These macroeconomic factors could adversely affect our business, operations, operating results and financial condition as well as the price of our common stock and our ability to raise additional capital when needed on acceptable terms. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our stock price and could require us to delay or abandon clinical development plans. In addition, any or all of these effects could disrupt our and our collaborators' supply chains and adversely affect our and our collaborators' ability to conduct ongoing and future clinical trials of our product candidates. The extent and duration of the military action, sanctions and resulting economic, market and other disruptions are impossible to predict, but could be substantial. Any such disruptions may magnify the impact of the other risks described herein.

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. 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 ZF 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. We expect to continue to incur additional operating losses for the next several years as we continue to develop 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 will need substantial additional funding to execute our operating plan and continue to operate as a going concern. We may be unable to raise additional capital on favorable terms, if at all, which would harm or preclude our ability to develop our technology and product candidates and could delay or terminate some or all of our programs. Future sales and issuances of equity securities could also result in substantial dilution to our stockholders.

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 available cash, cash equivalents, and marketable securities as of December 31, 2022 will be adequate to fund our currently planned operations through the next 12 months from the date our consolidated financial statements in this Annual Report on Form 10-K are issued, our future viability beyond one year from the date of issuance of such consolidated financial statements is dependent on our ability to raise substantial additional capital to finance our operations. Our estimate as to how long we expect our existing cash, cash equivalents, and marketable securities to be able to continue to fund our operations is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Further, changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned.

In order to mitigate substantial doubt about our ability to continue as a going concern, we will be required to raise substantial additional capital to fund our operations. In this regard, we are actively seeking additional capital, including through public or private equity or debt financings, royalty financings or other sources, such as strategic collaborations. However, additional capital may not be available to us, on terms that are acceptable or at all. If adequate funds are not available to us on a timely basis, or at all, we will be required to take additional actions to address our liquidity needs, including cost preservation measures such as reducing operating expenses and delaying, reducing the scope of, discontinuing or altering our research and development activities.

If we raise additional capital through public or private equity offerings, including sales pursuant to our at-the-market offering program with Jefferies LLC, the ownership interest of our existing stockholders will be diluted, and such dilution may be substantial, and the terms of any new equity securities may have a preference over, and include rights superior to, our common stock. If we raise additional capital through royalty financings or other collaborations, strategic alliances or licensing arrangements with third parties, we may need to relinquish certain valuable rights to our product candidates, technologies, future revenue streams or research programs or grant licenses on terms that may not be favorable. If we raise additional capital through debt financing, we may be subject to specified financial covenants or covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or pursuing certain transactions, any of which could restrict our ability to commercialize our product candidates or operate as a business.

In addition, as we focus our efforts on proprietary human therapeutics, we will need to seek regulatory approvals of our product candidates from the FDA or other comparable foreign regulatory authorities, a process that could cost in excess of hundreds of millions of dollars per product. We may experience difficulties in accessing the capital markets 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. For example, our ability to raise additional capital may be adversely impacted by global economic conditions and disruptions to and volatility in the credit and financial markets in the United States and worldwide, such as has been experienced recently due in part to, among other things, the impacts of the COVID-19 pandemic and the ongoing conflict between Russia and Ukraine. 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 adversely affect our business and our ability to develop our technology and products candidates.

Our ability to use net operating losses to offset future taxable income may be subject to limitations.

Although a certain amount of our federal net operating loss carryforwards carry forward indefinitely (but are subject to a percentage limitation), a significant amount of our federal and all of our state net operating loss carryforwards will begin to expire, if not utilized, beginning in 2024 and 2029, respectively. The net operating loss carryforwards subject to expiration could expire unused and be unavailable to offset future income tax liabilities. In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50 percentage point change in its equity ownership value over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income or taxes may be limited. We have experienced an ownership change in the past and we may also experience additional ownership changes in the future as a result of subsequent shifts in our stock ownership, some

of which may be outside of our control. If an ownership change occurs and our ability to use our net operating loss carryforwards is materially limited, it would harm our future operating results by effectively increasing our future tax obligations. In addition, at the state level, there may be periods during which the use of net operating loss carryforwards is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. As a result, if we earn net taxable income, we may be unable to use all or a material portion of our net operating loss carryforwards and other tax attributes, which could potentially result in increased future tax liability to us and adversely affect our future cash flows.

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 market price of 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.

Risks Relating to our Reliance on Third Parties

If conflicts arise with our contractors, collaborators or other business partners, these conflicts may limit our ability to implement our strategies and may harm our business and prospects.

If conflicts arise with our contractors, collaborators or other business partners, the other party will likely act in its self-interest, which may limit our ability to implement our strategies. For example, some of our collaborators are conducting multiple product development efforts within each area that is the subject of their collaboration with us. Our collaborators may develop, either alone or with others, product candidates in related fields that are competitive with the product candidates that are the subject of their collaborations with us. Competing products, either developed by the collaborators or to which the collaborators or have rights, may result in the withdrawal of their support for our product candidates.

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

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.

Any of these conflicts could harm our product development efforts and otherwise adversely affect our business and prospects.

Our collaborators control certain aspects of our product development efforts, including certain of our clinical trials, which could result in unanticipated delays and other obstacles in the commercialization of our product candidates.

We depend on collaborators to design and conduct certain of our clinical trials for some of our product candidates. As a result, these clinical trials may not be conducted in the manner or on the timeline we desire, which may negatively impact our product development efforts. For example, Pfizer is the trial sponsor of the Phase 3 AFFINE trial of giroctocogene fitelparvovec and we depended on the efforts of Pfizer to diligently seek to lift the clinical hold on the Phase 3 AFFINE trial and resume the trial. Although dosing in the AFFINE trial has now resumed, we cannot guarantee that we will not experience future delays in this trial or that the trial will be completed on the anticipated timeframe or at all.

Our lack of control over aspects of product development in our agreements with Novartis, Biogen, Kite, Takeda and Pfizer 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 licensing our ZF technologies may decide to adopt alternative technologies or products or may be unable or unwilling to develop commercially viable products with our ZF technologies, which would negatively impact our revenues and our strategy to develop product candidates using ZF technologies.

Several of our collaborations leverage our ZF technology platform. These collaborators may elect to adopt alternative technologies in the future, which could decrease the value of our ZF technology platform and impede the development of product candidates using the platform. Additionally, because many of our collaborators 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 and develop our ZF technology platform and would delay or terminate the development of our product candidates using the platform. Further, our collaborators may elect not to develop product candidates arising out of our collaborations or not to devote sufficient resources to the development, manufacturing, marketing or sale of these product candidates. If they terminate the collaborations with us and we wish to continue developing the product candidates, we will be required to seek the support of other collaborators or develop the products ourselves. We may not be able to identify a suitable partner or negotiate a favorable collaboration agreement, and we may not have sufficient resources and expertise internally, to allow us to continue the development of these product candidates.

Commercialization of our technologies will depend, in part, on collaborations with other companies. If we are not able to find collaborators in the future or if our collaborators 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 market value of our common stock.

We do not have financial resources ourselves to fully develop, obtain regulatory approval for and commercialize our product candidates. We rely significantly on our collaborations with other biopharmaceutical companies to provide funding for our research and development efforts, including preclinical studies and clinical tests, and expect to rely significantly on such collaborations to provide funding for the lengthy regulatory approval processes required to commercialize our product candidates.

For example, we have collaborations with Novartis to develop product candidates to treat certain neurodevelopment disorders, including autism and intellectual disability; with Biogen to develop product candidates to treat tauopathies including Alzheimer's disease, alpha-synuclein related diseases including Parkinson's disease and other neurological diseases; and with Kite to develop product candidates to treat cancer; with Pfizer to develop product candidates to treat hemophilia A and amyotrophic lateral sclerosis and frontotemporal lobar degeneration linked to mutations of the C9ORF72 gene.

In June 2022, we completed the transition of the rights and obligations of Sanofi S.A, or Sanofi, under our prior collaboration agreement back to us. Although we expect to complete the Phase 1/2 PRECIZIN-1 study of BIVV003, our product candidate to treat SCD, we cannot guarantee that we will be able to complete this study in a timely manner or at all. Also, we do not expect to make additional material investments in our SCD program and, accordingly, do not plan to continue developing BIVV003 beyond completion of this study. Although we are currently seeking a potential collaboration partner to advance the development of BIVV003 beyond this study, we cannot guarantee that we will be able to successfully secure any such collaboration in a timely manner, on acceptable terms or at all. In such case, the continued development of BIVV003 could be further delayed or precluded altogether, in which case may choose to discontinue the BIVV003 program. Any further delays to or discontinuance of this program could have an adverse impact on our business, results of operations, financial condition and prospects.

If we are unable to secure additional collaborations or if our collaborators are unable or unwilling to diligently advance the development, regulatory approval and commercialization of our product candidates, our growth may slow and adversely affect our ability to generate funding for development of our technologies and product candidates. In addition, our collaborators may sublicense or abandon development programs with little advance notice, or we may have disagreements or disputes with our collaborators, which would cause associated product development to slow or cease. In addition, the business or operations of our collaborators may change significantly through restructurings, acquisitions, other strategic transactions that may negatively impact their ability to advance our programs.

Under typical collaborations, we 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 any commercialized products. Achieving these milestones will depend, in part, on the efforts of our collaborators, which we have no control over, as well as our own efforts. In addition, business combinations, changes in a collaborator's business strategy and financial difficulties or other factors could result in that collaborator abandoning or delaying development of any product candidates covered by our collaboration agreement with that collaborator. For example, the transition back to us of the rights and obligations of Sanofi related to BIVV003 and the related termination for convenience by Sanofi of our prior collaboration agreement followed a change in Sanofi's strategic direction to focus on allogeneic universal genomic medicine approaches rather than autologous personalized cell therapies. Further, if we fail or any collaboration partner fails to meet specific milestones, then the collaboration agreement may be terminated, which would preclude our ability to earn any additional milestone payments under that collaboration agreement and would reduce our revenues. In addition, even if a collaboration product candidate is successfully developed and approved for marketing by relevant regulatory authorities, if sales of the commercialized product fails to meet expectations, we could receive lower royalties than expected. In any event, the milestone and royalty payment opportunities associated with our collaborations involve a substantial degree of risk to achieve and may never be received. Accordingly, investors should not assume that we will receive all of the potential milestone payments provided for under our collaborations and it is possible that we may never receive any further significant milestone payments or any royalty payments under our collaborations.

Risks Relating to our Intellectual Property

Because it is difficult, time consuming and costly to obtain, maintain and enforce patent protections for our technologies and product candidates, and because third parties may have made inventions that are similar to ours, we may not be able to secure optimal patent protections of our technologies and product candidates.

Our commercial success may depend in part on obtaining, maintaining and enforcing patent protection for our technologies and product candidates and successfully defending any of our patents that may be challenged. Obtaining, maintaining and enforcing biopharmaceutical patents is costly, time consuming and complex, and we may not be able to file and prosecute all necessary or desirable patent applications in all desired jurisdictions, or maintain, enforce and license any patents that may issue from such patent applications, at a reasonable cost or in a timely manner or at all. 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 biopharmaceutical 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. In addition, future patent laws, regulations, rules, and court decisions may affect the scope, validity, enforceability, and associated remedies of our current and future patent claims. Accordingly, we cannot predict the breadth of claims that may issue from any patent applications that we own or license, nor are we able to predict whether any third-party patents might issue with claims that are relevant to our product candidates or technologies. Even if patents do successfully issue and even if such patents cover our technologies and product candidates, third parties may challenge their validity, enforceability or scope, which may result in such patents being narrowed, invalidated or deemed unenforceable. There is no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found, the existence of which could invalidate a patent or prevent a patent from issuing from a pending patent application. Furthermore, if third parties have made similar inventions, there are multiple ways they could impact the coverage of our own applications.

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.

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 conceive and/or reduce to practice 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;
- the laws, regulations, rules, or court decisions in the United States and foreign countries will not change or be interpreted in a way that modifies our patent rights or impacts our ability to enforce or maintain our patent rights; 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 research, development or 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, selling, offering to sell, or importing into the United States 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 costly, lengthy and distracting litigation with unpredictable results.

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.

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

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 means to extend this expected expiration date may be available. Regardless, 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 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, collaborators, partners 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 "If our information technology systems or data, or those of third parties upon which we rely, are or were compromised, we could experience adverse consequences, including but not limited to regulatory investigations or actions, litigation, fines and penalties, disruptions of our business operations and reputational harm." 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, collaborators, partners 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 an 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.

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 adversely affect our business, results of operations and financial condition.

We may not be successful in obtaining or maintaining necessary rights to product components, platforms 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 TX200 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, including from other companies and academic institutions, that we may consider attractive. Other companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. Once an intellectual property right that we desire is licensed to another company, we may be precluded from obtaining our own license to such rights.

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.

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 an 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 an adverse effect on our business, financial condition, results of operations and prospects. As an example, Sangamo France has exclusively licensed the right to the CAR for use in TX200 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 acquisition of Sangamo France.

We may be involved in patent or intellectual property lawsuits or similar disputes involving patents under our control or patents of third parties claiming infringement, which lawsuits could be expensive, time-consuming and impair or prevent development and commercialization activities.

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, declaratory judgment lawsuits, invalidity proceedings, interferences, oppositions, ex parte or inter partes reexaminations, post-grant reviews and inter partes review proceedings before the 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 third parties related to certain vector and vector manufacturing methods that are related to 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 valid and in force at the time of commercialization, we may need to challenge these patents, use or develop non-infringing alternatives 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 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 or hinder 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 or processes for manufacture or methods of use, 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. Moreover, because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates may infringe.

In some instances, third parties may allege that we are infringing their patents or other proprietary rights even if they are not competitors or have an associated business. Such litigants would bring such infringement actions or threats of action with the goal of obtaining settlement money from us instead of engaging in costly and time-consuming litigation.

Defense of these claims, regardless of their merit, would involve substantial litigation expense, could expose proprietary information 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.

Competitors may also 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. Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover our product candidate. 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 an 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 expose us to significant monetary damages, result in the loss of valuable intellectual property, 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.

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 unable to license gene transfer technologies that we may need to commercialize our ZF technology and potential products, if approved.

In order to regulate or modify a gene in a cell, the ZFP must be efficiently delivered to the cell. We have licensed certain gene transfer technologies for our ZFP in research, including AAV and mRNA technology, and 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. We have not fully 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. For example, in addition to our own vector manufacturing methods currently being used in our product candidates, 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. However, we may not be able to license the gene transfer technologies on reasonable terms, if at all, required to develop and commercialize our product candidates. The inability to obtain a license to use gene transfer technologies with entities that 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.

Risks Relating to our Business Operations

If our information technology systems or data, or those of third parties upon which we rely, are or were compromised, we could experience adverse consequences resulting from such compromise, including but not limited to regulatory investigations or actions, litigation, fines and penalties, disruptions of our business operations, reputational harm and other adverse consequences.

We are increasingly dependent on information technology systems and infrastructure to operate our business, which are large and complex. In the ordinary course of our business, we and the third parties upon which we rely, may collect, receive, store, process, generate, use, transfer, disclose, make accessible, protect, secure, dispose of, share and transmit large amounts of proprietary, confidential and sensitive information, including intellectual property, trade secrets and personal data (such as health-related 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 have access to our computer networks or our confidential information. Many of those third parties in turn subcontract or outsource some of their responsibilities to other third parties. Our ability to monitor third parties' information security practices is limited, and these third parties may not have adequate information security measures in place.

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. Attacks of this nature are increasing in their frequency, levels of persistence, sophistication and intensity. Threats to information systems and data are increasingly difficult to detect and come from a variety of sources, including traditional computer "hackers," threat actors, "hacktivists," organized criminal threat actors, personnel (such as through theft or misuse), sophisticated nation-states and nation-state-supported actors. Some actors now engage and are expected to continue to engage in cyber-attacks, including nation-state actors for geopolitical reasons and in conjunction with military conflicts and defense activities. During times of war and other major conflicts, we and the third parties on which we rely may be vulnerable to a heightened risk of these attacks, including retaliatory cyber-attacks, that could materially disrupt our systems, operations and supply chain. We and the third parties upon which we rely may be subject to a variety of evolving threats, including but not limited to social-engineering attacks (including through phishing attacks), malicious code (such as viruses and worms), malware (including as a result of advanced persistent threat intrusions), denial-of-service attacks (such as credential stuffing), credential harvesting, personnel misconduct or error, ransomware attacks, supply-chain attacks, software bugs, server malfunctions, software or hardware failures, loss of data or other information technology assets, adware, telecommunications failures, natural disasters (such as earthquakes, fires, floods), war, terrorism and other similar threats. Ransomware attacks are becoming increasingly prevalent and severe and can lead to significant interruptions in our operations, loss of data and income, reputational harm and diversions of funds. Extortion payments may alleviate the negative impact of a ransomware attack, but we may be unwilling or unable to make such payments due to, for example, applicable laws or regulations prohibiting such payments. In addition, the effects of the COVID-19 pandemic and our updated work from home policies have intensified our dependence on information technology systems and could increase our cybersecurity risk as many of our critical business activities are currently being conducted remotely utilizing network connections, computers and devices outside our premises or network and our increased reliance on personnel working from home, while in transit and in public locations.

Any of the previously identified or similar threats could cause a data security incident or other interruption of our, our third-party vendors' and/or business partners' information technology systems that 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 and reputational harm to us. While we have implemented security measures designed to protect against data security incidents, there can be no assurance that these measures will be effective. We have not always been able in the past and may be unable in the future to detect vulnerabilities in our information technology systems because such threats and techniques change frequently, are often sophisticated in nature and may not be detected until after a data security incident has occurred. For example, in April 2018, we announced a data security incident involving the compromise of a senior executive's company email account. Our investigation of the incident did not reveal any evidence that our systems were otherwise compromised in connection with the incident or that personal data about patients or other individuals besides the executive were accessed or disclosed. 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. Any litigation or regulatory review or investigation arising from this incident could result in significant legal exposure to us. A security incident or other interruption could also 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 are 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 delay in the discovery of an attack may result in increased expense and may harm our reputation. Any security incident or interruption that we, or a third-party upon which we rely, experience (including the company email incident described above) could lead to adverse consequences, including government enforcement actions (for example, investigations, fines, penalties, audits and inspections), additional reporting requirements and/or oversight, restrictions on processing data (including personal data), litigation (including class claims), indemnification obligations, harm to our reputation, monetary fund diversions and financial loss. Applicable data privacy and security obligations may require us to notify relevant stakeholders of security incidents. Such disclosures are costly, and the disclosures or the failure to comply with such requirements could lead to adverse consequences. 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. We may expend significant resources or modify our business activities in an effort to protect against security incidents or other interruptions. Further, we may experience delays in developing and deploying remedial measures designed to address any such identified vulnerabilities. Our contracts may not contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages or claims related to our data privacy and security obligations. While we may be entitled to damages if our third-party partners fail to satisfy their privacy or data security-related obligations to us, any award may be insufficient to cover our damages, or we may be unable to recover such award.

Additionally, we cannot be sure that our insurance coverage, if any, will be adequate or sufficient to protect us from or mitigate liabilities arising out of our privacy and security practices, that such coverage will continue to be available on commercially reasonable terms, or at all, or that such coverage will pay future claims.

We have business operations in France and the United Kingdom, which exposes us to additional costs and risks.

Our business operations in France and the United Kingdom subject us to certain additional costs and risks associated with doing business outside the United States, including:

- the increased complexity and costs inherent in managing international operations in geographically disparate locations;
- challenges of complying with diverse regulatory, financial and legal requirements, which are subject to change at any time;
- potentially adverse tax consequences, including changes in applicable tax laws and regulations;
- potentially costly trade laws, tariffs, export quotas, custom duties or other trade restrictions, and any changes to them;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- 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;
- natural disasters, political and economic instability, including wars, terrorism and political unrest, including the conflict between Russia and Ukraine, outbreak of health epidemics, including the COVID-19 pandemic, and the resulting global economic and social impacts;
- workforce uncertainty in countries where labor unrest is more common than in the United States; and
- differing laws and regulations relating to data security and the unauthorized use of, or access to, commercial and personal information.

In addition, our international operations in France and the United Kingdom expose us to fluctuations in currency exchange rates between the Euro and the U.S. dollar and between the Pound Sterling 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 an adverse effect on our financial condition and results of operations. In any event, difficulties resulting from these and other risks related to our operations outside of the United States 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 have experienced and may continue to experience difficulties in hiring, integrating and retaining qualified skilled employees

The growth and stability of our organization is critical to our ability to successfully achieve our strategic objectives. We may not be able to hire, integrate and retain a sufficient number of qualified employees with the appropriate levels of experience and skills to accomplish our growth objectives.

There currently is a shortage of skilled individuals with substantial experience discovering, developing and manufacturing genomic medicines, which is likely to continue. As a result, competition for these individuals is intense and the turnover rate can be high. We have experienced, and may continue to experience, difficulty hiring, integrating and retaining employees with these skills on acceptable terms given the competition among numerous biopharmaceutical companies and academic institutions for individuals with these skills. In addition, any negative or unexpected results in our preclinical or clinical trials or applications for marketing approval would make it more challenging to hire and retain qualified skilled employees. If we do not achieve our growth objectives, the progress of our research, development, manufacturing and regulatory efforts will slow down, which will adversely impact our business, financial condition, results of operations and prospects.

We are dependent on certain key members of our executive team and certain of our scientific, clinical development and manufacturing personnel, the loss of whose services may impede the progress of our research, development, manufacturing and regulatory efforts. For example, in 2022, our former Senior Vice President, Head of Development, resigned from Sangamo, and we have experienced similar departures in recent years among senior finance and legal employees to pursue opportunities at various other biotechnology companies. We could experience resignations of other executives and employees in the future given the intensity of the competition for talent in the biotechnology industry, particularly in the San Francisco Bay Area.

Additional resignations could result in more significant disruptions and threats to our growth and stability. While we have entered into employment agreements with each of our executive officers, any of them could leave our employment at any time, as all of our employees are "at will" employees. We do not have "key person" insurance on any of our employees.

We may not be successful in our efforts to discover, license or acquire new potential product candidates and may fail to capitalize on product candidates with a greater commercial opportunity or for which there is a greater likelihood of success.

If 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 discovery, in-licensing or acquisitions. We may be unable to do so. If we do identify potential product candidates for licensing or acquisition, we may be unable to reach acceptable terms with the licensors or sellers. Further, there may be risks and liabilities associated with the product candidates which our due diligence efforts fail to discover, that are not disclosed to us, that we inadequately assess, or that we are unable to manage effectively. Additionally, we may not realize the anticipated benefits of such licenses or acquisitions for a variety of reasons, including the possibility that the product candidates prove not to be safe or effective in clinical trials, that we are unable to successfully integrate the product candidate into our operations, or that the anticipated benefits will not otherwise be realized within the expected timeframe.

Additionally, because we have limited resources, we may forego or delay pursuit of opportunities with certain product candidates or indications that later prove to have greater commercial potential. Our spending on current and future research and development programs may not yield any commercially viable products. If we do not accurately evaluate the commercial potential for a particular product candidate, we may relinquish valuable rights to that product candidate through strategic collaboration, licensing or other arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. Alternatively, we may allocate internal resources to a product candidate in a therapeutic area in which it would have been more advantageous to enter into a collaboration arrangement.

Risks Relating to our Common Stock and Corporate Organization

Our stock price has been volatile and will likely continue to be volatile, which could result in substantial losses for investors, and could be influenced by public perception of genomic medicines and the biotechnology sector.

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 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 or 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 or technologies or significant contracts, acquisitions, strategic relationships, joint ventures or capital commitments;
- announcement of changes in business and operations by our collaborators, or changes to our existing collaboration agreements;
- changes in public opinions of genomic medicines;
- regulatory developments, including increased regulatory scrutiny of genomic medicines;
- changes by one or more of our securities analysts in recommendations, ratings or coverage of our stock;
- additions or departures of key personnel; and
- sales of our common stock or other securities by us, officers or directors, liquidation of institutional funds that comprised large holdings of our stock and decreases in our cash balances.

In addition, the stock markets have recently experienced extreme price and volume fluctuations that have affected and continue to affect the market prices of equity securities of many companies, which has resulted in decreased stock prices for many companies notwithstanding the lack of a fundamental change in their underlying business models or prospects. These

fluctuations have often been unrelated or disproportionate to the operating performance of those companies. Broad market and industry factors, including worsening macroeconomic conditions and other adverse effects or developments relating to the COVID-19 pandemic, and political, geopolitical, regulatory and other market conditions, may negatively affect the market price of shares of our common stock, regardless of our actual operating performance.

Actual or potential sales of significant amounts of shares of our common stock into the market could cause the market price of our common stock to fall or prevent it from increasing for numerous reasons.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. Our outstanding shares of common stock generally may be freely sold in the public market at any time to the extent permitted by Rules 144 and 701 under the Securities Act of 1933, as amended, or the Securities Act, or to the extent the issuance of such shares has already been registered under the Securities Act and are held by non-affiliates of ours. In 2022, the restrictions applicable to the sale of the shares that we issued to Biogen lapsed, and accordingly, may be sold in the public market without restriction. Further, we also agreed, subject to certain limitations, to register for resale under the Securities Act any of the shares we issued to Biogen. We have also filed registration statements registering the shares of common stock that we may issue under our equity compensation plans. Such shares can be freely sold in the public market upon issuance, subject to volume limitations and black-out periods applicable to affiliates. Additionally, we are party to a sales agreement with Jefferies LLC which permits us from time to time at our discretion to sell up to $325.0 million of shares of our common stock in the public markets at prevailing market prices. As of February 22, 2023, we have sold 22,953,199 shares of our common stock under the sales agreement for net proceeds of approximately $117.7 million.

In addition, in accordance with the guidelines specified under Rule 10b5-1 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and our policies regarding stock transactions, certain of our employees, executive officers and 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. Our employees, executive officers, directors and affiliated stockholders also may buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material, nonpublic information. Actual or potential sales of our common stock by such persons could be viewed negatively by other investors and could cause the price of our common stock to fall or prevent it from increasing.

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 designate exclusive forums for the adjudication of certain disputes, which could limit our stockholders' ability to bring claims in a judicial forum it finds favorable for disputes with us or our directors, officers, or employees.

Our amended and restated bylaws provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware or, if such court does not have subject matter jurisdiction, the federal district court of the State of Delaware, will be 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.

Our amended and restated bylaws further provide that a federal district court of the United State is the sole and exclusive forum for any complaint asserting a cause of action arising under the Securities Act of 1933, as amended. These provisions further provide 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 these provisions.

These provisions 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 any of these provisions 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 87,700 square feet of office and research and development laboratory facilities in Brisbane, California, pursuant to a lease that expires in May 2029. We also lease approximately 59,485 square feet of research and office space, pursuant to a lease that expires in August 2031, and approximately 7,700 of office space, pursuant to a lease that expires in August 2026, in Richmond, California. We also lease approximately 26,600 square feet of office and research and development space in Valbonne, France, subject to leases that expire beginning in June 2025 through January 2030. We believe that our facilities are currently adequate to meet our needs. As we continue to expand our operations, we may need to lease or purchase additional facilities.

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 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."

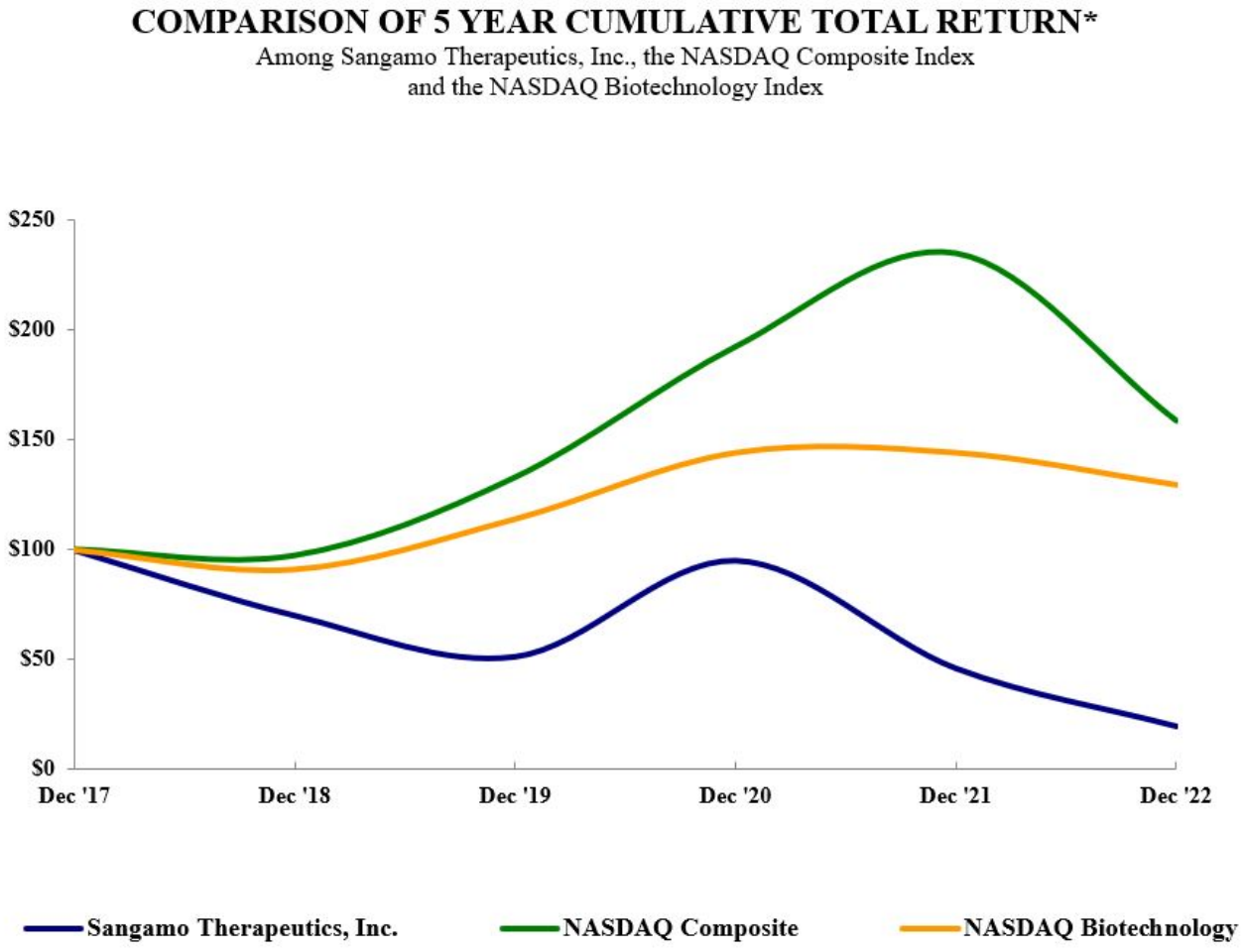
Holders

As of February 17, 2023, there were 60 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



*$100 invested on December 31, 2017 in stock or index, including reinvestment of dividends.
Fiscal year ending December 31.

The above Stock Performance Graph and related information shall not be deemed "soliciting material" or to be "filed" with the SEC nor shall such information be incorporated by reference into any future filing under the Securities Act or the Exchange Act, each as amended, except to the extent that we specifically incorporate it by reference into such filing.

ITEM 6 – [RESERVED]

Data responsive to Item 6 have not been presented in accordance with amendments to Item 301 of Regulation S-K contained in SEC Release No. 33-10890.

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, as amended, and Section 21E of the Exchange Act, as amended. These forward-looking statements include, without limitation, statements containing the words "anticipates," "believes," "continues," "could," "estimates," "expects," "intends," "may," "plans," "seeks," "should," "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 of this Annual Report on Form 10-K. You should read the following discussion and analysis along with the Consolidated Financial Statements and notes attached to those statements included elsewhere in this report.

In addition, the section of this "Management's Discussion and Analysis of Financial Condition and Results of Operations" generally discusses 2022 and 2021 items and year-to-year comparisons between 2022 and 2021. Discussions of 2020 items and year-to-year comparisons between 2021 and 2020 are not included in this Annual Report on Form 10-K and can be found in "Management's Discussion and Analysis of Financial Condition and Results of Operations" in Part II, Item 7 of our Annual Report on Form 10-K for the fiscal year ended December 31, 2021, filed with the SEC on February 24, 2022.

Overview

We are a clinical-stage genomic medicine company committed to translating ground-breaking science into medicines that transform the lives of patients and families afflicted with serious diseases. We plan to deliver on this mission through development of our clinical and preclinical product candidates, leveraging our novel science and our in-house manufacturing capabilities.

Our current clinical-stage product candidates are:

- Isaralgagene civaparvovec, also known as ST-920, our wholly-owned gene therapy product candidate for the treatment of Fabry disease, is currently being evaluated in our Phase 1/2 STAAR clinical study, and we are progressing plans for a potential Phase 3 clinical trial;
- TX200, our wholly-owned Chimeric Antigen Receptor, or CAR, engineered regulatory T cell, or CAR-Treg, cell therapy product candidate for the prevention of immune-mediated rejection in HLA-A2 mismatched kidney transplantation, is currently being evaluated in our Phase 1/2 STEADFAST clinical study;
- Giroctocogene fitelparvovec, also known as SB-525, a gene therapy product candidate for the treatment of moderately severe to severe hemophilia A, is currently being evaluated in the registrational Phase 3 AFFINE clinical trial. We are developing giroctocogene fitelparvovec with our collaborator Pfizer Inc., or Pfizer; and
- BIVV003, our zinc finger nuclease, or ZF nuclease, gene-edited cell therapy product candidate for the treatment of sickle cell disease, or SCD, is currently being evaluated in our Phase 1/2 PRECIZN-1 clinical study. BIVV003 is a wholly-owned Sangamo program following the transition from Sanofi S.A., or Sanofi, to Sangamo in June 2022. As discussed below, we recently made the strategic decision to halt further material investments in the BIVV003 program beyond completion of the Phase 1/2 PRECIZN-1 study in order to prioritize deployment of resources to our Fabry and TX200 programs.

Our preclinical development is focused in two innovative priority areas: (i) CAR-Treg cell therapies for autoimmune disorders and (ii) genome engineering for neurological diseases. Indications for our preclinical programs include neurodevelopmental disorders, cancer, inflammatory bowel disease, or IBD, tauopathies and neurodegenerative diseases such as amyotrophic lateral sclerosis, or ALS, multiple sclerosis, or MS, and Huntington's disease, some of which we are developing with our collaborators Biogen MA, Inc. and Biogen International GmbH, which we refer to together as Biogen, Novartis Institutes for BioMedical Research, Inc., or Novartis, Pfizer, Takeda Pharmaceutical Company Limited, or Takeda, and Kite Pharma, Inc.

Our multiple collaborations with biopharmaceutical companies bring us important financial and strategic benefits and reinforce the potential of our research and development efforts and our ZF technology platform. They leverage our

collaborators' therapeutic and clinical expertise and commercial resources with the goal to bring our medicines more rapidly to patients. We believe these collaborations reflect the value of our ZF technology platform and will potentially expand the addressable markets of our product candidates. To date, we have received approximately $815.0 million in upfront licensing fees, milestone payments and proceeds from the sale of our common stock to collaborators, and have the opportunity to earn up to $6.7 billion in potential future milestone payments from our collaborations, in addition to potential product royalties.

We believe that our in-house manufacturing capacity provides us a competitive advantage. We currently operate an adeno-associated virus, or AAV, manufacturing facility in our Brisbane, California headquarters and cell therapy manufacturing facilities in Brisbane, California and Valbonne, France. Our manufacturing strategy is to provide greater flexibility, quality and control by building a balanced and necessary capacity achieved through our in-house manufacturing and contract manufacturing organization, or CMO, partnerships, investing in manufacturing processes and analytics and developing a strong supply chain.

For additional information regarding our business, see "Business" in Part I, Item 1 of this Annual Report on Form 10-K.

Recent Business Highlights

Fabry Disease

- On February 22, 2023, we announced updated preliminary clinical data from our Phase 1/2 STAAR study evaluating isaralgagene civaparvovec, or ST-920, a wholly owned gene therapy product candidate for the treatment of Fabry disease, in advance of our presentation at the 19th Annual WORLD*Symposium* on February 24, 2023. This announcement included data on the 13 patients treated with isaralgagene civaparvovec as of the cutoff date of October 20, 2022, including kidney biopsy data on two patients. Since the cutoff date, an additional four patients have been dosed in the Phase 1/2 STAAR study, resulting in a total of 17 patients dosed to date. A total of 20 sites are now active and recruiting. Progress in the study continues with additional male and female patients currently in screening.
- The Phase 1/2 STAAR study expansion phase is ongoing and preparations for a potential Phase 3 clinical trial actively progress. A Phase 3 trial start is anticipated by the end of 2023, depending on regulatory interactions, and dosing of the first patient may occur as early as the first part of 2024. The completion of dosing in the Phase 1/2 expansion phase is expected by the end of 2023 and is not expected to be a gating factor for the commencement of the Phase 3 trial.
- In December 2022, one patient in the study expansion phase experienced a Grade 3 serious adverse event, or SAE, of shoulder enthesopathy requiring hospitalization that occurred 14 days following infusion. The event has since fully resolved, and the patient remains enrolled in the study. The Principal Investigator and the Safety Monitoring Committee for the study assessed the SAE as possibly related to treatment, and the SAE was reported to regulatory authorities. The Safety Monitoring Committee has since determined that the study may proceed without modification, and this event was reported to other investigators for awareness.

Renal Transplant Rejection

- In March 2022, we dosed the first patient in our Phase 1/2 STEADFAST study evaluating TX200, our wholly-owned autologous HLA-A2 CAR Treg cell therapy product candidate treating patients receiving an HLA-A2 mismatched kidney from a living donor, with the second patient dosed in September 2022. The third patient has received their kidney transplant and their personalized TX200 cell therapy has been manufactured, with dosing expected early in the second quarter of 2023. Manufacturing and clinical activities for the second cohort are progressing and dosing of the fourth patient is anticipated in the summer of 2023. Additional patients are in pre-screening for potential enrollment in the study. Opportunities to accelerate the dose escalation scheme are being explored with regulators.

Hemophilia A

- In September 2022, the voluntary pause initiated by Pfizer on the Phase 3 AFFINE clinical trial of giroctocogene fitelparvovec, our investigational gene therapy for the treatment of moderately severe to severe hemophilia A, was lifted and the trial re-opened recruitment and resumed enrollment. Dosing to support primary analysis resumed in November 2022 and is expected to be completed by the end of the first quarter of 2023. A pivotal readout is expected in the first half of 2024, with Pfizer anticipating a biologics license application, or BLA, submission in the second half of 2024.
- In December 2022, we and Pfizer presented updated follow-up data from the Phase 1/2 Alta study of giroctocogene fitelparvovec at ASH. As of the September 6, 2022 cutoff date:
    - At 156 weeks, the five patients in the highest dose 3e13 vg/kg cohort had mean factor VIII (FVIII) activity of 25.5% via chromogenic clotting assay.

- In this cohort, mean annualized bleeding rate was 0.0 in the first year post-infusion and was 1.2 throughout the total duration of follow-up. All bleeding events occurred after week 69 post-infusion. Two patients experienced bleeding events necessitating treatment with exogenous FVIII. No participants in the highest dose cohort had resumed prophylaxis.
- Giroctocogene fitelparvovec continued to be generally well-tolerated.

Sickle Cell Disease

- In December 2022, we presented updated preliminary proof-of-concept clinical data from the Phase 1/2 PRECIZN-1 study of BIVV003, a ZF nuclease gene-edited cell therapy candidate in development with Sanofi, at ASH. As of the September 30, 2022 cutoff date, five of the six patients achieving successful target yields of HSPCs had been infused with BIVV003.
- For the first four patients dosed received BIVV003 produced using the initial manufacturing process:
  - The effects of BIVV003 infusion on total Hb and HbF levels were maintained up to 30 months.
  - Three of the four patients had stable engraftment of ZF nuclease-modified HSPCs, resulting in sustained elevated HbF levels greater than 30% and an absence of severe vaso-occlusive crisis, or VOCs, post-BIVV003 administration.
- Patient 5 received BIVV003 manufactured using improved methods that had been shown in internal experiments to increase the number of long-term progenitor cells in the final product.
- The HbF level of 45% and total Hb of 12.4 g/dL at week 26 post-infusion for Patient 5 in the latest sample collected post cutoff date were greater than the levels observed in Group 1 at week 26.
- Since presenting updated data at ASH, clinical and manufacturing activities in preparation for the dosing of patient 7, the Phase 3 trial design, the CMC package and other requirements have been agreed with the FDA. In addition, we have progressed additional manufacturing improvements which have the potential to further strengthen clinical outcomes and reduce manufacturing costs in a potential Phase 3 trial.
- We recently made the strategic decision to halt further material investments in the BIVV003 program beyond completion of the Phase 1/2 PRECIZN-1 study in order to prioritize deployment of resources to our Fabry and TX200 programs. We remain committed to completing the Phase 1/2 PRECIZN-1 study for BIVV003, and we expect to conclude dosing in the study using the funds already committed. We intend to launch a search for a collaboration partner who can progress this program to a potential Phase 3 trial.

Manufacturing

- We currently operate an adeno-associated virus, or AAV, manufacturing facility in our Brisbane, California headquarters and cell therapy manufacturing facilities in Brisbane, California and Valbonne, France.

Impacts of the COVID-19 Pandemic

We have experienced and continue to experience impacts from the COVID-19 pandemic on our business and operations and could continue to experience these or potentially more severe impacts as the pandemic evolves in the United States, France, the United Kingdom and locations of our clinical studies and trials, such as the new sites for our STAAR study in Canada, Italy and Australia. For example, we have experienced periodic short-term disruptions to our onsite operations while addressing positive cases of COVID-19 in clinical trial patients, and our operations could experience longer term disruptions in the future in the event of a significant outbreak of COVID-19. Moreover, from time to time, we have been required to reorganize and prioritize our resources to mitigate moderate supply constraints due to the impact of COVID-19. If our programs encounter longer-term disruptions, it could impact our ability to support our biopharmaceutical partners as contemplated in our collaboration agreements and could result in adjustments to our timelines.

Additionally, our Phase 1/2 STAAR clinical study evaluating isaralgagene civaparvovec has experienced and continues to experience delays in its timeline due in part to COVID-19 impacts. For example, the study has experienced delays when certain patients have tested positive for COVID-19 prior to enrollment or dosing in the study. Moreover, we had experienced some short-term delays in sourcing the necessary raw materials to manufacture supplies for the STAAR study and in transporting clinical trial materials due to COVID-19 impacts. We estimated that these challenges set back our initial STAAR study timelines by approximately three to six months. Clinical timelines for this study could be revised again if COVID-19 impacts to our recruitment, screening, enrollment and dosing of patients and to our sourcing of raw materials for this study intensify because of vaccination delays, new COVID-19 variants or unexpected events.

In addition, our STEADFAST study evaluating TX200, our wholly-owned CAR-Treg cell therapy product candidate for the treatment of kidney transplant rejection, has experienced delays in its timeline due to COVID-19 impacts related to manufacturing and technology transfer challenges with our CMOs and due to patients and donors testing positive for COVID-19. Our timelines for this study could be adjusted if COVID-19 impacts result in additional delays.

Going forward, we will continue to monitor the impact of COVID-19 on our operations, research commitments and clinical trials and those of our collaborators, clinical trial sites and CMOs. Disruptions to these operations, and possibly more severe disruptions in the future that could arise due to restrictions applicable in the places we operate or our industry generally or to us and our facilities specifically, could impede our ability to conduct research in a timely manner, comply with our research obligations to our collaborators and advance the development of our therapeutic programs. These delays and disruptions could result in adverse material impacts to our business, operating results and financial condition.

We do not anticipate any material negative impact on our financial condition in 2023 as a result of the COVID-19 pandemic. We do not currently anticipate any material impairments to the valuation of the financial assets or goodwill on our balance sheet as a result of the COVID-19 pandemic. We do not believe that the remote workplace arrangements we have implemented for our office-based employees have affected our financial reporting or control systems.

The extent to which the COVID-19 pandemic will impact our business, operations and financial condition, either directly or indirectly, will depend on future developments that remain highly uncertain at the present time. These developments include the ultimate duration and severity of the pandemic, the impacts of new COVID-19 variants, travel restrictions, new public health restrictions in the United States, France, the United Kingdom and other countries, business disruptions and the effectiveness and timeliness of actions to contain and treat the disease, including the effectiveness and timing of vaccination programs. As our understanding of events evolves and additional information becomes available, we may materially change our guidance relating to our revenues, expenses and timelines for manufacturing, clinical trials and research and development.

See the section titled “Risk Factors” included in Part I, Item 1A of this Annual Report on Form 10-K for additional information on risks and uncertainties related to the COVID-19 pandemic.

Certain Components of Results of Operations

Our revenues have consisted primarily of revenues from upfront licensing fees, reimbursements for research services, milestone achievements and research grant funding. We expect revenues to continue to fluctuate from period to period and there can be no assurance that new collaborations or partner reimbursements will continue beyond their initial terms or that we are able to meet the milestones specified in these agreements.

We have incurred net losses since inception and expect to incur losses for at least the next several years as we continue our research and development activities. To date, we have funded our operations primarily through the issuance of equity securities and revenues from collaborations and research grants.

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 product candidates from research stage through clinical trials. Pursuant to the terms of our collaboration agreements with Biogen, Kite Pharma, Inc., or Kite, and Novartis and our termination and transition agreement with Sanofi, certain expenses related to research and development activities will be reimbursed to us. The reimbursement funds to be received from Biogen, Kite, and Novartis will be recognized as revenue as the related costs are incurred and collection is reasonably assured. The reimbursement funds to be received from Sanofi will decrease our research and development expense.

General and administrative expenses consist primarily of salaries and personnel related expenses for executive, finance and administrative personnel, stock-based compensation expense, 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 and administrative expenses.

Critical Accounting Policies and Estimates

Our Consolidated Financial Statements and the related disclosures have been prepared in accordance with generally accepted accounting principles in the United States. The preparation of these Consolidated 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.

We believe our critical accounting policies and estimates relating to revenue recognition and valuation of long-lived assets including goodwill and intangible assets are the most significant estimates and assumptions used in the preparation of our Consolidated Financial Statements.

For a complete description of our significant accounting policies, see Note 1 – *Organization, Basis of Presentation and Summary of Significant Accounting Policies* in the accompanying notes to the Consolidated Financial Statements included in Part II, Item 8, "Financial Statements and Supplementary Data" of this Annual Report on Form 10-K.

Revenue Recognition

Our revenues are primarily derived from collaboration arrangements which primarily include licensing intellectual property and providing research and development services. We recognize revenue when our customers obtain control of promised goods or services in a contract for an amount that reflects the consideration we expect to receive in exchange for those goods or services.

For most of our arrangements, the licenses granted to our intellectual property are not distinct from providing related research and development services and such combined performance obligations are satisfied over time. Such agreements may also contain options for additional goods and services that are considered to be material rights. For these agreements, we are required to estimate a transaction price and then allocate such transaction price based on the estimated standalone selling price of each distinct performance obligation. Most of our performance obligations are delivered over time. We generally recognize revenue using measure of progress based on an input method (e.g., cumulative actual level of effort, which includes the value of actual time incurred by our researchers plus third-party cost reimbursements, relative to the total estimated level of effort to be incurred, or cumulative actual hours incurred relative to total estimated hours to be incurred) which we believe best depicts our satisfaction of the relevant performance obligation. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

Estimating the standalone selling price of material rights including their likelihood of exercise requires significant judgment. Estimating the measure of progress is also complex, involves significant judgment, and is affected by our estimates of the total costs to be incurred to satisfy the respective performance obligation. Changes in these estimates can have a material effect on our revenue recognition.

For a further description of our revenue recognition, see Note 4 – *Major Customers, Partnerships and Strategic Alliances* in the accompanying notes to the Consolidated Financial Statements included in Part II, Item 8, "Financial Statements and Supplementary Data" of this Annual Report on Form 10-K.

Valuation of Long-lived Assets including Goodwill and Intangible Assets

We review goodwill and indefinite-lived intangible assets for impairment at least annually or more frequently if events or changes in circumstances would more likely than not reduce the fair value these assets below their carrying values. As of December 31, 2022, no impairment of goodwill or indefinite-lived intangible assets was identified.

Long-lived assets, including property and equipment and finite-lived intangible assets, are reviewed for possible impairment whenever events or circumstances indicate that the carrying amount of such assets may not be recoverable. The evaluation is performed at the lowest level for which identifiable cash flows are largely independent of the cash flows of other assets and liabilities. Recoverability of these assets is measured by a comparison of the carrying amounts to the future undiscounted cash flows the assets are expected to generate from the use and eventual disposition. If such review indicates that the carrying amount of property and equipment and intangible assets is not recoverable, the carrying amount of such assets is reduced to fair value. We have not recorded any significant impairment charges during the years presented.

Results of Operations

Years Ended December 31, 2022, 2021 and 2020

Revenues

	Year Ended December 31, (in thousands, except percentage values)							
	2022	2021	Change	%	2021	2020	Change	%
Revenues	$111,299	$110,701	$ 598	1 %	$110,701	$118,192	$ (7,491)	(6)%

Revenues consisted of amounts earned from our collaboration agreements. We anticipate revenues over the next several years will be derived primarily from our collaboration agreements with Biogen, Novartis, Kite, and Pfizer.

Revenues remained consistent in 2022 compared to 2021. There were increases of $13.1 million and $1.8 million in revenues related to our collaboration agreements with Kite and Novartis, respectively. These increases were partially offset by

decrease of $13.9 million in revenue related to our collaboration agreement with Biogen, $0.2 million in revenue related to our license agreement with Sigma-Aldrich Corporation and $0.2 million in revenue from sublicense fees related to our agreement with Dow AgroSciences LLC.

Operating Expenses

	Year Ended December 31, (in thousands, except percentage values)							
	2022	2021	Change	%	2021	2020	Change	%
Operating expenses:								
Research and development	$249,898	$230,819	$ 19,079	8 %	$230,819	$180,647	$ 50,172	28 %
General and administrative	62,682	63,219	(537)	(1)%	63,219	67,097	(3,878)	(6)%
Total operating expenses	$312,580	$294,038	$ 18,542	6 %	$294,038	$247,744	$ 46,294	19 %

Research and Development Expenses

Research and development expenses consisted primarily of compensation related expenses, including stock-based compensation, laboratory supplies, preclinical and clinical studies, manufacturing clinical supply, contracted research, and allocated facilities and information technology expenses.

The increase of $19.1 million in research and development expenses in 2022 compared to 2021 was primarily driven by an increase of $10.9 million in facilities and information technology costs driven by overall cost increases and progress made on projects resulting in reassignment of additional space to our research and development departments, an increase of $7.1 million in preclinical, clinical and lab supply expenses due to the timing of our trials and increased activity primarily attributable to our collaborations and research programs, an increase of $1.9 million in compensation and other personnel costs as a result of increased headcount to support our programs, clinical trials and manufacturing operations, and an increase of $1.3 million in travel and entertainment expenses. These increases were partially offset by $2.1 million in reimbursement of certain research and development expenses by Sanofi. Stock-based compensation expense included in research and development expenses was $18.4 million and $19.5 million for the years ended December 31, 2022 and 2021, respectively.

The table below shows research and development expenses related to our clinical, preclinical and other research and development programs. As shown in the table below, clinical programs contributed $34.2 million of the increase in our research and development expenses, offset by a decrease of $14.0 million in our preclinical and research programs in 2022 as compared to 2021, primarily driven by timing of activities related to our wholly-owned programs.

	Year Ended December 31, (in thousands)	
Programs	**2022**	**2021**
Clinical programs:		
Fabry clinical programs	$ 67,351	$ 58,880
TX200 clinical programs	26,185	14,557
Sickle cell clinical programs	14,547	483
Subtotal	108,083	73,920
Preclinical and research programs:		
Wholly-owned programs and early research activities	103,160	99,297
CNS partner programs	28,247	47,418
Oncology partner programs	2,222	894
Others	—	38
Subtotal	133,629	147,647
Other research and development programs	8,186	9,252
Total research and development expenses	$ 249,898	$ 230,819

(*) The amount is related to dissolution of the repayment obligation of the grant from CIRM associated with the ST-400 clinical program which was discontinued in 2021. See Note 4 – *Major Customers, Partnerships and Strategic Alliances* in the accompanying notes to the Consolidated Financial Statements included in Part II, Item 8, "Financial Statements and Supplementary Data" of this Annual Report on Form 10-K.

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 clinical programs and if we are able to progress our earlier stage product candidates into clinical trials.

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.

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

General and administrative expenses consist primarily of compensation related expenses including stock-based compensation for executive, legal, finance and administrative personnel, professional fees, allocated facilities and information technology expenses, and other general corporate expenses.

The decrease of $0.5 million in general and administrative expenses in 2022 compared to 2021 was primarily driven by a decrease of $7.4 million in allocated costs attributable to reassignment of additional space to our research and development departments. This decrease was offset by an increase of $3.3 million in compensation and other personnel costs as a result of increased headcount, an increase of $1.8 million of legal and professional fees, an increase of $1.3 million in facilities and information technology costs, and an increase of $0.4 million in travel and entertainment expenses. Stock-based compensation expense included in general and administrative expenses was $13.2 million and $13.4 million for the years ended December 31, 2022 and 2021, respectively.

Interest and other income, net

Interest and other income, net was $9.4 million and $5.3 million for the years ended December 31, 2022 and 2021, respectively. The increase of $4.1 million in 2022 compared to 2021 was primarily driven by an increase of $3.5 million in interest income reflecting increases in market interest rates, a benefit of $3.0 million of employee retention credit under the Coronavirus Aid, Relief, and Economic Security Act, and an increase of $0.5 million in research tax credits earned by Sangamo France. These increases were partially offset by a decrease of $1.9 million related to fluctuations in foreign currency exchange rates and a net benefit of $1.2 million recorded in 2021 related to dissolution of the repayment obligation of a grant from California Institute for Regenerative Medicine associated with the discontinuation of the ST-400 program.

Income tax expense

Provision for income taxes was $0.4 million, $0.3 million, and $0.3 million for 2022, 2021 and 2020, respectively. The income tax expense for all years was due to foreign income taxes and partially offset by a foreign deferred tax benefit.

Beginning in 2022, the 2017 Tax Cuts and Jobs Act amended Section 174 to eliminate current-year deductibility of research and experimentation, or R&E, expenditures and software development costs, collectively, R&E expenditures, and instead require taxpayers to charge their R&E expenditures to a capital account amortized over five years (15 years for expenditures attributable R&E activity performed outside the United States). We generated a deferred tax asset for capitalized R&E expenditures for the year ended December 31, 2022, which is fully offset with a valuation allowance.

As of December 31, 2022, we had net operating loss carryforwards for federal and state income tax purposes of approximately $689.7 million and $312.0 million, respectively. The federal net operating loss generated before 2018 will begin to expire in 2023 and will keep expiring through 2037, if not utilized. Federal net operating losses generated from 2018 will

carry forward indefinitely. If not utilized, the state net operating loss carryforwards will begin to expire in 2029. We also have federal and state research tax credit carryforwards of $36.8 million and $26.1 million, respectively. The federal research credits will begin to expire in 2022, 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 U.S. federal taxes related to income in the near future.

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.

As of December 31, 2022, we had cash, cash equivalents, and marketable securities totaling $307.5 million compared to $464.7 million as of December 31, 2021. Our most significant use of capital was for employee compensation and external research and development expenses, such as manufacturing, clinical trials and preclinical activity related to our therapeutic programs. Our cash and investment balances are held in a variety of interest-bearing instruments, including U.S. government-sponsored entity debt securities, commercial paper securities, money market funds, corporate debt securities, asset-backed securities and certificates of deposit. Cash in excess of immediate requirements is invested in accordance with our investment policy with a view toward capital preservation and liquidity.

In August 2020, we entered into an Open Market Sale Agreement℠, or the sales agreement, with Jefferies LLC, providing for the sale of up to $150.0 million of our common stock from time to time in 'at-the-market' offerings under an existing shelf registration statement, of which $35.0 million remained available as of December 31, 2022. In December 2022, we entered into Amendment No. 2 to the Open Market Sale Agreement℠ which increased the aggregate offering price under the sales agreement by an additional $175.0 million. During the year ended December 31, 2022, we sold 19,300,743 shares of our common stock under the sales agreement for net proceeds of approximately $84.9 million. From January 1, 2023 to the date of this Annual Report on Form 10-K, we sold 1,644,524 shares of our common stock under the sales agreement for net proceeds of approximately $5.7 million.

Under Accounting Standards Codification, or ASC, Topic 205-40, *Presentation of Financial Statements—Going Concern*, we have the responsibility to evaluate whether conditions and/or events could raise substantial doubt about our ability to meet our future financial obligations as they become due within twelve months after the date that the consolidated financial statements included in this Annual Report on Form 10-K are issued. We have identified several potential actions including cost preservation measures that would be initiated in a timely manner to address our liquidity needs, as follows:

- Deferral and reprioritization of certain research and development programs that would involve reduced program and headcount spend;
- Pause on any new hiring and reduction in ancillary expenses such as travel and recruitment expenses; and
- Reduction in non-critical capital and operating expenditures including additional equipment, lab improvements, efficiency projects, and business support spend.

We believe management's plans, as described above, sufficiently alleviate the risk of substantial doubt about our ability to continue as a going concern for at least twelve months from the date that the consolidated financial statements included in this Annual Report on Form 10-K are issued.

We will be required to raise additional capital to fund our operations and support our product development endeavors. In this regard, we are actively seeking substantial additional capital, including through public or private equity or debt financings, royalty financings or other sources, such as strategic collaborations. However, additional capital may not be available to us, on terms that are acceptable or at all. If adequate funds are not available to us on a timely basis, or at all, we will be required to take additional actions to address our liquidity needs, including cost preservation measures such as reducing operating expenses and delaying, reducing the scope of, discontinuing or altering our research and development activities. If we raise additional capital through public or private equity offerings, including sales pursuant to our at-the-market offering program with Jefferies LLC, the ownership interest of our existing stockholders will be diluted, and such dilution may be substantial, and the terms of any new equity securities may have a preference over, and include rights superior to, our common stock. If we raise additional capital through royalty financings or other collaborations, strategic alliances or licensing arrangements with third parties, we may need to relinquish certain valuable rights to our product candidates, technologies, future revenue streams or research programs or grant licenses on terms that may not be favorable. If we raise additional capital

through debt financing, we may be subject to specified financial covenants or covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or pursuing certain transactions, any of which could restrict our ability to commercialize our product candidates or operate as a business. In addition, management's planned cost reductions are intended to reduce our operating expenses and optimize our cash resources. Based on the timing of these cost reduction plans, we expect to start realizing the benefit of our efforts beginning in the third quarter of 2023; however, there can be no assurance that we realize the benefits of the cost reduction plans on the anticipated timeline, or at all.

Cash Flows

Operating activities

Net cash used in operating activities was $223.6 million in 2022, primarily reflecting our net loss of $192.3 million, a decrease in deferred revenues of $91.3 million, an increase in prepaid expenses and other assets of $4.9 million, and a decrease in lease liabilities by $2.2 million. These decreases were partially offset by $51.0 million of non-cash expenses related to stock-based compensation, depreciation and amortization, amortization of operating lease right-of-use assets, and net amortization of premium (discount) on marketable securities, an increase in accounts payable and other accrued liabilities of $13.3 million, and an increase in accounts receivable of $2.3 million.

Net cash used in operating activities was $233.3 million in 2021, primarily reflecting our net loss of $178.3 million, a decrease in deferred revenues of $84.2 million, a decrease in accounts payable and other accrued liabilities of $7.7 million, an increase in prepaid expenses and other assets of $7.2 million, a decrease for adjustment of CIRM award liability related to termination of the grant of $6.4 million, and a decrease in lease liabilities of $4.3 million. These decreases were partially offset by $53.4 million of non-cash expenses related to stock-based compensation, depreciation and amortization, amortization of operating lease right-of-use assets, and net amortization of premium (discount) on marketable securities, and an increase in non-current liabilities of $1.2 million.

Investing activities

Net cash provided by investing activities was $59.3 million in 2022, primarily related to maturities of marketable securities of $354.6 million and sales of marketable securities of $2.3 million, partially offset by purchases of marketable securities of $277.4 million and purchases of property and equipment of $20.2 million.

Net cash provided by investing activities was $248.2 million in 2021, primarily related to maturities of marketable securities of $602.9 million and sales of marketable securities of $6.9 million, partially offset by purchases of marketable securities of $338.2 million and purchases of property and equipment of $23.3 million.

Financing activities

Net cash provided by financing activities was $84.7 million in 2022, primarily related to $87.1 million of proceeds from the at-the-market offering, netted by offering expenses of $2.2 million, and an increase of $1.8 million related to proceeds from the issuance of common stock under our employee stock purchase plan, offset by a decrease of $2.1 million for taxes paid related to net share settlement of equity awards.

Net cash provided by financing activities was $32.9 million in 2021, primarily related to $27.9 million of proceeds from the at-the-market offering, netted by offering expenses of $0.8 million, an increase of $5.6 million related to proceeds from the exercise of stock options, and an increase of $3.4 million related to proceeds from the issuance of common stock under our employee stock purchase plan, offset by a decrease of $3.3 million for 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 and need to raise substantial additional capital. The effects of the current macroeconomic environment, including the COVID-19 pandemic, the effects of war in Ukraine, inflation, climate change, rising interest rates and other economic uncertainty and volatility, has resulted and may continue to result in significant disruption of global financial markets, which could impair our ability to access capital on terms that are acceptable or at all, and in turn could negatively affect our liquidity. Future capital requirements beyond the next 12 months will be substantial, and we need to raise substantial additional capital to fund the development, manufacturing and potential commercialization of our product candidates. In this regard, we are actively seeking substantial additional capital, including through public or private equity or debt financings, royalty financings or other sources, such as strategic collaborations. However, additional capital may not be available to us, on terms that are acceptable or at all. If adequate funds are not available to us on a timely basis, or at all, we will be required to take additional actions to address our liquidity needs, including cost preservation measures such as reducing operating expenses and delaying, reducing the scope of, discontinuing or altering our research and development activities, which could have a material adverse effect on our business.

As we focus our efforts on proprietary human therapeutics, we will need to seek FDA approvals of our product candidates, a process that could cost in excess of hundreds of millions of dollars per product. 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. 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, including the costs associated with such acquisitions and investments; and
- the costs of potential disputes and litigation.

Contractual Obligations

Our contractual obligations as of December 31, 2022 relate primarily to (i) operating leases consisting of base rents for facilities we occupy in Brisbane, California; Richmond, California; and Valbonne, France, (ii) purchase obligations related to manufacturing, facilities, and equipment, and (iii) license obligations for ongoing license maintenance fee associated with cancellable in-licensed patent agreements. These agreements are enforceable and legally binding and specify all significant terms, including fixed or minimum services to be used, fixed, minimum or variable price, and the approximate timing of the actions under the contracts. For more information regarding our contractual obligations and commitments as of December 31, 2022, see Note 7 – *Commitments and Contingencies* in the accompanying notes to the Consolidated Financial Statements included in Part II, Item 8, "Financial Statements and Supplementary Data" of this Annual Report on Form 10-K.

ITEM 7A – QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Our exposure to market risk relates to our cash, cash equivalents, and marketable securities. 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 and are classified as available-for-sale. The majority of these available-for-sale securities are short-term in nature and subject to minimal interest rate risk. Our investments currently consist of U.S. government-sponsored entity debt securities, commercial paper securities, corporate debt securities, asset-backed securities and certificates of deposit. 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 are carried at market value, which approximates cost. We do not use derivative financial instruments in our investment portfolio. If market interest rates were to increase or decrease by one hundred basis points, the fair value of our investment portfolio would increase or decrease by an immaterial amount.

Foreign Currency Exchange Risk

We have operations in the United States as well as in Europe. The functional currency of each foreign subsidiary is 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 our subsidiaries' 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, 2022 by approximately $3.3 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 United States and Europe. In 2022, we incurred foreign currency transaction losses of $3.1 million. A 10% unfavorable change in the Euro and U.S. dollar exchange rate on December 31, 2022 would have had an immaterial impact on foreign currency transaction losses for 2022.

We did not maintain any cash balances denominated in a foreign currency in the United States as of December 31, 2022.

ITEM 8 – FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

SANGAMO THERAPEUTICS, INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and the Board of Directors 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, 2022 and 2021, 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, 2022, 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, 2022 and 2021, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2022, 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, 2022, 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 February 22, 2023 expressed an unqualified opinion thereon.

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.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing separate opinions on the critical audit matter or on the accounts or disclosures to which it relates.

Revenue recognition for collaboration arrangements

Description of the Matter

The Company's contract revenues are derived from collaboration arrangements which primarily include licensing intellectual property and providing research and development services. As discussed in Note 1 of the consolidated financial statements, in determining the amount of revenue to be recognized as the Company 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; (iii) measurement of the transaction price, including the 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. Revenues are recognized over time by measuring progress towards satisfaction of the relevant performance obligation, using the input method (i.e., cumulative actual costs incurred relative to total estimated costs).

Auditing the Company's accounting for revenues under collaboration arrangements was complex primarily due to significant judgment involved in evaluating the standalone selling price of material rights including the likelihood of exercise, as well as the Company's estimates of the total costs required to complete each performance obligation and its periodic reassessment of the estimates of total costs expected to complete the performance obligations. Changes in these estimates can have a material effect on revenue recognized.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design, and tested the operating effectiveness of internal controls over the Company's process for accounting for new collaboration arrangements or modifications related to existing arrangements. For example, we tested management's controls over the determination of the standalone selling price of the material rights, including the likelihood of exercise as well as the Company's estimates of the total costs required to complete each performance obligation and its periodic reassessment of the estimates of total costs expected to complete the performance obligations.

Our audit procedures included, among others, inspecting the agreements and evaluating the identification of performance obligations. We tested the Company's estimates of standalone selling prices of identified material right performance obligations by performing inquiries of the research and development personnel responsible for the specific development projects, and inspecting the minutes of the relevant quarterly joint steering committee meetings to evaluate management's assumptions of the likelihood of the customers exercising the material rights. In addition, we performed sensitivity analyses over these assumptions used in the estimate of the standalone selling prices to evaluate the changes in the estimated standalone selling prices resulting from significant changes in the assumptions. To test the initial and subsequent remeasurement of the total costs required to complete each performance obligation, we performed inquiries of the research and development personnel responsible for the specific development projects, inspected the minutes of the relevant quarterly joint steering committee meetings to evaluate management's assumptions used in the Company's estimates of total expected costs by project, and evaluated changes in the total expected costs by project. We also performed sensitivity analysis of changes to the total expected costs to evaluate the changes in the total expected costs resulting from significant changes to the assumptions. We compared previous estimates of total expected costs by project to actual costs incurred, to assess the accuracy of the forecasts. We also tested the amount of cumulative actual costs incurred under each project and recalculated the resulting revenue recognized under the Company's models.

/s/ ERNST & YOUNG LLP

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

San Mateo, California
February 22, 2023

SANGAMO THERAPEUTICS, INC.

CONSOLIDATED BALANCE SHEETS

(in thousands, except share and per share amounts)

	December 31, 2022	December 31, 2021
ASSETS		
Current assets:		
Cash and cash equivalents	$ 100,444	$ 178,872
Marketable securities	177,188	197,676
Interest receivable	794	349
Accounts receivable	3,678	6,013
Prepaid expenses and other current assets	18,223	15,859
Total current assets	300,327	398,769
Marketable securities, non-current	29,845	88,169
Property and equipment, net	63,531	51,523
Intangible assets	50,729	53,760
Goodwill	37,552	39,702
Operating lease right-of-use assets	62,002	73,181
Other non-current assets	17,023	15,319
Restricted cash	1,500	1,500
Total assets	$ 562,509	$ 721,923
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 22,418	$ 9,759
Other accrued liabilities	16,007	11,577
Accrued compensation and employee benefits	21,506	20,840
Deferred revenues	51,780	85,711
Total current liabilities	111,711	127,887
Deferred revenues, non-current	109,377	166,776
Long-term portion of lease liabilities	38,986	44,055
Deferred income tax	6,270	6,645
Other non-current liabilities	1,207	1,217
Total liabilities	267,551	346,580
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, $0.01 par value, 5,000,000 shares authorized, and no shares issued or outstanding	—	—
Common stock, $0.01 par value; 320,000,000 shares authorized; 166,793,320 and 145,921,530 shares issued and outstanding at December 31, 2022 and 2021, respectively	1,668	1,459
Additional paid-in capital	1,450,239	1,334,138
Accumulated deficit	(1,148,545)	(956,267)
Accumulated other comprehensive loss	(8,404)	(3,987)
Total stockholders' equity	294,958	375,343
Total liabilities and stockholders' equity	$ 562,509	$ 721,923

See accompanying Notes to Consolidated Financial Statements.

SANGAMO THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS

(in thousands, except per share amounts)

	Year Ended December 31,		
	2022	**2021**	**2020**
Revenues	$ 111,299	$ 110,701	$ 118,192
Operating expenses:			
Research and development	249,898	230,819	180,647
General and administrative	62,682	63,219	67,097
Total operating expenses	312,580	294,038	247,744
Loss from operations	(201,281)	(183,337)	(129,552)
Interest and other income, net	9,432	5,346	8,775
Loss before income taxes	(191,849)	(177,991)	(120,777)
Income tax expense	429	306	345
Net loss	(192,278)	(178,297)	(121,122)
Net loss attributable to non-controlling interest	—	(11)	(126)
Net loss attributable to Sangamo Therapeutics, Inc. stockholders	$ (192,278)	$ (178,286)	$ (120,996)
Basic and diluted net loss per share attributable to Sangamo Therapeutics, Inc. stockholders	$ (1.25)	$ (1.23)	$ (0.90)
Shares used in computing basic and diluted net loss per share attributable to Sangamo Therapeutics, Inc. stockholders	154,345	144,568	134,449

See accompanying Notes to Consolidated Financial Statements.

SANGAMO THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS

(in thousands)

	Year Ended December 31,		
	2022	**2021**	**2020**
Net loss	$ (192,278)	$ (178,297)	$ (121,122)
Foreign currency translation adjustment	(4,606)	(8,351)	8,345
Net pension gain (loss)	786	(716)	(193)
Change in unrealized loss on marketable securities, net of tax	(597)	(339)	(284)
Comprehensive loss	(196,695)	(187,703)	(113,254)
Comprehensive loss attributable to non-controlling interest	—	(11)	(126)
Comprehensive loss attributable to Sangamo Therapeutics, Inc.	$ (196,695)	$ (187,692)	$ (113,128)

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 Capital	Accumulated Deficit	Accumulated Other Comprehensive (Loss) Income	Non-Controlling Interest	Total Stockholders' Equity
	Shares	Amount					
Balances at December 31, 2019	115,972,708	$ 1,160	$ 1,090,828	$ (656,985)	$ (2,449)	$ 185	$ 432,739
Issuance of common stock upon exercise of stock options and in connection with restricted stock units, net of tax	1,395,956	14	8,545	—	—	—	8,559
Issuance of common stock under employee stock purchase plan	274,382	3	2,012	—	—	—	2,015
Issuance of common stock in connection with the Biogen collaboration agreement, net of issuance costs	24,420,157	244	142,282	—	—	—	142,526
Stock-based compensation	—	—	25,708	—	—	—	25,708
Acquisition of additional shares of Sangamo France	—	—	—	—	—	(927)	(927)
Foreign currency translation adjustment	—	—	—	—	8,345		8,345
Net pension losses	—	—	—	—	(193)	—	(193)
Net unrealized loss on marketable securities, net of tax	—	—	—	—	(284)	—	(284)
Net loss	—	—	—	(120,996)	—	(126)	(121,122)
Balances at December 31, 2020	142,063,203	1,421	1,269,375	(777,981)	5,419	(868)	497,366
Issuance of common stock in connection with at-the-market offering, net of offering expenses	2,007,932	20	27,079	—	—	—	27,099
Issuance of common stock upon exercise of stock options and in connection with restricted stock units, net of tax	1,417,288	14	2,375	—	—	—	2,389
Issuance of common stock under employee stock purchase plan	433,107	4	3,366	—	—	—	3,370
Stock-based compensation	—	—	32,956	—	—	—	32,956
Acquisition of additional shares of Sangamo France	—	—	(70)	—	—	(64)	(134)
Foreign currency translation adjustment	—	—	—	—	(8,351)	—	(8,351)
Net pension losses	—	—	—	—	(716)	—	(716)
Net unrealized loss on marketable securities, net of tax	—	—	—	—	(339)	—	(339)
Buy-out of non-controlling interest	—	—	(943)	—	—	943	—
Net loss	—	—	—	(178,286)	—	(11)	(178,297)
Balances at December 31, 2021	145,921,530	1,459	1,334,138	(956,267)	(3,987)	—	375,343
Issuance of common stock in connection with at-the-market offering, net of offering expenses	19,300,743	193	84,676	—	—	—	84,869
Issuance of common stock upon exercise of stock options and in connection with restricted stock units, net of tax	994,097	10	(1,990)	—	—	—	(1,980)
Issuance of common stock under employee stock purchase plan	576,950	6	1,765	—	—	—	1,771
Stock-based compensation	—	—	31,650	—	—	—	31,650
Foreign currency translation adjustment	—	—	—	—	(4,606)	—	(4,606)
Net pension gains	—	—	—	—	786	—	786
Net unrealized loss on marketable securities, net of tax	—	—	—	—	(597)	—	(597)
Net loss	—	—	—	(192,278)	—	—	(192,278)
Balances at December 31, 2022	166,793,320	$ 1,668	$ 1,450,239	$ (1,148,545)	$ (8,404)	$ —	$ 294,958

See accompanying Notes to Consolidated Financial Statements.

SANGAMO THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

(in thousands)

	Year Ended December 31,		
	2022	**2021**	**2020**
Operating Activities:			
Net loss	$ (192,278)	$ (178,297)	$ (121,122)
Adjustments to reconcile net loss to net cash (used in) provided by operating activities:			
Depreciation and amortization	12,108	9,439	5,682
Amortization of (discount) premium on marketable securities	(1,242)	2,844	(825)
Amortization and other changes in operating lease right-of-use assets	8,454	8,199	7,687
Stock-based compensation	31,650	32,956	25,708
Gain on free shares	—	(18)	(63)
Net (gain) loss on disposal of property and equipment	—	(52)	222
Adjustment of CIRM award liability related to termination of the grant	—	(6,427)	—
Net changes in operating assets and liabilities:			
Interest receivable	(445)	686	(353)
Accounts receivable	2,335	(789)	31,685
Prepaid expenses and other assets	(4,909)	(7,175)	(10,411)
Accounts payable and other accrued liabilities	13,348	(7,664)	10,703
Accrued compensation and employee benefits	941	373	6,877
Deferred revenues	(91,331)	(84,202)	216,546
Lease liabilities	(2,249)	(4,340)	(3,761)
Other non-current liabilities	(9)	1,216	1,300
Net cash (used in) provided by operating activities	(223,627)	(233,251)	169,875
Investing Activities:			
Purchases of marketable securities	(277,391)	(338,159)	(570,779)
Maturities of marketable securities	354,587	602,885	314,570
Sales of marketable securities	2,260	6,870	—
Purchases of property and equipment	(20,171)	(23,278)	(14,714)
Purchase of additional Sangamo France shares	—	(119)	(704)
Net cash provided by (used in) investing activities	59,285	248,199	(271,627)
Financing Activities:			
Proceeds from at-the-market offering, net of offering expenses	84,869	27,099	—
Proceeds from issuance of common stock in connection with the Biogen collaboration agreement, net of issuance costs	—	—	142,526
Taxes paid related to net share settlement of equity awards	(2,104)	(3,258)	(765)
Proceeds from issuance of common stock under employee stock purchase plan	1,771	3,369	2,015
Proceeds from exercise of stock options	124	5,648	9,324
Net cash provided by financing activities	84,660	32,858	153,100
Effect of exchange rate changes on cash and cash equivalents, and restricted cash	1,254	(263)	(447)
Net (decrease) increase in cash, cash equivalents, and restricted cash	(78,428)	47,543	50,901
Cash, cash equivalents, and restricted cash, beginning of period	180,372	132,829	81,928
Cash, cash equivalents, and restricted cash, end of period	$ 101,944	$ 180,372	$ 132,829
Supplemental cash flow disclosures:			
Property and equipment included in unpaid liabilities	$ 6,539	$ 1,535	$ 4,569
Tenant improvement allowance included in contra-lease liability	$ 243	$ —	$ —
Buy-out of non-controlling interest	$ —	$ 943	$ —
Right-of-use assets obtained in exchange for lease obligations	$ —	$ 10,418	$ 1,333

See accompanying Notes to Consolidated Financial Statements

NOTE 1 – ORGANIZATION, BASIS OF PRESENTATION AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Organization and Description of Business

Sangamo Therapeutics, Inc. ("Sangamo" or "the Company") was incorporated in the State of Delaware in June 1995 and changed its name from Sangamo Biosciences, Inc. in January 2017. Sangamo is a clinical-stage genomic medicine company committed to translating ground-breaking science into medicines that transform the lives of patients with serious diseases.

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. For consolidated entities where the Company owns or is exposed to less than 100% of the economics, the Company records net loss attributable to non-controlling interests on its Consolidated Statements of Operations equal to the percentage of the economic or ownership interest retained in such entities by the respective non-controlling parties.

Liquidity, Capital Resources and Management's Plans

Sangamo is currently working on a number of long-term development projects that involve experimental technologies. The projects may require several years and substantial expenditures to complete and ultimately may be unsuccessful. In recent years, the Company's operations have been funded primarily through collaborations and strategic partnerships, research grants and from the issuance of equity securities. As of December 31, 2022, the Company had capital resources of $307.5 million consisting of cash, cash equivalents, and marketable securities. Management believes that the Company's existing cash, cash equivalents, and marketable securities will be sufficient to fund its operations for at least the next 12 months from the date these Consolidated Financial Statements are issued.

Under Accounting Standard Codification ("ASC") Topic 205-40, *Presentation of Financial Statements—Going Concern* ("ASC Topic 205-40"), the Company has the responsibility to evaluate whether conditions and/or events raise substantial doubt about its ability to meet its future financial obligations as they become due within one year after the date that the Consolidated Financial Statements are issued. As required under ASC Topic 205-40, management's evaluation should initially not take into consideration the potential mitigating effects of management's plans that have not been fully implemented as of the date the Consolidated Financial Statements are issued.

Substantial Doubt Raised

In performing the first step of the evaluation, the Company concluded that the following conditions raised substantial doubt about its ability to continue as a going concern:

- Net loss of $192.3 million and $178.3 million for the years ended December 31, 2022 and 2021, respectively, and history of recurring net losses; and
- Accumulated deficit of $1,148.5 million and $956.3 million as of December 31, 2022 and 2021, respectively.

Consideration of Management's Plans

In performing the second step of this assessment, the Company is required to evaluate whether it is probable that its plans will be effectively implemented within one year after the consolidated financial statements are issued and whether it is probable those plans will alleviate the substantial doubt about its ability to continue as a going concern.

The Company has identified several potential actions including cost preservation measures that would be initiated in a timely manner to address the Company's liquidity needs over the twelve-month period from the date the Consolidated Financial Statements are issued, as follows:

- Deferral and reprioritization of certain research and development programs that would involve reduced program and headcount spend;
- Pause on any new hiring and reduction in ancillary expenses such as travel and recruitment expenses; and

- Reduction in non-critical capital and operating expenditures including additional equipment, lab improvements, efficiency projects, and business support spend.

Management Assessment of Ability to Continue as a Going Concern

The Company believes management's plans, as described more fully above, will provide sufficient liquidity to meet its financial obligations and maintain levels of liquidity over the twelve-month period from the date the Consolidated Financial Statements are issued. Therefore, management concluded these plans alleviate the substantial doubt that was raised about the Company's ability to continue as a going concern for at least twelve months from the date that the Consolidated Financial Statements are issued.

The accompanying Consolidated Financial Statements have been prepared assuming the Company will continue to operate as a going concern, which contemplates the realization of assets and the settlement of liabilities in the normal course of business. The Consolidated Financial Statements do not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or the amounts of liabilities that may result from uncertainty related to the Company's ability to continue as a going concern.

Future Plans and Considerations

The Company will be required to raise additional capital to fund its operations and support its product development endeavors. In this regard, the Company is actively seeking substantial additional capital, including through public or private equity or debt financings, royalty financings or other sources, such as strategic collaborations. However, additional capital may not be available to the Company, on terms that are acceptable or at all. If adequate funds are not available to the Company on a timely basis, or at all, it will be required to take additional actions to address its liquidity needs, including cost preservation measures such as reducing operating expenses and delaying, reducing the scope of, discontinuing or altering its research and development activities. If the Company raises additional capital through royalty financings or other collaborations, strategic alliances or licensing arrangements with third parties, it may need to relinquish certain valuable rights to its product candidates, technologies, future revenue streams or research programs or grant licenses on terms that may not be favorable. If the Company raises additional capital through public or private equity offerings, including sales pursuant to its at-the-market offering program with Jefferies LLC, the ownership interest of its existing stockholders will be diluted, and such dilution may be substantial, and the terms of any new equity securities may have a preference over, and include rights superior to, its common stock. If the Company raises additional capital through royalty financings or other collaborations, strategic alliances or licensing arrangements with third parties, it may need to relinquish certain valuable rights to its product candidates, technologies, future revenue streams or research programs or grant licenses on terms that may not be favorable. If the Company raises additional capital through debt financing, it may be subject to specified financial covenants or covenants limiting or restricting its ability to take specific actions, such as incurring additional debt, making capital expenditures or pursuing certain transactions, any of which could restrict its ability to commercialize its product candidates or operate as a business. In addition, management's planned cost reductions are intended to reduce the Company's operating expenses and optimize its cash resources. Based on the timing of these cost reduction plans, the Company expects to start realizing the benefit of its efforts beginning in the third quarter of 2023; however, there can be no assurance that the Company will realize the benefits of the cost reduction plans on the anticipated timeline, or at all.

Summary of Significant Accounting Policies

Use of Estimates

The preparation of the Consolidated Financial Statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the amounts reported in the Consolidated 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, income taxes, 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.

During the year ended December 31, 2021, the Company recorded adjustments to revenue related to changes in estimates in connection with the collaboration agreement with Sanofi S.A. ("Sanofi"). These changes in estimates were driven by a change in project scope and related project costs in September 2021 and subsequent notification of termination of the collaboration agreement, effective June 28, 2022, which resulted in changes to the measure of proportional cumulative performance. These adjustments decreased revenue by $1.6 million, increased net loss by $1.6 million and increased the Company's basic and diluted net loss per share by $0.01 for the year ended December 31, 2021.

During the year ended December 31, 2020, the Company recorded adjustments to revenue related to changes in estimates in connection with the collaboration agreements with Sanofi and Pfizer Inc. ("Pfizer"). These changes in estimates were driven by changes in project scope and related project costs which resulted in changes to the measure of proportional cumulative performance. These adjustments increased revenue by $8.9 million, decreased net loss by $8.9 million and decreased the Company's basic and diluted net loss per share by $0.06 for the year ended December 31, 2020.

Revenue Recognition

The Company accounts for its revenues pursuant to the provisions of Accounting Standards Codification ("ASC") Topic 606, *Revenue from Contracts with Customers* ("ASC Topic 606"). The Company's contract revenues are derived from collaboration agreements including licensing arrangements and research services. Research and licensing agreements typically include nonrefundable upfront signing or license fees, payments at negotiated rates for time incurred by Company researchers, third-party cost reimbursements, additional target selection fees, sublicense fees, milestone payments tied to ongoing development and product commercialization, and royalties on future licensees' product sales. All funds received from the Company's collaboration partners are generally not refundable. Non-refundable upfront fees are fixed at the commencement of the contract. All other fees represent variable consideration in contracts. One of the Company's contracts also contains a provision where we reimburse its customer for certain costs they incur which is accounted for as a reduction to the contract transaction price as we do not acquire any distinct goods or services in exchange for such payments. Deferred revenue primarily represents the portion of nonrefundable upfront fees or milestone payments received but not earned.

In determining the appropriate amount of revenue to be recognized as the Company 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.

Most of the Company's performance obligations in its collaboration agreements represent distinct bundles of licenses of intellectual property and research and development services, with these components being individually non-distinct. Options to license our intellectual property and/or acquire research and development services also represent performance obligations when they grant customers a material right, e.g. a right to a discount the customer would not have received if they did not purchase our services under the existing contract.

Revenues from bundles of licenses of intellectual property and research and development services are recognized over time using a proportional performance method. Under this method, revenue is recognized by measuring progress towards satisfaction of the relevant performance obligation using a measure that best depicts the progress towards satisfaction of the relevant performance obligation. For most of the Company's agreements the measure of progress is an input measure based on a level of effort incurred, which includes the value of actual time by Company researchers plus third-party cost reimbursements.

Consideration allocated to options that include material rights is deferred until the options are exercised or expire. The exercise of such options is accounted for as contract continuation, with target selection fees and estimated variable consideration included in the transaction price at that time and allocated specifically to the respective target's performance obligation.

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. Changes in these estimates can have a material effect on revenue recognized. 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. For variable consideration, 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. A cumulative catch-up is then recorded in the current period to reflect the updated transaction price and the updated measure of progress. The estimated period of performance and level of effort, including the value of Company researchers' time and third-party costs, are reviewed quarterly and adjusted, as needed, to reflect the Company's current expectations.

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, discount rates and probabilities of exercise of technical and regulatory success, and the expected level of effort for research and development services.

Certain disclosures associated with our revenue recognition and major customers, partnerships and strategic alliances have been updated to conform with immaterial changes associated with prior periods.

Revenues from major collaboration agreements and research activity grants as a percentage of total revenues were as follows:

	Year Ended December 31,		
	2022	2021	2020
Novartis Institutes for BioMedical Research, Inc.	36 %	34 %	4 %
Kite Pharma, Inc.	35 %	23 %	24 %
Biogen MA, Inc.	26 %	38 %	24 %
Sanofi S.A.	3 %	3 %	5 %
Pfizer Inc.	— %	— %	40 %

Accounts Receivable

Accounts receivable consists of amounts billed to the Company's collaboration partners for cost reimbursements for research services. 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. The Company records trade receivables net of allowances for credit losses. The Company applies an aging method to estimate credit losses and considers its historical loss information, adjusted to account for current conditions, and reasonable and supportable forecasts of future economic conditions affecting its customers. As of December 31, 2022, the Company had not incurred any losses related to these receivables. As of December 31, 2022 and 2021, the percentage of accounts receivable by collaboration partners who individually accounted for 10% or more of accounts receivable were as follows:

	As of December 31,	
	2022	2021
Novartis Institutes for BioMedical Research, Inc.	59 %	32 %
Kite Pharma, Inc.	19 %	2 %
Biogen MA, Inc.	14 %	46 %
Sanofi S.A.	— %	11 %

Goodwill and Intangible Assets

Goodwill represents the excess of consideration transferred over the fair values of assets acquired and liabilities assumed in a business combination. 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. Goodwill and intangible assets with indefinite useful lives are not amortized. 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. The Company tests goodwill and indefinite-lived intangible assets 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 the fair values of the assets are below their respective carrying amounts. As of December 31, 2022, no impairment of goodwill or indefinite-lived intangible assets was identified.

Valuation of Long-lived Assets

Long-lived assets, including property and equipment and finite-lived intangible assets, are reviewed for impairment whenever facts or circumstances either internally or externally may suggest that the carrying value of an asset may not be recoverable. Recoverability of these assets is measured by comparison of the carrying amount of each asset to the future undiscounted cash flows expected to result from the use of the asset and its eventual disposition. If the asset is considered to be impaired, the amount of any impairment is measured as the difference between the carrying value and the fair value of the impaired asset. As of December 31, 2022, no impairment of long-lived assets was identified.

Fair Value Measurements

The carrying amounts for financial instruments consisting of cash and cash equivalents, accounts receivable, accounts payable and other accrued liabilities approximate fair value due to their short-term maturities. Marketable securities are stated at their estimated fair values.

Cash, Cash Equivalents, and Restricted Cash

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 cash, deposits in demand money market accounts and U.S. government-sponsored entity debt securities. Restricted cash consists of a letter of credit for $1.5 million, representing a deposit for the lease of the corporate headquarters in Brisbane, California.

A reconciliation of cash, cash equivalents, and restricted cash reported within the accompanying Consolidated Balance Sheets to the amounts reported within the accompanying Consolidated Statements of Cash Flows is as follows (in thousands):

	As of December 31,		
	2022	2021	2020
Cash and cash equivalents	$ 100,444	$ 178,872	$ 131,329
Non-current restricted cash	1,500	1,500	1,500
Cash, cash equivalents, and restricted cash as reported within the Consolidated Statements of Cash Flows	$ 101,944	$ 180,372	$ 132,829

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 income (loss) ("AOCI"). The Company classifies those investments that are not required for use in current operations and that mature in more than 12 months as non-current marketable securities in the accompanying Consolidated Balance Sheets.

The Company's investments are subject to a periodic impairment review. 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 marketable securities are included in interest and other income, net, which are determined using the specific identification method. Credit losses related to the marketable securities are recorded in interest and other income (expense), net in the Consolidated Statements of Operations through an allowance for credit losses rather than as a reduction in the amortized cost basis of the securities.

Concentrations of Credit Risk and Other Risks

Cash, cash equivalents, and marketable securities consist of financial instruments that potentially subject the Company to a concentration of credit risk to the extent of the fair value recorded in the Consolidated Balance Sheets. The Company invests cash that is not required for immediate operating needs primarily in highly liquid instruments that bear minimal risk. The Company has established policies relating to the quality, diversification, and maturities of securities to enable the Company to manage its credit risk. The Company is exposed to credit risk in the event of a default by the financial institutions or issuers of investments holding its cash, cash equivalents, and investments to the extent recorded on the Consolidated Balance Sheets.

Certain materials and key components that the Company utilizes in its operations are obtained through single suppliers. Since the suppliers of key components and materials must be named in an investigational new drug application ("IND") filed with the U.S. Food and Drug Administration for a product, significant delays can occur if the qualification of a new supplier is required. If delivery of material from the Company's suppliers were interrupted for any reason, the Company may be unable to supply any of its product candidates for clinical trials.

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 which is 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.

Research and Development Expenses

Research and development expenses consist primarily of personnel costs, including salaries, benefits and stock-based compensation, clinical studies performed by contract research organizations, materials and supplies and overhead allocations consisting of various support and facility-related costs. Research and development costs are expensed as incurred.

General and Administrative Expenses

General and administrative expenses consist of finance, human resources, legal and other administrative activities. These expenses consist primarily of personnel costs, including salaries, benefits and stock-based compensation, facilities and overhead costs, legal expenses, and other general and administrative costs.

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 Stock Purchase Plan ("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, expected dividend yield of stock 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. The Company accounts for forfeitures in the period they occur.

Income Taxes

Income tax expense has been calculated 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 includes accrued interest and penalties with the related income tax liability within other accrued liabilities on its Consolidated Balance Sheets. The Company evaluates uncertain tax positions on a regular basis and makes adjustments to these accruals when facts and circumstances change, such as the closing of a tax audit or the refinement of an estimate.

Leases

The Company determines if an arrangement is or contains a lease at inception by assessing whether the arrangement contains an identified asset and whether it has the right to control the identified asset. Right-of-use ("ROU") assets represent the Company's right to use an underlying asset for the lease term and lease liabilities represent the Company's obligation to make lease payments arising from the lease. Lease liabilities are recognized at the lease commencement date based on the present value of future lease payments over the lease term. ROU assets are based on the measurement of the lease liability and also include any lease payments made prior to or on lease commencement and exclude lease incentives and initial direct costs incurred, as applicable.

As the implicit rate in the Company's leases is generally unknown, the Company uses its incremental borrowing rate based on the information available at the lease commencement date in determining the present value of remaining lease payments. The incremental borrowing rate represents an estimate of the interest rate the Company would incur at lease commencement to borrow an amount equal to the lease payments on a collateralized basis over the term of a lease in a similar economic environment. The Company considers its credit risk, term of the lease, and total lease payments and adjusts for the impacts of collateral, as necessary, when calculating its incremental borrowing rates. The lease terms may include options to extend or terminate the lease when it is reasonably certain the Company will exercise any such options. Rent expense for the Company's operating leases is recognized on a straight-line basis over the lease term.

The Company has elected not to separate lease and non-lease components for its real estate and copier leases and, as a result, accounts for any lease and non-lease components as a single lease component. The Company has also elected not to apply the recognition requirement to any leases with a term of 12 months or less and does not include an option to purchase the underlying asset that the Company is reasonably certain to exercise.

Foreign Currency Translation

The functional currency of the Company's foreign subsidiaries is primarily the Euro. 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 AOCI within stockholders' equity. Revenues and expenses from the Company's 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 the Company's Consolidated Statements of Operations.

Net Loss Per Share

Basic net loss per share attributable to Sangamo Therapeutics, Inc. stockholders has been computed by dividing net loss attributable to Sangamo Therapeutics, Inc. stockholders by the weighted-average number of shares of common stock outstanding during the period. Diluted net loss per share attributable to Sangamo Therapeutics, Inc. stockholders is calculated by dividing net loss attributable to Sangamo Therapeutics, Inc. stockholders by the weighted-average number of shares of common stock plus potentially dilutive securities outstanding during the period.

The total number of shares subject to stock options and RSUs outstanding and the ESPP shares reserved for issuance, which are all anti-dilutive, were excluded from consideration in the calculation of diluted net loss per share attributable to Sangamo Therapeutics, Inc. stockholders. Stock options and RSUs outstanding and ESPP shares reserved for issuance as of December 31, 2022, 2021 and 2020 were 18,560,755, 15,159,908, and 14,237,871, 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, 2022 and 2021, the majority of the Company's property and equipment were maintained in the United States. For the years ended December 31, 2022, 2021 and 2020, all of the Company's revenues were generated and incurred in the United States.

Recent Accounting Pronouncements

None.

NOTE 2 – FAIR VALUE MEASUREMENTS

The Company measures certain financial assets and liabilities at fair value on a recurring basis, including cash equivalents and marketable securities. 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 measurements and unobservable (*i.e.,* supported by little or no market activity).

The fair value measurements of the Company's cash equivalents and marketable securities are identified at the following levels within the fair value hierarchy (in thousands):

	December 31, 2022			
	Fair Value Measurements			
	Total	Level 1	Level 2	Level 3
Assets:				
Cash equivalents:				
Money market funds	$ 50,820	$ 50,820	$ —	$ —
Total	50,820	50,820	—	—
Marketable securities:				
U.S. government-sponsored entity debt securities	18,417	—	18,417	—
Commercial paper securities	101,165	—	101,165	—
Corporate debt securities	11,670	—	11,670	—
Asset-backed securities	24,792	—	24,792	—
U.S. treasury bills	7,938		7,938	
Certificates of deposit	37,461	—	37,461	—
Agency bonds	5,590		5,590	
Total	207,033	—	207,033	—
Total cash equivalents and marketable securities	$ 257,853	$ 50,820	$ 207,033	$ —

	December 31, 2021			
	Fair Value Measurements			
	Total	Level 1	Level 2	Level 3
Assets:				
Cash equivalents:				
Money market funds	$ 119,919	$ 119,919	$ —	$ —
Total	119,919	119,919	—	—
Marketable securities:				
U.S. government-sponsored entity debt securities	30,614	—	30,614	—
Commercial paper securities	105,757	—	105,757	—
Corporate debt securities	33,682	—	33,682	—
Asset-backed securities	70,701	—	70,701	—
Certificates of deposit	45,091	—	45,091	—
Total	285,845	—	285,845	—
Total cash equivalents and marketable securities	$ 405,764	$ 119,919	$ 285,845	$ —

Cash Equivalents and Marketable Securities

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 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.

NOTE 3 – CASH EQUIVALENTS AND MARKETABLE SECURITIES

The table below summarizes the Company's cash equivalents and marketable securities (in thousands):

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
December 31, 2022				
Assets				
Cash equivalents:				
Money market funds	$ 50,820	$ —	$ —	$ 50,820
Total	50,820	—	—	50,820
Marketable securities:				
U.S. government-sponsored entity debt securities	18,710	—	(293)	18,417
Commercial paper securities	101,336	22	(193)	101,165
Corporate debt securities	11,760	—	(90)	11,670
Asset-backed securities	24,970	2	(180)	24,792
U.S. treasury bills	7,950	—	(12)	7,938
Certificates of deposit	37,599	4	(142)	37,461
Agency bonds	5,598	—	(8)	5,590
Total	207,923	28	(918)	207,033
Total cash equivalents and marketable securities	$ 258,743	$ 28	$ (918)	$ 257,853
December 31, 2021				
Assets				
Cash equivalents:				
Money market funds	$ 119,919	$ —	$ —	$ 119,919
Total	119,919	—	—	119,919
Marketable securities:				
U.S. government-sponsored entity debt securities	30,700	1	(87)	30,614
Commercial paper securities	105,792	7	(42)	105,757
Corporate debt securities	33,723	1	(42)	33,682
Asset-backed securities	70,807	1	(107)	70,701
Certificates of deposit	45,116	1	(26)	45,091
Total	286,138	11	(304)	285,845
Total cash equivalents and marketable securities	$ 406,057	$ 11	$ (304)	$ 405,764

The fair value of marketable securities by contractual maturity were as follows (in thousands):

	December 31,	
	2022	2021
Maturing in one year or less	$ 177,188	$ 197,676
Maturing after one year through five years	29,845	88,169
Total	$ 207,033	$ 285,845

Realized gains and losses on the sales of investments were not material during the years ended December 31, 2022, 2021 and 2020. Total unrealized gains for securities with net gains in accumulated other comprehensive income were not material for the year ended December 31, 2022.

The Company manages credit risk associated with its investment portfolio through its investment policy, which limits purchases to high-quality issuers and also limits the amount of its portfolio that can be invested in a single issuer. The Company did not record an allowance for credit losses or other impairment charges related to its marketable securities for the years ended December 31, 2022, 2021, or 2020.

The Company had unrealized losses related to its marketable securities for the years ended December 31, 2022, 2021 and 2020. The Company had no material unrealized losses, individually and in the aggregate, for marketable securities that are in a continuous unrealized loss position for greater than 12 months as of December 31, 2022 and 2021. Based on the scheduled maturities of its investments, the Company determined that it was more likely than not that it will hold these investments for a period of time sufficient for a recovery of its amortized cost basis. These unrealized losses were not attributed to credit risk and were associated with changes in market conditions. The Company periodically reviews its marketable securities for indications of credit losses. The Company considers factors such as the duration, the magnitude and the reason for the decline in value, the potential recovery period, creditworthiness of the issuers of the securities and its intent to sell. For marketable securities, it also considers whether (i) it is more likely than not that the Company will be required to sell the debt securities before recovery of their amortized cost basis, and (ii) the amortized cost basis cannot be recovered as a result of credit losses. No significant facts or circumstances have arisen to indicate that there has been any significant deterioration in the creditworthiness of the issuers of the securities held by the Company. Based on the Company's review of these securities, including the assessment of the duration and severity of the unrealized losses and the Company's ability and intent to hold the investments until maturity, the Company determined that no allowance for credit losses related to its marketable securities was required at either December 31, 2022 or 2021.

NOTE 4 – MAJOR CUSTOMERS, PARTNERSHIPS AND STRATEGIC ALLIANCES

Novartis Institutes for BioMedical Research, Inc.

On July 27, 2020, the Company entered into a collaboration and license agreement with Novartis Institutes for BioMedical Research, Inc. ("Novartis") for the research, development and commercialization of gene regulation therapies to treat three neurodevelopmental disorders. Under the agreement, which was effective upon execution, the Company granted Novartis an exclusive, royalty bearing and worldwide license, under its relevant patents and know-how, to develop, manufacture and commercialize certain of its zinc finger ("ZF") transcriptional regulators ("ZF-TRs") targeted to three undisclosed genes that are associated with certain neurodevelopmental disorders, including autism spectrum disorder and intellectual disability. The Company is performing early research activities over the collaboration period for each gene target and manufacture the ZF-TRs required for such research, costs of which are funded by Novartis. Novartis is responsible for additional research activities, studies enabling INDs, clinical development, regulatory approvals, manufacturing of preclinical, clinical and approved products, and global commercialization. Subject to certain exceptions set forth in the agreement, the Company is prohibited from developing, manufacturing or commercializing any therapeutic product targeting any of the three genes that are the subject of the collaboration. Novartis also has the option to license certain of the Company's proprietary adeno-associated viruses ("AAVs") for the sole purpose of developing, manufacturing and commercializing licensed products arising from the collaboration.

Under the agreement, Novartis paid the Company a $75.0 million upfront license fee in August 2020. In addition to this fee and the cost reimbursements for early research activities, the Company is eligible to earn from Novartis up to $420.0 million in development milestones and up to $300.0 million in commercial milestones. The Company is also eligible to earn from Novartis tiered high single-digit to sub-teen double-digit royalties on potential net commercial sales of licensed products arising from the collaboration. These royalty payments will be subject to reduction due to patent expiration, loss of market exclusivity and payments made under certain licenses for third-party intellectual property. The agreement will continue, on a product-by-product and country-by-country basis, until the expiration of the applicable royalty term. Novartis has the right to terminate the agreement, in its entirety or on a target-by-target basis, for any reason after a specified notice period. Each party also has the right to terminate the agreement on account of the other party's bankruptcy or material, uncured breach.

All payments received under the agreement, when earned, are non-refundable and non-creditable. The transaction price of $95.1 million includes the upfront license fee of $75.0 million and estimated research costs of $20.1 million to be provided over the estimated research period. All clinical or regulatory milestone amounts were considered fully constrained at inception of the agreement. 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.

The Company assessed the agreement with Novartis in accordance with ASC Topic 606 and concluded that Novartis is a customer. The Company has identified a single performance obligation within this arrangement as a license to the technology and ongoing research services. The Company concluded that the license is not discrete as it does not have stand-alone value to Novartis 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 of the ongoing research services through the estimated research period. The estimation of progress towards the satisfaction of performance obligation and project cost is reviewed quarterly and adjusted, as needed, to reflect the Company's current assumptions regarding the timing of its performance

obligation. As of December 31, 2022 and 2021, the Company had a receivable of $2.2 million and $1.9 million, respectively, and deferred revenue of $9.6 million and $40.9 million, respectively, related to this agreement. These amounts are expected to be recognized over the period through 2023.

Revenues recognized under the agreement were as follows (in thousands):

	Year Ended December 31,		
	2022	2021	2020
Revenue related to Novartis agreement:			
Recognition of upfront license fee	$ 31,344	$ 29,945	$ 4,143
Research services	8,384	7,999	1,109
Total	$ 39,728	$ 37,944	$ 5,252

The Company paid $1.5 million for financial advisory fees during the year ended December 31, 2020, equal to 2% of $75.0 million received for the upfront license fee related to the collaboration and license agreement with Novartis. The Company recognized $1.5 million as a contract asset as such amount represents a cost of obtaining the agreement. This balance is amortized and included in general and administrative expenses on a systematic basis consistent with the transfer of the services to Novartis in accordance with ASC Topic 340, *Other Assets and Deferred* Costs ("ASC Topic 340"). The Company amortized $0.6 million and $0.6 million during the years ended December 31, 2022 and 2021, respectively.

Biogen MA, Inc.

In February 2020, the Company entered into a collaboration and license agreement with Biogen MA, Inc. ("BIMA") and Biogen International GmbH (together with BIMA, "Biogen") for the research, development and commercialization of gene regulation therapies for the treatment of neurological diseases. The companies plan to leverage the Company's proprietary ZF technology delivered via AAV to modulate expression of key genes involved in neurological diseases. Concurrently with the execution of the collaboration agreement, the Company entered into a stock purchase agreement with BIMA, pursuant to which BIMA agreed to purchase 24,420,157 shares of the Company's common stock (the "Biogen Shares"), at a price per share of $9.2137, for an aggregate purchase price of approximately $225.0 million.

The collaboration agreement became effective in April 2020 following the termination of the waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, and satisfaction of other customary closing conditions, including the payment of $225.0 million for the purchase of the Biogen Shares.

Under the collaboration agreement, Biogen paid the Company an upfront license fee of $125.0 million in May 2020. The Company is also eligible to receive research, development, regulatory and commercial milestone payments that could total up to approximately $2.4 billion if Biogen selects all of the targets allowed under the agreement and all the specified milestones set forth in the agreement are achieved, which includes up to $925.0 million in pre-approval milestone payments and up to $1.5 billion in first commercial sale and other sales-based milestone payments. In addition, the Company is eligible to receive tiered high single-digit to sub-teen royalties on potential net commercial sales of licensed products arising from the collaboration. 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.

Under the collaboration agreement, the Company granted to Biogen an exclusive, royalty bearing and worldwide license, under its relevant patents and know-how, to develop, manufacture and commercialize ZF and/or AAV-based products directed to certain neurological disease gene targets selected by Biogen. Biogen has already selected four of these: ST-501 to treat tauopathies, ST-502 to treat synucleinopathies including Parkinson's disease, a third product candidate targeting DM1, a neuromuscular disease, and a fourth undisclosed neurological disease gene target. Biogen has exclusive rights to nominate up to seven additional targets over the remaining period of five years from the effective date of the collaboration agreement. For each gene target selected by Biogen, the Company performs early research activities, costs of which are shared by the companies, aimed at the development of the combination of proprietary central nervous system delivery vectors and ZF-TRs (or potential other ZF products) targeting therapeutically relevant genes. Biogen has assumed responsibility and costs for the IND-enabling studies, clinical development, related regulatory interactions, and global commercialization. The Company is responsible for manufacturing activities for the initial clinical trials for the first three products of the collaboration and plans to leverage its in-house manufacturing capacity, where appropriate, which is currently in development. Biogen is responsible for manufacturing activities beyond the first clinical trial for each of the first three products. The Company's research activities for any targets will be performed over the period not to exceed seven years from the effective date of the agreement (i.e., through April 2027). Subject to certain exceptions set forth in the collaboration agreement, the Company is prohibited from developing, manufacturing or commercializing any therapeutic product directed to the targets selected by Biogen.

The collaboration agreement continues on a product-by-product and country-by-country basis until the expiration of all applicable royalty terms. Biogen has the right to terminate the collaboration agreement, in its entirety or on a target-by-target

basis, for any reason after a specified notice period, and also has the right to replace up to eight targets. Each party has the right to terminate this agreement on account of the other party's bankruptcy or material, uncured breach. In addition, the Company may terminate the collaboration agreement if Biogen challenges any patents licensed by the Company to Biogen.

Pursuant to the terms of the stock purchase agreement, Biogen has agreed not to, without the Company's prior written consent and subject to specified conditions and exceptions, directly or indirectly acquire shares of the Company's outstanding common stock, seek or propose a tender or exchange offer or merger between the parties, solicit proxies or consents with respect to any matter, or undertake other specified actions related to the potential acquisition of additional equity interests in the Company. Such standstill restrictions expire on the earlier of the three-year anniversary of the effectiveness of the collaboration agreement and the date that Biogen beneficially owns less than 5% of the Company's common stock.

The Company assessed the collaboration agreement with Biogen in accordance with ASC Topic 606 and concluded that Biogen is a customer. The transaction price includes the upfront license fee of $125.0 million and the excess consideration from the stock purchase of $79.6 million, which represents the difference between the $225.0 million received for the purchase of the Biogen Shares and the $145.4 million estimated fair value of the equity issued. The equity issued to Biogen was valued using an option pricing model to reflect certain holding period restrictions. None of the clinical or regulatory milestones have been included in the transaction price, as none of the milestones have yet been achieved, and all such amounts are fully constrained. As part of its evaluation of the constraint, the Company considers 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 transaction price also includes actual and estimated cost-sharing payments by Biogen for the work by Company researchers and reimbursement of the Company's costs incurred with third-parties. The amounts paid and expected to be paid to Biogen for the use of Biogen's resources and its expenses are consideration paid to a customer. Since the Company does not acquire distinct goods or services in exchange for these payments, they reduce the transaction price and are recorded as reduction in revenue. The Company uses the expected value method to estimate cost sharing payments, taking into account the impact of constraint. Variable consideration is included in the transaction price only to the extent it is probable a significant reversal of cumulative revenues recognized would not occur. Target selection fees are included in the transaction price when the options for the associated targets are exercised. The Company re-evaluates the transaction price as uncertain events are resolved or other changes in circumstances occur.

The Company concluded that the licenses to its intellectual property are not distinct from the related research and development activities as the licensed technology is not shared with and cannot be utilized by Biogen without the research services to be performed by the Company pursuant to the agreement. On the other hand, each combination of a license to the Company's intellectual property as applied to a specific target and the related research and development activities are a discrete research project that is distinct from any other target's project. The targets Biogen could select in the future are options that provide Biogen with material rights, as the exercise of the options does not require payment of a fee commensurate with the value of the incremental license rights. As a result, such options also represent performance obligations.

At contract inception, the Company allocated fixed consideration of $204.6 million included in the initial transaction price to the existing targets' license and research services performance obligations and those performance obligations for options that include material rights, based on their relative standalone selling prices. Through December 31, 2022, one material right has expired, and seven material rights remain outstanding and will expire if not exercised in 2023 or in 2025.

As of December 31, 2022 and 2021, the Company had a receivable of $0.5 million and $2.8 million, respectively, and deferred revenue of $132.2 million and $154.0 million, respectively, related to this agreement. Changes in deferred revenue balances relate primarily to progress in delivery of the performance obligations. The amounts of transaction price remaining to be recognized were $151.3 million and $182.2 million as of December 31, 2022 and 2021, respectively. These amounts are expected to be recognized over the period through 2027. The timing of recognition will be affected by the volume of annual activity under the agreement and by whether and when Biogen exercises options for additional targets and could be subject to significant changes.

Revenues recognized under the agreement were as follows (in thousands):

	Year Ended December 31,		
	2022	2021	2020
Revenue related to Biogen agreement:			
Recognition of license and other fixed consideration	$ 21,820	$ 29,224	$ 21,356
Cost-sharing payments for research services, net variable consideration	6,599	13,076	6,545
Total	$ 28,419	$ 42,300	$ 27,901

The Company paid $7.0 million for financial advisory fees during the year ended December 31, 2020, equal to 2% of $225.0 million received for the sale of shares and 2% of $125.0 million received for the upfront fee. The fees incurred related to

both the collaboration agreement with Biogen and to the stock purchase agreement for the sale of shares. The Company believes that the allocation of fees on a relative fair value basis between the two agreements is reasonable. The Company recognized $4.1 million, which represents 2% of the initial transaction price of $204.6 million, as a contract cost asset. This balance is released into general and administrative expenses on a systematic basis consistent with the transfer of the services to Biogen in accordance with ASC Topic 340. The Company recognized as expense $0.4 million, $0.6 million and $0.4 million during the years ended December 31, 2022, 2021 and 2020, respectively. The Company recognized $2.9 million, which represented 2% of the $145.4 million estimated fair value of the equity issued, as a share issuance cost and recorded this amount in equity as a reduction in net proceeds during the year ended December 31, 2020.

Kite Pharma, Inc.

In February 2018, the Company entered into a global collaboration and license agreement with Kite Pharma, Inc. ("Kite"), a Gilead Sciences, Inc. subsidiary, which became effective on April 5, 2018 ("Effective Date"), and was amended and restated in September 2019, for the research, development, and commercialization of potential engineered cell therapies for cancer. In this collaboration, Sangamo is working together with Kite on a research program under which the companies are designing zinc finger nucleases ("ZFNs") and viral vectors to disrupt and insert certain genes in T-cells and natural killer cells ("NK-cells") including the insertion of genes that encode chimeric antigen receptors ("CARs"), T-cell receptors ("TCRs"), and NK-cell receptors ("NKRs") directed to mutually agreed targets. Kite is responsible for all clinical development, manufacturing and commercialization of any resulting products.

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 ZFNs and viral vectors 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, 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, 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, the Company received a $150.0 million upfront payment from Kite. In addition, Kite reimburses the Company's direct costs to conduct the joint research program. Sangamo is also eligible to receive contingent development- and sales-based milestone payments that could total up to $3.0 billion if all of the specified milestones set forth in this agreement are achieved. Of this amount, approximately $1.3 billion relates to the achievement of specified research, clinical development, regulatory and first commercial sale milestones, and approximately $1.8 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 10 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 is entitled to receive escalating, tiered royalty payments with a percentage in the single digits based on future annual worldwide net sales of 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.

The initial research term in the agreement is six years from the Effective Date. Kite has an option to extend the research term for up to two additional one-year periods for a separate upfront fee of $10.0 million per year. All contingent payments under the agreement, when earned, will be non-refundable and non-creditable. Through the amendment and restatement of the agreement in September 2019, the Company and Kite agreed to expand the scope of the collaboration program to incorporate the use of lentiviral or retroviral vectors provided by Kite. 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 assessed the agreement with Kite in accordance with ASC Topic 606 and concluded that Kite is a customer. The transaction price includes the upfront license fee of $150.0 million and estimated reimbursable service costs for the research projects over the estimated performance period. None of the clinical or regulatory milestones have been included in the transaction price, as none of the milestones have yet been achieved, and all 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 transaction price also includes actual and estimated payments by Kite for the work by Company researchers and reimbursement of the Company's costs incurred with third-parties. The Company uses the expected value method to estimate payments related to the Company's researchers' work, taking into account the impact of constraint. Variable consideration is included in the transaction price only to the extent it is probable a significant reversal of cumulative revenues recognized would not occur. 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.

The Company has identified four performance obligations within the Kite agreement as follows: (1) a license to the technology combined with the obligation to perform research and development services to apply the Company's technology to Kite-selected targets; (2) production of research materials; and (3-4) two material rights, each for an extension of the research period for an additional one-year term. Such extensions contain material rights because their exercise does not require payment of a fee that is commensurate with the value of the incremental research term. The license to the Company's intellectual property is not distinct from the related research and development activities as the licensed technology is not shared with and cannot be utilized by Kite without the research services performed by the Company.

The Company allocated variable consideration (payments by Kite for the work performed by the Company's researchers and third party costs, as well as any future milestones and royalties) to the specific performance obligations to which they relate, as such allocation would meet the allocation objective in ASC Topic 606. The Company allocated the fixed consideration of $150.0 million to the performance obligations based on their relative standalone selling prices. Standalone selling prices of optional research years are similar to those of the initial year, but additionally take into account the intrinsic value of the discount upon exercise and the likelihood of exercise.

Fees allocated to options with material rights are deferred until the options are exercised or expire. The exercise of options is accounted for as contract continuation, with target selection fees and estimated variable consideration included in the transaction price at that time and allocated specifically to the respective target's performance obligation.

Revenue for the combined license and research services performance obligations is recognized over time, as Kite consumes the benefit of such services as they are being performed by the Company. For the license combined with research and development services performance obligation, the Company recognizes revenue based on proportional performance of the ongoing research services over the period during which the Company performs the services. The estimation of progress towards the satisfaction of this performance obligation and project costs are reviewed quarterly and adjusted, as needed, to reflect the Company's assumptions regarding the estimated volume of required activities. The production of research materials performance obligation is accounted for under the right to invoice practical expedient, as the Company has the right to invoice Kite for these services in an amount that corresponds directly with the value of the services.

As of December 31, 2022, and 2021 the Company had a receivable of $0.7 million and $0.1 million, respectively, and deferred revenue of $19.4 million and $56.5 million, respectively, related to this agreement. Changes in deferred revenue balances relate primarily to progress in delivery of the performance obligations. The amounts of transaction price (excluding the amounts recognized as invoiced for the production of research materials performance obligation) remaining to be recognized were $19.7 million and $51.4 million as of December 31, 2022 and 2021, respectively. These amounts are expected to be recognized over the period through 2024. The timing of recognition will be affected by the volume of annual activity under the agreement and by whether and when Kite exercises options for additional years of services, and could be subject to significant changes.

Revenues recognized under the agreement were as follows (in thousands):

	Year Ended December 31,		
	2022	2021	2020
Revenue related to Kite agreement:			
Recognition of license fee fixed consideration	$ 37,032	$ 24,977	$ 25,046
Research services variable consideration	1,560	476	3,562
Total	$ 38,592	$ 25,453	$ 28,608

Pfizer Inc.

Giroctocogene Fitelparvovec 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 giroctocogene fitelparvovec, 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 for certain manufacturing activities for giroctocogene fitelparvovec, while Pfizer is responsible for subsequent worldwide development, manufacturing, marketing and commercialization of giroctocogene fitelparvovec. Sangamo may also collaborate in the research and development of additional AAV-based gene therapy products for hemophilia A.

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 giroctocogene fitelparvovec 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 is 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 giroctocogene fitelparvovec 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 giroctocogene fitelparvovec in the terminated country or countries.

Upon execution of the agreement, the Company received an upfront fee of $70.0 million and 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 giroctocogene fitelparvovec 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 agreement, is up to $475.0 million, which includes up to $300.0 million for giroctocogene fitelparvovec 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 14% - 20% of the annual worldwide 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, two milestones of $55.0 million in aggregate have been achieved and paid, however no products have been approved and therefore no royalty fees have been earned under the agreement.

The Company assessed the agreement with Pfizer in accordance with ASC Topic 606 and concluded that Pfizer was a customer. The total transaction price under this agreement was $134.0 million, which represented the upfront fee and research services fees of $79.0 million and fees related to two achieved milestones in an aggregate amount of $55.0 million. Sangamo was responsible for internal and external research costs as part of the upfront fee and had the ability to request additional reimbursement from Pfizer if certain conditions were met. None of the constrained clinical or regulatory milestones were included in the transaction price. As part of its evaluation of the constraint, the Company considered numerous factors, including the fact that achievement of the milestones at the time was uncertain and contingent upon future periods when the uncertainty related to the variable consideration is resolved.

The Company has identified the performance obligations within the agreement as a license to the technology and ongoing research services. The Company concluded that the license was not discrete as it did not have stand-alone value to Pfizer apart from the research services to be performed by the Company pursuant to the agreement. As a result, the Company recognized revenue from the upfront payment based on proportional performance of the ongoing research services through 2020, the period during which the Company performed research services. The estimation of progress towards the satisfaction of its performance obligation and project cost was reviewed quarterly and adjusted, as needed, to reflect the Company's assumptions regarding the timing of its deliverables.

In December 2020, the Company satisfied the deliverables and research services responsibilities within the arrangement. As a result, the Company recognized the remaining deferred revenue from the upfront payment in December 2020 and no revenues have been recognized during the years ended December 31, 2022 and 2021.

In December 2019, the Company entered into an amendment to the collaboration agreement, pursuant to which the Company transferred the IND for giroctocogene fitelparvovec to Pfizer. Upon this transfer the Company achieved a $25.0 million milestone as the conditions for achieving the milestone were met. The cumulative revenue recognized in

connection with this milestone was $25.0 million as of December 31, 2020 and included $1.3 million recognized during the year ended December 31, 2020.

In September 2020, the Company determined that there was a high probability of achievement of a $30.0 million milestone with Pfizer for giroctocogene fitelparvovec. The milestone was subsequently achieved upon dosing of the first subject in a Phase 3 clinical trial in early October 2020. The cumulative revenue recognized in connection with this milestone was $30.0 million during the year ended December 31, 2020.

Revenues recognized under the agreement were as follows (in thousands):

	Year Ended December 31,		
	2022	2021	2020
Revenue related to Pfizer giroctocogene fitelparvovec agreement:			
Recognition of upfront fee and research services	$ —	$ —	$ 3,111
Milestone achievement	—	—	31,338
Total	$ —	$ —	$ 34,449

In March 2020, the Company recorded an adjustment to revenue related to a change in estimate in connection with the giroctocogene fitelparvovec collaboration agreement with Pfizer. This adjustment was a direct result of the decision to decrease the project scope and the corresponding costs, after the successful IND transfer of the giroctocogene fitelparvovec product candidate to Pfizer, both of which resulted in an increase in the measure of proportional cumulative performance. This adjustment increased revenue by $2.4 million, decreased net loss by $2.4 million and decreased the Company's basic net loss per share by $0.02 for year ended December 31, 2020.

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 ZF-TRs to treat amyotrophic lateral sclerosis and frontotemporal lobar degeneration 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 ZF-TRs that bind to and specifically reduce expression of the mutant form of the *C9ORF72* gene.

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 ZF-TRs 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) 15 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 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 in commercial milestone payments if annual worldwide net sales of the licensed products reach specified levels. In addition, Pfizer will pay the Company royalties of 14% - 20% 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. To date, a milestone of $5.0 million has been achieved and paid, however no products have been approved and therefore no royalty fees have been earned under the *C9ORF72* Pfizer agreement.

The Company assessed the agreement with Pfizer in accordance with ASC Topic 606 and concluded that Pfizer was a customer. The Company concluded the total transaction price under this agreement was $17.0 million, which represented the upfront fees of $12.0 million and fees related to achievement of one milestone in the amount of $5.0 million. None of the constrained clinical or regulatory milestones were included in the transaction price. As part of its evaluation of the constraint, the Company considered numerous factors, including the fact that achievement of the milestones at the time was uncertain and contingent upon future periods when the uncertainty related to the variable consideration is resolved.

The Company had identified the performance obligations within this agreement as a license to the technology and ongoing research 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 recognized revenue from the upfront payment based on proportional performance of the ongoing research services through 2020, the period the Company performed research services.

The Company satisfied the deliverables and research services responsibilities within the arrangement in September 2020, and as a result, earned a $5.0 million milestone, which the Company recognized on a cumulative basis during the year ended December 31, 2020. In addition, the Company recognized the remaining deferred revenue from the upfront payment in September 2020, and no revenues have been recognized during the year ended December 31, 2022 and 2021.

Revenues recognized under the agreement were as follows (in thousands):

	Year Ended December 31,		
	2022	2021	2020
Revenue related to Pfizer *C9ORF72* agreement:			
Recognition of upfront fee	$ —	$ —	$ 7,985
Milestone achievement	—	—	5,000
Total	$ —	$ —	$ 12,985

During the year ended December 31, 2020, the Company recorded adjustments to revenue related to changes in estimate in connection with the *C9ORF72* collaboration agreement with Pfizer. These adjustments were a direct result of the decision to decrease the project scope and the corresponding costs due to advancement of the program, which resulted in an increase in the measure of proportional cumulative performance. These adjustments increased revenue by $8.8 million, decreased net loss by $8.8 million and decreased the Company's basic net loss per share by $0.06 for the year ended December 31, 2020.

Sanofi S.A.

In January 2014, the Company entered into an exclusive worldwide collaboration and license agreement ("2014 Collaboration Agreement") to develop therapeutics for hemoglobinopathies, focused on beta thalassemia and sickle cell disease ("SCD"). The 2014 Collaboration Agreement was originally signed with BIMA, who subsequently assigned it to Bioverativ Inc., which was later acquired by Sanofi. Under the 2014 Collaboration Agreement, the Company was originally jointly conducting two research programs: a beta thalassemia program, which was discontinued in the third quarter of 2021, and the SCD program, which resulted in the development of SAR445136 (now known as BIVV003), a ZFN, gene-edited cell therapy product candidate for the treatment of SCD. In December 2021, Sanofi notified the Company of its termination for convenience, effective June 28, 2022 (the "Termination Date"), of the 2014 Collaboration Agreement. A termination and transition agreement (the "Termination and Transition Agreement") was executed by the parties on September 6, 2022.

In the SCD program, the Company and Sanofi were jointly responsible for research and development activities prior to filing of an IND, but Sanofi was responsible for subsequent worldwide clinical development, manufacturing and commercialization of licensed products developed under the agreement. Subject to the terms of the agreement, the Company had granted Sanofi an exclusive, royalty-bearing license, with the right to grant sublicenses, to use certain ZF and other technology controlled by the Company for the purpose of researching, developing, manufacturing and commercializing licensed products developed under the agreement. The Company had also granted Sanofi 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 was 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 2014 Collaboration Agreement, the Company received an upfront license fee of $20.0 million and was eligible to receive additional payments upon the achievement of specified clinical development, regulatory milestones, and sales milestones, as well as royalty payments for each licensed product based on net sales of such product. Sanofi was also to reimburse Sangamo for agreed upon costs incurred in connection with research and development activities conducted by Sangamo. Through the Termination Date, a total of $13.5 million was received based on achievement of clinical development milestones. No products have been approved and therefore no royalty fees have been or will be earned under the 2014 Collaboration Agreement.

In its termination notice to the Company, Sanofi indicated that its termination relates to Sanofi's change in strategic direction to focus on allogeneic universal genomic medicine approaches rather than autologous personalized cell therapies. As of the Termination Date, the 2014 Collaboration Agreement was terminated in its entirety and following the Termination Date, the Company will not be entitled to receive any further milestone payments or royalties from Sanofi. As of the Termination Date, Sanofi has no further obligations under the 2014 Collaboration Agreement to develop or to fund the development of any collaboration research programs under the 2014 Collaboration Agreement. The licenses granted to Sanofi under the 2014 Collaboration Agreement have been terminated, and the license rights have reverted to the Company.

As part of the Termination and Transition Agreement, Sanofi granted to the Company exclusive, worldwide, fully paid, royalty-free, perpetual, irrevocable licenses, with the right to grant sublicenses through multiple tiers, to certain of its intellectual property, to develop, manufacture, have manufactured, use, sell, offer to sale, import and otherwise commercialize BIVV003, the product candidate in development under the SCD program. The Company agreed to take on responsibilities for all clinical trials related to BIVV003, including completion of the ongoing clinical trial and the related long-term follow-up study. The Company also assumed all regulatory responsibilities related to BIVV003. Sanofi transferred and assigned to the Company all documentation, materials and contracts with third parties related to BIVV003, and the right to use certain Sanofi-owned or leased equipment related to BIVV003.

Sanofi has also agreed to reimburse the Company for the costs of conducting the ongoing clinical trial of BIVV003 and the costs of the long-term follow-up study through December 31, 2023, up to $7.0 million. In addition, should the Company elect not to continue the development of BIVV003 past December 31, 2023, Sanofi will become obligated to reimburse the Company for the costs of the long-term follow-up study incurred after 2023, up to $5.3 million. Sanofi's reimbursement obligations will terminate upon certain triggering events, including the Company's entering into a contract with a third party for collaboration, partnership, sale, licensing, or divestiture of BIVV003, or if the FDA permits early closure of the clinical trial and/or the long-term follow-up study.

The Company assessed the 2014 Collaboration Agreement in accordance with ASC Topic 606 and concluded that Sanofi was a customer, under that arrangement. The Company identified the performance obligation within this arrangement as a license to the technology combined with ongoing research services activities. The Company concluded that the license was not distinct as it did not have stand-alone value to Sanofi without the research services. As a result, the Company recognized revenue from the upfront payment and the milestones based on progress of performance of the ongoing research services. The estimation of progress towards the satisfaction of the performance obligation and project cost was reviewed quarterly and adjusted, as needed, to reflect the Company's then current assumptions regarding the timing of its deliverables. Related costs and expenses under these arrangements have historically approximated the revenues recognized. Sanofi's December 2021 notice of termination of the 2014 Collaboration Agreement represented a modification that reduced the expected scope of the Company's services and the estimated transaction price and shortened the remaining performance timeline. Consistent with this change, all services provided by the Company under the 2014 Collaboration Agreement were completed by June 28, 2022, and all amounts ultimately included in the transaction price were recognized by such date. The final transaction price of $96.3 million included the upfront license fee of $20.0 million, two milestone payments in the aggregate amount of $13.5 million and reimbursement of research costs of $62.8 million. As of December 31, 2022 and 2021, the Company had a receivable of zero and $0.6 million, respectively, related to the 2014 Collaboration Agreement. Deferred revenue related to the 2014 Collaboration Agreement was zero and $1.1 million, respectively.

The Company concluded that Sanofi is not a customer under the Termination and Transition Agreement as Sanofi is not entitled to receive and cannot use the results of the ongoing clinical trial or the long-term follow-up study. This relationship is also not a collaboration in the scope of ASC Topic 808, *Collaborative Arrangements*. The Company concluded that the assets acquired from Sanofi do not represent a business, as substantially all of their value is concentrated in the acquired or re-acquired licenses to intellectual property. The Company has no obligation to repay Sanofi for its ongoing funding of the clinical trial or long-term follow-up study costs. Therefore, the Company will recognize Sanofi reimbursements as reductions to its research and development expense. During the year ended December 31, 2022, the Company decreased its research and development expense by $2.1 million, of which $1.1 million is included within prepaid expenses and other current assets on the Company's Consolidated Balance Sheet as of December 31, 2022.

Revenues recognized under the agreement were as follows (in thousands):

	Year Ended December 31,		
	2022	2021	2020
Revenue related to Sanofi agreement:			
Recognition of upfront fee	$ 677	$ 34	$ 298
Research services	2,126	3,057	4,823
Milestone achievement	457	23	201
Total	$ 3,260	$ 3,114	$ 5,322

During the year ended December 31, 2021, the Company recorded adjustments to revenue related to changes in estimates in connection with the collaboration agreement with Sanofi. These changes in estimates were driven by a change in project scope and related project costs in September 2021 and subsequent notification of termination of the collaboration agreement which resulted in changes to the measure of proportional cumulative performance. These adjustments decreased revenue by $1.6 million, increased net loss by $1.6 million and increased the Company's basic and diluted net loss per share by $0.01 for the year ended December 31, 2021.

During the year ended December 31, 2020, the Company recorded an adjustment to revenue related to a change in estimate in connection with the collaboration agreement with Sanofi. This adjustment was a direct result of the decision in March 2020 to increase the project scope and the corresponding costs, both of which resulted in a decrease in the measure of proportional cumulative performance. This adjustment decreased revenue by $2.2 million, increased net loss by $2.2 million and increased the Company's basic net loss per share by $0.02 for the year ended December 31, 2020.

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 ZF therapeutic for the treatment of beta thalassemia based on the application of Sangamo's ZF nuclease genome editing technology. The grant provided matching funds to support ST-400, a gene-edited cell therapy candidate for people with transfusion-dependent beta thalassemia. Under the terms of the CIRM grant, the Company was 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 had the option to decline any and all amounts awarded by CIRM and as an alternative to revenue sharing, the Company had the option to convert the award to a loan, however no such election had been made as of December 31, 2020. The Company had received $5.2 million under the award as of December 31, 2020. The Company had recorded $6.4 million, including accrued interest of $1.2 million, as a loan related to this award in other non-current liabilities on the Consolidated Balance Sheet as of December 31, 2020.

As a result of the November 2021 decision to discontinue the development of ST-400 in order to prioritize the development of other product candidates, the grant was terminated. In connection with the termination and discontinuation of the program, the Company elected not to convert the award to a loan and recognized the non-refundable award amount of $5.2 million as a reduction of research and development expenses, and $1.2 million of accrued interest on the award as interest and other income, net, on the Company's Consolidated Statements of Operations for the year ended December 31, 2021. No amounts related to this award were included on the Consolidated Balance Sheets as of December 31, 2022 and 2021.

Agreement with Sigma-Aldrich Corporation

In 2007, Sangamo entered into a license agreement with Sigma-Aldrich Corporation ("Sigma") to provide Sigma with access to Sangamo's proprietary ZF 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 Dow AgroSciences LLC ("DAS"), a wholly-owned subsidiary of Dow Chemical Company. Sangamo developed laboratory research reagents using its ZF technology over a three-year research services period. Sangamo has since transferred the ZF 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 ZF-modified cell lines for commercial production of protein pharmaceuticals and certain ZF-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, 2022, 2021 and 2020, were $0.9 million, $1.1 million and $0.5 million, respectively.

Agreement with DAS

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 ZF 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 ZF-TRs 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 ZF 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. 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 provided that DAS has the right to enter into certain sublicenses with third parties to use ZF products derived from Company's ZF technology ("Licensing Program") and also provided for minimum annual payment obligations each year due to Sangamo every October, provided the Licensing Program is not terminated by DAS. Annual fees ranged from $0.3 million to $3.0 million and totaled $25.3 million over 11 years, with the last payment being in October 2020 in the amount of $3.0 million. The Company had identified the performance obligation within this arrangement as a license to the technology. In July 2021, DAS gave notice to the Company of termination of the Licensing Program, effective as of September 2021. However, Sangamo's sublicense to DAS remains in effect, as does the DAS agreement itself. In the event of any termination of the agreement, all rights to use the Company's ZF technology will revert to Sangamo, and DAS will no longer be permitted to practice Sangamo's ZF technology or to develop or, except in limited circumstances, commercialize any products derived from the Company's ZF technology.

Revenues recognized under the agreement with DAS for the years ended December 31, 2022, 2021 and 2020 were zero, $0.2 million, and $3.0 million, respectively.

NOTE 5 – ACQUISITION OF SANGAMO FRANCE

In 2018, Sangamo entered into various agreements with the goal of eventually acquiring 100% of Sangamo France's share capital, including arrangements with the holders of approximately 477,000 free shares of Sangamo France pursuant to which the Company had the right to purchase such shares from the holders (a call option), and such holders had the right to sell to the Company such shares from time to time through mid-2021 (a put option) (collectively the "Free Shares Options"). As of December 31, 2021, the Company acquired all of the 477,000 free shares, resulting in 100% ownership of Sangamo France.

The acquisition of Sangamo France was accounted for as a business combination in accordance with ASC Topic 805, *Business Combinations*, in exchange for total consideration of approximately $45.9 million at the Acquisition Date. The operating results of Sangamo France after the Acquisition Date have been included in the Company's Consolidated Statements of Operations. There was no goodwill impairment during the years ended December 31, 2022, 2021 or 2020.

Non-controlling Interest

Prior to the acquisition of all the free shares, the fair value of the remaining non-controlling interest was determined based on the number of outstanding free shares comprising the non-controlling interest and the $2.99 acquisition price per share as of the Acquisition Date. The non-controlling interest was presented as a component of stockholders' equity on the Company's Consolidated Balance Sheet as of December 31, 2020. As of December 31, 2022 and 2021, after acquisition of 100% of ordinary shares of Sangamo France, the carrying amount of the non-controlling interest was recorded as additional paid-in capital on the Company's Consolidated Balance Sheet.

NOTE 6 – OTHER BALANCE SHEET DETAILS

Property and Equipment, Net

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

	December 31,	
	2022	2021
Laboratory equipment	$ 39,080	$ 31,988
Leasehold improvements	26,559	21,970
Furniture and fixtures	9,744	9,080
Manufacturing equipment	9,908	8,781
Construction in progress	14,770	4,729
	100,061	76,548
Less: accumulated depreciation and amortization	(36,530)	(25,025)
Property and equipment, net	$ 63,531	$ 51,523

Depreciation and amortization expense was $12.1 million in 2022, $9.4 million in 2021 and $5.7 million in 2020.

Intangible Assets

The changes in intangible assets were as follows (in thousands):

	December 31,	
	2022	2021
Balance at beginning of year	$ 53,760	$ 58,128
Foreign currency translation adjustment	(3,031)	(4,368)
Balance at end of year	$ 50,729	$ 53,760

Goodwill

The changes in goodwill were as follows (in thousands):

	December 31,	
	2022	2021
Balance at beginning of year	$ 39,702	$ 42,798
Foreign currency translation adjustment	(2,150)	(3,096)
Balance at end of year	$ 37,552	$ 39,702

Other Accrued Liabilities

Other accrued liabilities consist of the following (in thousands):

	December 31,	
	2022	2021
Accrued research and development expenses	$ 7,115	$ 4,878
Operating lease liabilities – current	4,122	4,026
Accrued professional fees	1,704	869
Other	3,066	1,804
Total other accrued liabilities	$ 16,007	$ 11,577

NOTE 7 – COMMITMENTS AND CONTINGENCIES

Leases

Sangamo occupies approximately 87,700 square feet of office and research and development laboratory facilities in Brisbane, California pursuant to a lease that expires in May 2029. Sangamo also occupies approximately 59,485 square feet of research and office space, subject to a lease that expires in August 2031, and approximately 7,700 of office space, subject to a lease that expires in August 2026, in Richmond, California. In addition, the Company leases approximately 26,600 square feet of office and research and development space in Valbonne, France, subject to leases that expire beginning in June 2025 through January 2030.

In May 2020, the Company entered into an amendment to an existing lease to acquire approximately 8,500 square feet of additional research and office space in Richmond, California. The amended lease was effective October 1, 2020, and the Company recorded a lease liability and corresponding right-of-use asset of $1.3 million upon inception of this amended lease.

In January 2021, the Company entered into an amendment to an existing lease to acquire approximately 5,000 square feet of research and office space in Richmond, California. With this amendment, the existing lease expires in August 2026. Total lease payments over the life of this amended lease are approximately $0.9 million. Variable lease payments include the Company's allocated share of costs incurred and expenditures made by the landlord in the operation and management of the building. On February 1, 2021, the lease commencement date, the Company recorded an operating lease right-of-use asset and a corresponding lease liability of $0.7 million.

In January 2021, the Company also entered into a new lease to acquire approximately 5,800 square feet of research and office space in Valbonne, France, which expires in January 2030. Total lease payments over the life of this amended lease are approximately $0.8 million. Variable lease payments include the Company's allocated share of costs incurred and expenditures made by the landlord in the operation and management of the building. On January 29, 2021, the lease commencement date, the Company recorded an operating lease right-of-use asset and a corresponding lease liability of $0.6 million.

In October 2021, the Company entered into an agreement to extend the lease of its research and office space in Richmond, California by five years until August 2031. The Company also leased an additional 7,997 square feet of office space at the same location from November 2021 through August 2031. The amended lease was effective October 1, 2021, and the Company recorded an adjustment to the lease liability and the corresponding right-of-use asset of $9.1 million upon inception of this amended lease. Pursuant to the terms of the amended lease, the landlord agreed to reimburse the Company up to $2.6 million, related to a tenant improvement allowance.

Certain of these leases include renewal options at the election of the Company to renew or extend the lease for an additional five to ten years. These optional periods have not been considered in the determination of the ROU assets or lease liabilities associated with these leases as the Company did not consider it reasonably certain it would exercise the options.

The Company performed evaluations of its contracts and determined each of its identified leases are operating leases. Components of operating leases were as follows (in thousands):

	December 31,	
	2022	2021
Operating lease cost	$ 11,029	$ 10,839
Variable lease cost	3,305	2,831
Total	$ 14,334	$ 13,670

Variable lease expenses were not included in the measurement of the Company's operating ROU assets and lease liabilities. This variable expense consists primarily of the Company's proportionate share of operating expenses, property taxes and insurance and is classified as lease expense, due to the Company's election to not separate lease and non-lease components.

Cash paid for amounts included in the measurement of operating lease liabilities for the year ended December 31, 2022, 2021 and 2020 was $10.1 million, $6.9 million, and $6.4 million, respectively and was included in net cash used in operating activities in the Company's Consolidated Statements of Cash Flows.

Rent expense related to lease agreements was $11.0 million, $10.8 million, and $10.4 million for the years ended December 31, 2022, 2021 and 2020, respectively. Future minimum payments under lease obligations at December 31, 2022 consist of the following (in thousands):

	Total
2023	$ 6,832
2024	7,318
2025	7,552
2026	7,533
2027	7,480
Thereafter	15,807
Total lease payments	52,522
Less:	
Imputed interest	(9,171)
Tenant improvement allowance included in contra-lease liability	(243)
Total	$ 43,108

Reported as of December 31, 2022:	
Short-term portion of lease liabilities (included in other accrued liabilities on the Consolidated Balance Sheet)	$ 4,122
Long-term portion of lease liabilities	38,986
Total	$ 43,108

As of December 31, 2022, the weighted-average remaining lease term is 7.0 years and the weighted-average incremental borrowing rate used to determine the operating lease liability was 5.6% for the Company's operating leases.

Contractual Commitments

The Company's non-cancelable material contractual commitments under manufacturing-related supplier arrangements as of December 31, 2022 related to Lonza Netherlands, B.V. amount to $7.5 million and expire in December 2023. The Company also had $0.6 million of license obligations related to its intellectual property as of December 31, 2022.

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 8 – STOCKHOLDERS' EQUITY

Preferred Stock

The Company's Certificate of Incorporation authorizes the Company to issue up to 5,000,000 shares of preferred stock, which may be issued at the discretion of the Company's Board of Directors. As of December 31, 2022, no shares of the Company's preferred stock have been issued or are outstanding.

Common Stock

In June 2020, the Company's stockholders approved an amendment to the Company's Certificate of Incorporation to increase the total number of shares of the Company's common stock authorized for issuance from 160,000,000 shares to 320,000,000 shares. As of December 31, 2022, 166,793,320 shares of the Company's common stock are outstanding.

In connection with the collaboration agreement with BIMA described in Note 4 of these Consolidated Financial Statements, the Company entered into a stock purchase agreement with BIMA, pursuant to which BIMA agreed to purchase the Biogen Shares at a price per share of $9.2137, for an aggregate purchase price of $225.0 million. The Company closed the sale of the Biogen Shares in April 2020.

At-the-Market Offering Agreement

In August 2020, the Company entered into an Open Market Sale Agreement℠ with Jefferies LLC ("Jefferies") with respect to an at-the-market offering program under which the Company may offer and sell, from time to time at its sole discretion, shares of the Company's common stock having an aggregate offering price of up to $150.0 million through Jefferies as the Company's sales agent or principal. In December 2022, the Company entered into Amendment No. 2 to the Open Market

Sale Agreement℠ which increased the aggregate offering price under the at-the-market offering program by an additional $175.0 million. The Company is not obligated to sell any shares under the sales agreement. As of December 31, 2022, the Company sold 19,300,743 shares of its common stock for net proceeds of approximately $84.9 million. As of December 31, 2021, the Company sold 2,007,932 shares of its common stock for net proceeds of approximately $27.1 million.

2018 Equity Incentive Plan

In May 2020, the Company's stockholders approved an amendment and restatement of the 2018 Equity Incentive Plan (the "2018 Plan"), to, among other things, increase the aggregate number of shares of the Company's common stock reserved for issuance under the 2018 Plan by 9,900,000 shares. Additionally, in May 2022, the Company's stockholders approved an amendment and restatement of the 2018 Plan to, among other things, increase the aggregate number of shares of the Company's common stock reserved for issuance under the 2018 Plan by 7,900,000 shares.

The exercise price of a stock option granted under the 2018 Plan may not be less than 100% of the fair market value of the Company's common stock subject to the stock option on the date of grant, and the option term will not exceed 10 years. If the person to whom the stock option is granted is a 10% stockholder of the Company, and the stock option granted qualifies as an incentive stock option, 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 three or four years and expire 10 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.

As of December 31, 2022, there were 9,869,961 shares of the Company's common stock reserved for future awards under the Company's 2018 Plan.

2020 Employee Stock Purchase Plan

In May 2021, the Company's stockholders approved the Company's 2020 Employee Stock Purchase Plan ("the ESPP"). The ESPP provides for a total of 5.0 million shares of common stock reserved for issuance thereunder. Eligible employees may purchase common stock at 85% 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. As of December 31, 2022, there were 4,205,502 shares of the Company's common stock reserved for future issuance under the ESPP.

Stock Option Activity

A summary of the Company's stock option activity is as follows:

	Number of Shares	Weighted-Average Exercise per Share Price	Weighted-Average Remaining Contractual Term	Aggregate Intrinsic Value
			(in years)	(in thousands)
Options outstanding at December 31, 2021	11,963,277	$ 10.36		
Options granted	3,399,360	$ 5.75		
Options exercised	(28,354)	$ 4.40		
Options canceled	(2,159,288)	$ 10.09		
Options outstanding at December 31, 2022	13,174,995	$ 9.22	6.96	$ —
Options exercisable at December 31, 2022	7,823,318	$ 10.30	5.83	$ —

The intrinsic value of options exercised was zero, $2.8 million and $5.4 million during the years ended December 31, 2022, 2021 and 2020, respectively.

Restricted Stock Units

During the years ended December 31, 2022, 2021 and 2020, the Company awarded 4,349,795, 2,140,785, and 2,517,101 RSUs, respectively. The RSUs awarded in the years ended December 31, 2022, 2021 and 2020 had an average grant date fair value per award of $5.52, $11.16 and $8.06, respectively. These awards generally vest over three years. The aggregate fair value of RSUs vested during the years ended December 31, 2022, 2021 and 2020 was $13.1 million, $9.0 million and $3.7 million, respectively.

A summary of the Company's RSU activity is as follows:

	Number of Shares	Weighted-Average Remaining Contractual Term	Aggregate Intrinsic Value
		(in years)	(in thousands)
RSUs outstanding at December 31, 2021	3,139,594		
RSUs awarded	4,349,795		
RSUs released	(1,346,660)		
RSUs forfeited	(898,831)		
RSUs outstanding at December 31, 2022	5,243,898	1.03	$ 16,466

RSUs that vested in the years ended December 31, 2022, 2021 and 2020 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 380,917, 293,120, and 90,617 for the years ended December 31, 2022, 2021 and 2020, 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 $2.1 million, $3.3 million and $0.8 million in the years ended December 31, 2022, 2021 and 2020, 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.

NOTE 9 – 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,		
	2022	2021	2020
Research and development	$ 18,404	$ 19,534	$ 13,523
General and administrative	13,246	13,422	12,185
Total stock-based compensation expense	$ 31,650	$ 32,956	$ 25,708

As of December 31, 2022, total stock-based compensation expense to be recognized in future periods related to unvested stock options was $23.3 million, which is expected to be expensed over a weighted-average period of 2.07 years. As of December 31, 2022, total stock-based compensation expense to be recognized in future periods related to unvested RSUs was $23.7 million, which is expected to be expensed over a weighted-average period of 1.90 years. There was no capitalized stock-based employee compensation expense as of December 31, 2022, 2021 or 2020.

Valuation Assumptions

Employee stock-based compensation expense was determined using the Black-Scholes option valuation model for stock options and employee share purchases under the ESPP. Option valuation models require the input of subjective assumptions and these assumptions can vary over time. The fair value of RSUs was based on the closing price of the underlying common stock on the date of grant.

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 the years ended December 31, 2022, 2021 and 2020 was $3.73, $7.34, and $5.25, 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 were as follows:

	Year Ended December 31,		
	2022	2021	2020
Risk-free interest rate	2.15-3.69%	0.95-1.22%	0.34-0.61%
Expected term (in years)	5.46-5.49	5.46-5.52	5.51-5.57
Expected dividend yield of stock	—	—	—
Expected volatility	72.38-76.01%	77.30-79.77%	77.61-80.32%

Employees purchased 576,950, 433,107 and 274,382 shares of common stock through the ESPP at a weighted-average exercise price of $3.07, $7.78, and $7.34 per share during the years ended December 31, 2022, 2021 and 2020, respectively. The weighted-average estimated fair values of shares purchased under the Company's ESPP during the years ended December 31, 2022, 2021 and 2020 were $1.85, $4.48 and $8.02, respectively, based upon the assumptions used in the Black-Scholes valuation model.

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

	Year Ended December 31,		
	2022	2021	2020
Risk-free interest rate	1.62-4.61%	0.01-2.80%	1.53-2.80%
Expected term (in years)	0.5-2.0	0.0-2.0	0.5-2.0
Expected dividend yield of stock	—	—	—
Expected volatility	57.97-72.14%	32.54-97.88%	51.02-91.96%

NOTE 10 – 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 100% in 2022 and 2021 and 50% for the first 8% in 2020, up to a limit of $4,000 in 2022, 2021 and 2020. Matching funds are fully vested when contributed. Contributions to the Sangamo 401(k) Plan by the Company were $1.5 million, $1.5 million, and $1.2 million for the years ended December 31, 2022, 2021 and 2020, respectively.

NOTE 11 – INCOME TAXES

The domestic and foreign components of loss before income taxes were as follows (in thousands):

	Year Ended December 31,		
	2022	2021	2020
Domestic	$ (216,573)	$ (185,216)	$ (126,624)
Foreign	24,724	7,225	5,847
Loss before income taxes	$ (191,849)	$ (177,991)	$ (120,777)

Income tax expense consisted of the following (in thousands):

	Year Ended December 31,		
	2022	2021	2020
Income tax expense:			
Current:			
Federal	$ —	$ —	$ —
State	—	—	133
Foreign	500	886	686
Subtotal	500	886	819
Deferred:			
Federal	—	—	—
State	—	—	—
Foreign	(71)	(580)	(474)
Subtotal	(71)	(580)	(474)
Income tax expense	$ 429	$ 306	$ 345

The difference between the income tax expense and the amount computed by applying the federal statutory income tax rate to loss before income taxes is explained as follows (in thousands):

	Year Ended December 31,		
	2022	2021	2020
Tax at federal statutory rate	$ (40,288)	$ (37,372)	$ (25,363)
State taxes, net	(6,895)	(6,734)	(3,168)
Foreign rate differential	309	362	376
Global Intangible Low-taxed Income	1,002	637	1,335
Non-deductible stock-based compensation	3,545	2,770	4,232
Research credits	(6,694)	(5,230)	(3,657)
Change in valuation allowance	44,005	45,373	26,537
Transfer pricing settlement	4,343	—	—
Other	1,102	500	53
Income tax expense	$ 429	$ 306	$ 345

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 and liabilities are as follows (in thousands):

	December 31,	
	2022	2021
Assets:		
Deferred tax assets:		
Net operating loss carryforwards	$ 174,129	$ 159,740
Research and development tax credit carryforwards	44,264	35,260
Stock-based compensation	7,695	6,691
Deferred revenue	38,700	61,114
Capitalized research	37,985	—
Fixed assets	10,087	10,130
Lease liability	10,074	11,279
Accruals and reserves	1,603	1,119
Other	283	106
Total deferred tax asset	324,820	285,439
Valuation allowance	301,840	259,820
Deferred tax assets	22,980	25,619
Liabilities:		
Intangible assets	(13,512)	(13,856)
Operating lease right-of-use assets	(14,620)	(17,348)
Deferred tax liabilities	(28,132)	(31,204)
Total net deferred tax liabilities	$ (5,152)	$ (5,585)

The deferred tax assets and liabilities based on tax jurisdictions are presented on the Consolidated Balance Sheets as follows (in thousands):

	December 31,	
	2022	2021
Deferred tax assets (included in Other non-current assets on the Consolidated Balance Sheets)	$ 1,118	$ 1,060
Deferred tax liabilities	(6,270)	(6,645)
Net deferred tax liabilities	$ (5,152)	$ (5,585)

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 increased by $42.0 million, $45.5 million and $26.6 million for the years ended December 31, 2022, 2021 and 2020, respectively.

As of December 31, 2022, Sangamo had net operating loss carryforwards for federal and state income tax purposes of approximately $689.7 million and $312.0 million, respectively. The federal net operating loss generated before 2018 will begin to expire in 2023 and will keep expiring through 2037, if not utilized. Federal net operating loss generated from 2018 will carry forward indefinitely. If not utilized, the state net operating loss carryforwards will begin to expire in 2029, respectively. The Company's French net operating loss carryforward balance is $115.6 million, which carries over indefinitely. The Company also has federal and state research tax credit carryforwards of $36.8 million and $26.1 million, respectively. The federal research credits will begin to expire in 2023 and will keep expiring through 2042, 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.

The Company's policy is to reinvest the earnings of its non-U.S. subsidiaries in those operations. The Company does not provide for U.S. 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 U.S. taxes and withholding taxes. Due to the cumulative losses generated in foreign countries there are no earnings to repatriate.

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 the United Kingdom and French income tax returns, and the tax years from 2008 and thereafter remain open in the United Kingdom, and the tax years 2018 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, 2022, the Company had $0.2 million 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 amount that would impact the effective tax rate was $1.2 million, $1.2 million, and $0.6 million as of December 31, 2022, 2021 and 2020, respectively.

The following table summarizes the activity related to the Company's unrecognized tax benefits (in thousands):

	December 31,		
	2022	2021	2020
Beginning balance	$ 15,062	$ 12,892	$ 11,630
Additions based on tax positions related to the current year	3,177	2,454	2,834
Additions for tax positions of prior years	278	130	1,982
Reductions for tax positions of prior years	(338)	(414)	(3,554)
Ending balance	$ 18,179	$ 15,062	$ 12,892

NOTE 12 – RELATED PARTY TRANSACTION

There were no material related party transactions during the year ended December 31, 2022 and 2021.

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 SEC'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, 2022. Based on that evaluation, as of December 31, 2022, 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, 2022.

The effectiveness of our internal control over financial reporting as of December 31, 2022 has been audited by Ernst & Young LLP, an independent registered public accounting firm, as stated in their report, which is included herein.

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, 2022 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 Stockholders and the Board of Directors 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, 2022, 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, 2022, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the 2022 consolidated financial statements of the Company and our report dated February 22, 2023 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

San Mateo, California
February 22, 2023

ITEM 9B – OTHER INFORMATION

None.

ITEM 9C – DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

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 2023 Proxy Statement, no later than 120 days following the end of the fiscal year covered by this Annual Report on Form 10-K, and certain information to be included in the 2023 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 2023 Proxy Statement as follows:

- The information relating to our directors and nominees for director is to be included in the section entitled "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 and audit committee financial expert is to be included in the section entitled "Election of Directors – Audit Committee;"
- The information relating to our code of ethics is to be included in the section entitled "Election of Directors – Code of Business Conduct and Ethics;"
- The information relating to the procedures by which stockholders may recommend nominees to our Board of Directors is to be included in the section entitled "Questions and Answers About These Proxy Materials and Voting;" and
- The information regarding compliance with Section 16(a) of the Exchange Act is to be included in the section entitled "Delinquent Section 16(a) Reports."

Such information is incorporated herein by reference to our 2023 Proxy Statement, provided that if the 2023 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 2023 Proxy Statement under the sections entitled "Executive Compensation," "Director Compensation," "Election of Directors – Compensation Committee Interlocks and Insider Participation" and "Compensation Committee Report" and is incorporated herein by reference, provided that if the 2023 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 2023 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 2023 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 2023 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 2023 Proxy Statement under the sections entitled "Certain Relationships and Related Transactions" and "Election of Directors—Board Independence" and is incorporated herein by reference, provided that if the 2023 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 2023 Proxy Statement under the section entitled "Ratification of Independent Registered Public Accounting Firm" and is incorporated herein by reference, provided that if the 2023 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 AND 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	Fourth Certificate of Amendment of the Seventh Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed May 22, 2020).
3.3	Fifth Amended and Restated Bylaws (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed December 19, 2022).
4.1	Description of Capital Stock
4.2	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(+)	Amended and Restated 2018 Equity Incentive Plan (the "2018 Plan") (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed May 25, 2022).
10.3(+)	2018 Equity Incentive Plan French Stock-Options Sub-Plan (the "French Options Sub-Plan") (incorporated by reference to Exhibit 10.3 to the Company's Annual Report on Form 10-K filed March 1, 2019).
10.4(+)	2018 Equity Incentive Plan French Restricted Stock Unit Award Sub-Plan (the "French RSU Sub-Plan") (incorporated by reference to Exhibit 10.4 to the Company's Annual Report on Form 10-K filed March 1, 2019).
10.5(+)	2020 Employee Stock Purchase Plan (incorporated by reference to Exhibit 99.1 to the Company's Registration Statement on Form S-8 filed October 15, 2020).
10.6(+)	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).
10.7(+)	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).
10.8(+)	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).
10.9(+)	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).
10.10(+)	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).
10.11(+)	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).
10.12(+)	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
10.13(+)	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).
10.14(+)	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).
10.15(+)	Form of Stock Option Grant Notice (French employees) under the 2018 Plan and the French Options Sub-Plan (incorporated by reference to Exhibit 10.14 to the Company's Annual Report on Form 10-K filed March 1, 2019).
10.16(+)	Form of Stock Option Agreement (French Employees) under the 2018 Plan and the French Options Sub-Plan (incorporated by reference to Exhibit 10.15 to the Company's Annual Report on Form 10-K filed March 1, 2019).
10.17(+)	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).
10.18(+)	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).
10.19(+)	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).
10.20(+)	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. (incorporated by reference to Exhibit 10.19 to the Company's Annual Report on Form 10-K filed March 1, 2019).
10.21(+)	Amended and Restated Severance Plan (incorporated by reference to Exhibit 10.20 to the Company's Annual Report on Form 10-K filed March 1, 2019).
10.22(+)	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).
10.23(+)	Form of Indemnity Agreement (incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q filed May 11, 2020).
10.24(+)	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).
10.25(+)	Employment Agreement between the Company and Rolf Andrew (Andy) Ramelmeier effective as of November 1, 2017 (incorporated by reference to Exhibit 10.26 to the Company's Annual Report on Form 10-K filed February 28, 2020).
10.26(+)	Letter Agreement Regarding Andrew Ramelmeier Special Bonus (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed August 5, 2020).
10.27(+)	Letter Agreement between the Company and Jason Fontenot dated as of January 28, 2019 (incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q filed May 4, 2021).
10.28(+)	Letter Agreement between the Company and Robert J. Schott dated as of January 6, 2021 (incorporated by reference to Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q filed May 4, 2021).
10.29(+)	Letter Agreement between the Company and Prathyusha Duraibabu dated as of May 21, 2021 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed August 5, 2021).
10.30(+)	Letter Agreement between the Company and Scott Willoughby dated as of August 2, 2021 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed November 4, 2021).
10.31(+)	Letter Agreement between the Company and David Mark McClung dated November 1, 2021 (incorporated by reference to Exhibit 10.34 to the Company's Annual Report on Form 10-K filed February 24, 2022).
10.32(+)	Letter Agreement between the Company and Nathalie Dubois-Stringfellow dated as of September 28, 2022 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed November 3, 2022).
10.33(+)	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 filed February 24, 2000).

Exhibit Number	Description of Document
10.34	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).
10.35	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).
10.36	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).
10.37	Fourth Amendment to Triple Net Laboratory Lease between the Company and Point Richmond R&D Associates II, LLC, dated June 10, 2016 (incorporated by reference to Exhibit 10.33 to the Company's Annual Report on Form 10-K filed March 1, 2019).
10.38	Fifth Amendment to Triple Net Laboratory Lease between the Company and Point Richmond R&D Associates II, LLC, dated July 10, 2017 (incorporated by reference to Exhibit 10.34 to the Company's Annual Report on Form 10-K filed March 1, 2019).
10.39	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).
10.40	Seventh Amendment to Triple Net Laboratory Lease between the Company and Point Richmond R&D Associates II, LLC, dated May 20, 2020 (incorporated by reference to Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q filed August 5, 2020).
10.41	Eighth Amendment to Triple Net Laboratory Lease between the Company and Point Richmond R&D Associates II, LLC, dated May 29, 2020 (incorporated by reference to Exhibit 10.5 to the Company's Quarterly Report on Form 10-Q filed August 5, 2020).
10.42	Ninth Amendment to Triple Net Laboratory Lease between the Company and Point Richmond R&D Associates II, LLC, dated January 4, 2021 (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed May 4, 2021).
10.43	Amended and Restated Office and Laboratory Lease between the Company and Point Richmond R&D Associates II, LLC, dated October 18, 2021 (incorporated by reference to Exhibit 10.34 to the Company's Annual Report on Form 10-K filed February 24, 2022).
10.44	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).
10.45	First Amendment to Lease Agreement between the Company and Marina Boulevard Property, LLC dated January 1, 2019 (incorporated by reference to Exhibit 10.37 to the Company's Annual Report on Form 10-K filed March 1, 2019).
10.46	Open Market Sale Agreement between the Company and Jefferies LLC, dated August 5, 2020 (incorporated by reference to Exhibit 1.1 to the Company's Quarterly Report on Form 10-Q filed August 5, 2020).
10.47	Amendment No. 1 to Open Market Sale Agreement between the Company and Jefferies LLC, dated May 5, 2021 (incorporated by reference to Exhibit 1.3 to the Company's Registration Statement on Form S-3 filed May 5, 2021).
10.48	Amendment No. 2 to Open Market Sale Agreement between the Company and Jefferies LLC, dated December 23, 2022 (incorporated by reference to Exhibit 1.1 to the Company's Current Report on Form 8-K filed December 23, 2022).
10.49†	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).
10.50†	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).
10.51†	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).
10.52†	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).

Exhibit Number	Description of Document
10.53‡	Collaboration and License Agreement between the Company and Pfizer Inc., dated May 10, 2017.
10.54‡	Letter Amendment, dated December 17, 2019, to the Collaboration and License Agreement between the Company and Pfizer Inc., dated May 10, 2017 (incorporated by reference to Exhibit 10.45 to the Company's Annual Report on Form 10-K filed February 28, 2020).
10.55†	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).
10.56†	Amendment No. 1 to Research Collaboration and License Agreement between the Company and Pfizer Inc., dated March 21, 2019 (incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q filed May 8, 2019).
10.57‡	Amendment No. 2 to Research Collaboration and License Agreement between the Company and Pfizer Inc., dated July 31, 2020 (incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q filed November 4, 2020).
10.58†	Amended and Restated Collaboration and License Agreement between the Company and Kite Pharma, Inc., dated September 11, 2019 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed November 6, 2019).
10.59‡	Collaboration and License Agreement among the Company, Biogen MA, Inc. and Biogen International GmbH, dated February 26, 2020 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed May 11, 2020).
10.60	Stock Purchase Agreement between the Company and Biogen MA, Inc., dated February 26, 2020 (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed May 11, 2020).
10.61‡	Collaboration and License Agreement between the Company and Novartis Institutes for BioMedical Research, Inc., dated July 27, 2020 (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q filed November 4, 2020).
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 - the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL 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
104	The cover page from Sangamo's Annual Report on Form 10-K for the year ended December 31, 2022, is formatted in Inline XBRL and it is contained in Exhibit 101

† *Confidential treatment has been granted for certain information contained in this document pursuant to an order of the SEC. Such information has been omitted and filed separately with the SEC.*

‡ Certain portions of this exhibit (indicated by "[*]") have been omitted in accordance with 17 CFR § 229.601(b).

(+) 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.*

The agreements and other documents filed as exhibits to this Annual Report on Form 10-K are not intended to provide factual information or other disclosure other than with respect to the terms of the agreements or other documents themselves, and you should not rely on them for that purpose. In particular, any representations and warranties made by us in these agreements or

other documents were made solely within the specific context of the relevant agreement or document and may not describe the actual state of affairs as of the date they were made or at any other time.

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 February 22, 2023.

Date: February 22, 2023

SANGAMO THERAPEUTICS, INC.

By: / S / ALEXANDER D. MACRAE

Alexander D. Macrae
President and Chief Executive Officer

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Alexander D. Macrae and Scott Willoughby, 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 D. MACRAE **Alexander D. Macrae, M.B., Ch.B., Ph.D.**	President, Chief Executive Officer (Principal Executive Officer) and Director	February 22, 2023
/ S / PRATHYUSHA DURAIBABU **Prathyusha Duraibabu**	Senior Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)	February 22, 2023
/ S / H. STEWART PARKER **H. Stewart Parker**	Director and Chair of the Board	February 22, 2023
/ S / COURTNEY BEERS **Courtney Beers, Ph.D**	Director	February 22, 2023
/ S / ROBERT F. CAREY **Robert F. Carey**	Director	February 22, 2023
/ S / KENNETH J. HILLAN **Kenneth J. Hillan, M.B., Ch.B.**	Director	February 22, 2023
/ S / MARGARET A. HORN **Margaret A. Horn, J.D.**	Director	February 22, 2023
/ S / JOHN H. MARKELS **John H. Markels, Ph.D.**	Director	February 22, 2023
/ S / JAMES R. MEYERS **James R. Meyers**	Director	February 22, 2023
/ S / KAREN L. SMITH **Karen L. Smith, M.D., Ph.D., M.B.A., L.L.M.**	Director	February 22, 2023